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# ABSTRACT SUPPLEMENT

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# JAPAN COLLEGE OF RHEUMATOLOGY ABSTRACT SUPPLEMENT

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## Presidential Lecture

### PL

**Friend or foe? -Biological host response around artificial hip joints-**

Michiaki Takagi
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Conflict of interest: Yes

Artificial hip joint and its surgery have contributed treatment of end-staged disorders of hip joints. They are applied to those of rheumatoid arthritis and other inflammatory arthritis, osteoarthritis, and osteonecrosis of femoral head. Rheumatologists know them well. Better function and durability have been achieved by improvement of artificial materials combined with advance of surgical procedures. It becomes a great boon to the patients with disability of hips. Human beings equip immune system to exclude invaders of foreign body. From the other perspective, the patients, who received the surgery, has encountered huge “foreign bodies” only within a century, which they have never experienced in their long, long history. Orthopaedic surgeons have undergone various unfavorable biological host response and have to deal with them. Four major unfavorable biological host responses are picked up here, namely, 1) foreign body reaction, and periprosthetic osteolysis, characterized by implant loosening and fractures due to extensive foreign body granuloma with marked bone resorption, 2) periprosthetic joint infection, observed both in initial and late stages, and complicated often by biofilm formation and decreased immunity, 3) aseptic lymphocytic vasculitis associated lesion (ALVAL)/ adverse reaction to metal debris (ARMD), first reported as bizarre pseudotumor, and accompanied with lymphocytic infiltration and involvement of macrophages, and 4) periprosthetic fracture, due to characteristics of implants, and not uncommonly induced by senile change with osteoporosis. These pathologic conditions not seldom make the treatment troublesome due to extensive bone and/or soft tissue destruction. Is biological host response friend or foe? From the view point of the response and inflammation, understanding of these different pathologic events is indispensable to seek better outcome and survivorship of total hip joints through the previous and current translational research.

## Representative Session

### RS

**From Housewife to Prime Minister. Reflections on Finland’s Way towards a Gender Equal Society**

Nina Santavirta
Faculty of Edulational Sciences, University of Helsinki, Finland

Conflict of interest: None

Although different in population size, Japan and Finland have common things: appreciation to nature, both like the forest and houses built of wood. Both nations struggle with a decline in the working age population and aging societies. But when it comes to gender equality women have a more equal status in Finland compared to women in Japan according to the latest OECD report. The purpose of this presentation is to shed light on Finland’s way towards a gender equality. The process has been rapid, 100 years with a burst from1970 onwards and it has presupposed reforms in labor economics, social reforms and changes in cultural norms and attitudes. Regarding gender roles and norms Finnish women may feel more confident and self-efficient than Japanese women. This might partly be explained by the fact that Finland is a young nation while Japan has a long history of a sophisticated culture which makes the shift from the traditional male breadwinner - female housewife arrangement to a woman participating in the labor forces under the same conditions as her male counterparts more challenging. The association between strivings toward gender equality and equity and a declining birth rate is intriguing. In the postmodern society traditional family values and the perception of marriage, family life and child-rearing are under debate and change. It seems evident that policies that make it easier for couples to adopt gender symmetry in child caring promote gender egalitarianism, but the causal links are multifactorial and related to education and socio-economic factors. However, when asked, a large majority of women prefer to combine employment and economic autonomy with motherhood and family. This presupposes an institutional environment supporting this development: a full-day childcare of high quality for all and a mother-friendly labor market and both parents sharing the burden of childcare. The Nordic countries and Finland appear to have advanced in this direction.

# Special Symposium

## SS1-1

**Diversity Promotion Initiatives at Nagasaki University**

Masako Ito
Nagasaki University

Conflict of interest: None

I have been involved in supporting female physicians and researchers at Nagasaki University Hospital's Medical Work-Life Balance Center and Center for Diversity & Inclusion. Despite carrying a workload and responsibilities equal to their male counterparts, many female physicians and researchers face challenges in pursuing their desired roles amid the lingering convention that household and childcare responsibilities are primarily female duties. A society where all talents thrive requires the crucial realization of work-life balance and positive action as dual driving forces. While significant strides have been made in improving the working environment for women, and it is becoming less unnatural for women to occupy high-ranking positions, it is still not sufficient. Cultural shifts are not easily achieved, and women have faced criticism for being favored or deemed support efforts as futile. The recently highlighted concept of "unconscious bias" poses a threat to the momentum of these dual efforts. Drawing on my experience working at the Diversity Promotion Center, I would like to discuss the initiatives and challenges ahead. Additionally, I will touch upon the efforts at Nagasaki University Hospital's Medical Work-Life Balance Center. List of initiatives implemented at the Center for Diversity & Inclusion: 1) Work-life balance support: Establishment of on-campus daycare. Summer childcare programs. Workstyle reassessment programs. Encouragement of paid leave uptake. Promotion of male parental leave. Establishment of caregiving concierge and consultation services. 2) Positive action: Aim for a 30% ratio of female faculty members. Transparency in recruitment and selection processes. Enhancement of research capabilities (awards for female researchers, etc). Overseas dispatch program for female researchers. Support for English paper writing, etc. 3) Elimination of unconscious bias 4) Other: Support for high school girl students in choosing STEM career paths.

## SS2-1

**Musculoskeletal ultrasound for Rheumatic musculoskeletal diseases in resource limited set up**

Farzana Shumy
Square Hospitals Ltd., Dhaka, Bangladesh

Conflict of interest: None

After the first description of musculoskeletal ultrasound (Msk usg) in inflammatory arthropathies in late 70s, it has been incorporated by clinical rheumatologists, researchers, radiologists, and physicians of other subspecialities who manage patients with rheumatological conditions. In 2007, a survey in United Kingdom revealed that 33% of rheumatologist and in USA, 34% were doing it by themselves. In Asia, only 17% in China, 10.8% rheumatologist in Japan are using. Its widespread acceptance has been augmented by dramatic improvement in quality of image, its role in diagnosis, monitoring of disease. MSK USG performs better than clinical examination in detection of synovial effusion, subclinical synovitis (detects it in 13% of clinically normal joint), urate crystal detection in asymptomatic joints leading to diagnosis. By incorporating Msk usg, 42.1% undifferentiated arthritis can be classified as Rheumatoid arthritis (RA). Adding USG in 2012 ACR/EULAR classification criteria of polymyalgia rheumatica increases its sensitivity to 61%, specificity to 88%. It has become a first line investigation in assessment of temporal and axillary artery in giant cell arteritis as per 2023 EULAR recommendation. USG also showed similar efficacy in diagnosis of CTS, Rotator cuff tear, Achilles tendinopathy and Baker's cyst. It has a higher accuracy rate (more than 95%) in daily procedure and usg guided synovial biopsy has lower complication rate (around 11.2%). Thirty percent of all MRI diagnoses could have been made with MSUS and that replacing MRI with MSUS would lead to an estimated savings of $6.9 billion as per a report published with data of patients in the period from 2006 to 2020. In resource limited setting, MSK USG can be an excellent tool for its low resource consumption and in some instances, it replaces MRI because of its convenience, lower cost than MRI, ability to perform with ease in multiple joints, point of care USG significantly reduces rheumatological referrals and subsequent health expenditure. Despite all the advantages, cost, lack of physician time to incorporate it into their practice due to gross shortage of rheumatologists in resource limited settings and long learning curve. Lack of access to a rheumatology training program were seen as significant obstacle to Its more widespread use. However, because of its cost effectiveness, anchoring it into training curriculum of rheumatologists of late, arranging extensive training programs can help to overcome all the hindrances.

## SS2-2

**Pregnancy and Rheumatic diseases in APLAR region**

Samar Al Emadi
Department of Medicine, Rheumatology section, Hamad Medical Corporation, Qatar

Conflict of interest: None

Autoimmune rheumatic diseases (ARD) can affect women and men during fertile age, therefore reproductive health is a priority issue in rheumatology. Many topics need to be considered during preconception counselling: fertility, the impact of disease-related factors on pregnancy outcomes, the influence of pregnancy on disease activity, the compatibility of medications with pregnancy and breastfeeding. Risk stratification and individualized treatment approach elaborated by a multidisciplinary team minimize the risk of adverse pregnancy outcomes (APO). in my 20 minutes talks i will focus on data from the APLAR region and how we can work together.

## SS2-3

**Systemic autoinflammatory disease in adults: diagnostic approach and treatment**

Hugh C Caterson
Prince of Wales Hospital, Sydney, Australia

Conflict of interest: None

Systemic autoinflammatory diseases (SAIDs), although rare, are an increasingly acknowledged cause of patients presenting with fever or inflammation of unknown origin. This talk outlines a clinical approach to the recognition and diagnosis of SAIDs in this setting. The approach involves the use of clinical history and exam; patterns of inflammation seen in serial measurement of C reactive protein and serum amyloid A; and the appropriate use and interpretation of genetic testing. The relative incidence of specific SAIDs is reviewed to elucidate which conditions are seen in adult populations in real-world settings. Mimics of SAID are examined, including malignancy, obesity, drug fever, and occult autoinflammatory diseases. The diagnosis and genetics of familial Mediterranean fever, the archetypal monogenic SAID, are reviewed. VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is reviewed to highlight the role of somatic mutations. A focused study is also made of important specific non-monogenic SAIDs: adult-onset Still's disease, Schnitzler syndrome, PFAPA (periodic fever, aphthous stomatitis, pharyngitis and adenitis), and idiopathic recurrent pericarditis. The diagnosis of these conditions is through recognition of clinical patterns and is of high-value as it allows access to effective therapy. Despite advances in SAID diagnostic tools and the discovery of new conditions, a proportion of patients still remain in the category of undifferentiated SAID. The utility of a trial of therapy, both as a diagnostic and therapeutic tool, is outlined with a focus upon the optimal use of colchicine.

## SS2-4

**Synovial tissue heterogeneity and predominant inflammatory signal in Japanese patients with rheumatoid arthritis**

Sotaro Nakajima[1], Haruka Tsuchiya[1], Mineto Ota[1,2], Megumi Ogawa[1], Yamada Saeko[1], Ryochi Yoshida[1], Junko Maeda[1], Harumi Shirai[1], Taro Kasai[3], Jun Hirose[3], Keita Ninagawa[4], Yuichiro Fujieda[4], Takeshi Iwasaki[5], Yoshimi Aizaki[6], Hiroshi Kajiyama[6], Masakazu Matsushita[7], Eiryo Kawakami[8,9], Naoto Tamura[7], Toshihide Mimura[6], Koichiro Ohmura[5], Akio Morinobu[5], Tatsuya Atsumi[4], Yoshiya Tanaka[10], Tsutomu Takeuchi[11], Sakae Tanaka[3], Tomohisa Okamura[2], Keishi Fujio[1]
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Conflict of interest: None

[Objective] Recent advances in single-cell RNA sequencing technology have revealed the immunological landscape of rheumatoid arthritis (RA). However, much is still not known about the relationship between synovial diversity and clinical findings in Asians. We aimed to stratify synovial membranes of Japanese RA patients by their immune cell compositions to gain insight into the inflammatory factors of each synovial phenotype. [Methods] Synovial tissues were obtained from 41 patients undergoing articular surgery. The cellular composition was quantified by a deconvolution approach using a public single-cell-based reference. Inflammatory pathway activity was calculated by gene set variation analysis, and chromatin accessibility was evaluated using Assay of Transposase Accessible Chromatin sequencing. [Results] We stratified RA synovium into three distinct subtypes based on the hierarchical clustering of cellular composition data. Synovial type 1 (ST1) was characterized by abundant HLA-DRA$^{high}$ synovial fibroblasts, autoimmune-associated B cells, *GZMK*$^{+}$ *GZMB*$^{+}$ CD8$^{+}$ T cells, IL1-β$^{+}$ monocytes, and plasmablasts. ST2 was dominated by two types of monocytes, while there were higher proportions of naïve and memory B cells and follicular/peripheral helper T cells in ST3. In ST1, TNF-α, IFNs, and IL-6 signaling were highly activated, and the expression of various chemokines was significantly enhanced. ST3 had limited cytokine signaling and was characterized by increased expression of molecules associated with degeneration. ST2 had intermediate feature, with increased IFNs and IL-6 signaling. Moreover, RA risk locus in the *IRF4* region was accessible in ST1 and ST2, suggesting the influences of genetic background in these subtypes. [Conclusion] This study adds insights into the synovial heterogeneity in Japanese patients, and shows a promising link with predominant inflammatory signals. Evaluating the site of inflammation has the potential to lead to precision medicine.

## SS2-5

**Single cell analysis reveals the diversity of rheumatic diseases**

Masayuki Nishide, Atsushi Kumanogoh
Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine

Conflict of interest: None

Elucidating the immune abnormalities underlying diverse symptoms of rheumatic and connective tissue diseases from the single-cell diversity can help optimize the diagnosis and treatment of each case. This short lucture will summarize findings from single-cell analysis studies of rheumatic and connective tissue disease patient samples, including our recent work on ANCA-associated vasculitis. We will further focus on the challenges of applying single-cell analysis to clinical settings, as well as future treatment strategies to address unmet needs specific to each disease pathology.

## SS3-1

**EULAR: past, present, and future**

Daniel Aletaha
Division of Rheumatology, Medical University of Vienna, Austria

Conflict of interest: None

EULAR is a grown society with a history of more than 75 years. EULAR today is the umbrella of a large number of national European specialty societies in the field of rheumatology, and is a prime provider of education, research facilitation, quality of care, and advocacy activities on the European level. Looking at the challenges of tomorrow, EULAR is determined to help overcoming inequity across Europe, and bring rheumatology care to each and every patient, regardless of their place of living. In its mission EULAR joins other national and international societies and umbrella organisations worldwide.

## SS3-2

**Imaging and AI in rheumatology**

Annamaria Iagnocco
University of Turin, Italy

Conflict of interest: None

The potential of advanced imaging for assessing inflammation and structural lesions in rheumatology is well known. More recently the use of artificial intelligence (AI) for imaging techniques has shown significant potential for disease diagnosis, staging, and management. By using the capabilities of AI algorithms to analyse complex imaging data, decision-making processes can be optimized, stratification and phenotyping of patients can be improved and plans for treatment strategies can be enhanced. The improvements in AI techniques based on imaging interpretation have demonstrated that a computer-based analysis can equal and even exceed the human eye and recent studies in the field of AI have investigated how specific algorithms could distinguish between tissues, diagnose rheumatic pathology, and grade different signs of early inflammation, all of them being crucial for tracking disease activity. The lecture “Imaging and AI in rheumatology” will present and critically discuss an updated state-of-art in the field of innovative imaging tools and AI developments in RMDs.

## SS3-3

**Getting the diagnosis right: now and in the future - rheumatoid arthritis as an example**

Gerd R Burmester
Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin, Berlin

Conflict of interest: None

Rheumatoid arthritis is a heterogeneous disease which can be, based on data combining genetic risk factors and autoantibodies, subclassified in ACPA positive and negative RA. The presence of ACPA and RF as well as rising CRP levels years before onset of clinical symptoms indicate that relevant immune responses for RA development are initiated very early. ACPA are highly specific for RA, whereas RF can also be found among healthy (elderly) individuals and patients with other autoimmune diseases. The most important genetic risk factor for RA development, the shared epitope alleles, resides in the MHC class II region. Shared epitope alleles only predispose to the development of ACPA positive RA. This review presentation will focus on the development of new diagnostic strategies including biomarkers and imaging strategies. Early diagnosis will also be enabled by integrating elements of artificial intelligence such as ChatGPT and clinical parameters which will be outlined as well.

## SS3-4

**Management of Psoriatic Arthritis**

Iain B McInnes
College of Medical, Veterinary & Life Sciences (MVLS), University of Glasgow, Glasgow, UK

Conflict of interest: Yes

Psoriatic arthritis comprises a clinically heterogeneous condition that

includes cutaneous psoriasis, synovitis, enthesitis, dactylitis, nail disease and axial disease and can also associate with uveitis and inflammatory bowel disease. Significant cardiovascular metabolic and psychologic co-morbidities are common. Early detection of disease, assisted by identification of prognostic risk factors is important to optimise long term outcomes. Immune dysregulation is critical to the manifestation of PsA; different processes may be dominant in different disease tissue compartments. A range of therapeutic modes of action are available, or including biologic cytokine inhibitors, JAK inhibitors, PDE4 inhibitors. These agents should be used according to national or international recommendations, along with careful multi-disciplinary care.

## SS3-5

**Management of rheumatoid arthritis**

Josef S Smolen
Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Austria

Conflict of interest: Yes

In 2024 we have almost 20 DMARDs available to treat RA - conventional synthetic, biological and targeted synthetic DMARDs, aside from biosimilar and generic compounds. To bring some order into this array of options, task forces have been brought together to develop management recommendations. While ACR guidelines have last been updated in 2020, EULAR recommendations for RA management have reassessed in an update performed in 2022, taking into account the most recent advances regarding efficacy and safety of DMARDs as well as strategic approaches to treatment. Since then, new data have become available as well as some new regulatory safety statements that all support the decisions and recommendations of the EULAR task force. Furthermore, several new drugs are currently studied and may expand the therapeutic armament in the future, but as always data have to be seen critically as long as large phase 3 trial results are not available. Finally, clinical trials and especially also the increasing placebo response rates have come under scrutiny and thoughts to improve clinical trial design for future drug studies will be brought forward. Other important issues are the questions of predicting response to certain drugs as well as timelines to modify therapeutic approaches. In this presentation, all these aspects will be brought together and synthesized into a practical and feasible approach of studying and managing RA.

## SS4-1

**A systems biology approach to Lupus Nephritis**

Andrea Fava
Division of Rheumatology, Johns Hopkins University, Baltimore, USA

Conflict of interest: None

Lupus nephritis (LN) is a leading cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE), resulting in end-stage kidney disease in 20% of cases, especially in people of non-European descent. Despite optimal treatment, only 30%-40% of patients with LN achieve a complete renal response at 1 year. Thus, there is a pressing need to identify novel treatment strategies to prevent kidney damage and mortality. We live in the midst of 3 simultaneous revolutions. We have unprecedented ability to systematically measure biological phenomena (i.e. omics), access advanced computational power, and connect with people across the world. These factors shaped our ability to systematically study complex diseases through the lens of systems biology. This presentation will review the recent discoveries of systems biology applied to lupus nephritis including pathogenic insights, novel biomarkers, and potential therapeutic targets.

## SS4-2

**Pathologic Bone Resorption and New Bone Formation in Psoriatic Arthritis and Rheumatoid Arthritis, and Implications for Therapy**

Christopher Ritchlin
Allergy, Immunology and Rheumatology Division, University of Rochester Medical Center, Rochester, NY, USA

Conflict of interest: None

The composition and structure of bone is tightly regulated through the interaction of innate and acquired immune cells and stromal cells in the bone marrow and the skeleton. In this presentation, I will review basic osteoimmunology to introduce the pivotal effector cells and signaling pathways that maintain the balance between bone resorption and formation. I will then discuss the immunobiology of rheumatoid arthritis as it relates to bone remodeling and pathologic resorption. I will show the contrast in bone phenotypes between rheumatoid and psoriatic arthritis with attention focused on the combination of both pathologic resorption and formation. The contribution of the bone marrow environment and biomechanical forces that stress the enthesis and the contribution of innate cells to bone phenotypes will be outlined. Lastly, I will present contrasting therapeutic approaches to rheumatoid arthritis and PsA based on our understanding of basic underlying mechanisms.

## TREG Session

### TS-1

**Update from ACR Convergence 2023: Systemic Lupus Erythematosus (SLE) and Autoimmune Rheumatic Disorders**

Allan Gibofsky
Hospital for Special Surgery-Weill Cornell Medicine, USA

Conflict of interest: None

ACR Convergence2023 was noteworthy for many significant presentations of advances in the diagnosis and management of SLE and other autoimmune rheumatic diseases. This presentation will highlight several of the more significant papers preseneted, with a focus on diagnostic challenges of lupus nephritis, including better testing and prognostic biomarkers. Methods for how to improved cardiovascular risk in these patients will be discussed, as well as strategies to reduce corticosteroid doses and improved treatment of comorbidities. Select strategies for enriching enrollment in SLE clinical trials will also be reviewed.

### TS-2

**New molecules in Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Sjögren's (pSS), Systemic Sclerosis (dSSc) and Behcet's disease (BD) presented at EULAR and ACR 2023**

Roy M Fleischmann
University of Texas Southwestern Medical Center, USA

Conflict of interest: Yes

Results of trials of multiple new medications for the treatment of SLE, RA, pSS, dSSc and BD were reported in 2023 at EULAR and ACR. The ones of most interest to the TREG faculty will be discussed here. In SLE positive results were seen in a small trial of ianalumab (BAFF inhibitor) and a large trial of telitacicept (BlyS/APRIL inhibitor), early proof of concept studies with molecules that target TLR7/8 (afimetoran) or TLR7 (DS-7011a), a key pathway in the pathogenesis of SLE, and a mAb against CD6 which blocks its interaction with ALCAM, to inhibit Teff cell activity/trafficking (Itolizumab). Several abstracts reported positive results with jakinibs, including upadacitinib (JAK1), baricitinib (JAK1/2) and deucravacitinib (TYK2). In addition, several interesting abstracts were presented evaluating the safety and effectiveness of CAR-T therapy which are contrasted with the use of obinutuzumab, an effective CD20 inhibitor. In RA, dramatic results were reported with 2 drugs from China, one a dual inhibitor of JAK1/TYK2 and the other a JAK1 inhibitor, both of which achieved clinical responses superior to approved JAKi. In addition, there were presentations on two PD-1 agonists which are designed to target natural immune regulatory mechanisms to modulate immune cells driving disease theoretically dampening the inflammatory cycle and restore immune balance. A small study of an IgG1 mAb that blocks neonatal Fc receptor preventing recirculation (nipocalimab), failed. A small phase 2 study of an oral G protein-coupled receptor 68 proton sensing antagonist which inhibits pro-fibrotic pathways in systemic sclerosis (FT011) was positive as was a small study in dermatomyositis with a humanized IgG1 anti-IFNβ (PF-06823859 (dazukibart). Several molecules that inhibit CD40 (iscalimab and Dazodalibep) as well a BLys/APRI inhibitor (telitacicept) demonstrated efficacy in Sjögren's syndrome. Finally, an oral PDE4i, mufemilast, showed efficacy in Behçet's disease.

### TS-3

**Progress in the Therapeutic Approach to Rheumatoid Arthritis (RA)**

Arthur Kavanaugh
University of California, San Diego, La Jolla, California, USA

Conflict of interest: Yes

There has been continued progress in deciphering the cellular and molecular mechanisms of RA. As a result, a number of therapeutic agents and treatment strategies have emerged, allowing optimized clinical outcomes for affected patients. With this success, the goals of therapy have been elevated, with remission being the ultimate goal. Despite advances, challenges remain. Currently there are nearly 20 disease modifying antirheumatic drugs (DMARDs) available for treating RA, including biologic DMARDs, targeted synthetic DMARDs and older DMARDs. However, RA is heterogeneous, and we still lack "precision medicine", wherein it could be predicted *a priori,* what the most effective and best tolerated therapy for an individual patient would be. Much research is proceeding to help delineate this, including detailed immunophenotyping. It has long been known that RA patients tend to respond better earlier in their disease course. There has been interest therefore in treating RA at its very earliest stage, even before the disease is actually classifiable RA. While some studies have shown promise in perhaps slowing the development of RA for some patients, a major challenge is identifying the subset of such patients (clinically suspect arthralgia) who indeed go on to develop RA as opposed to those with self limited symptoms. The concern is that although RA treatments are generally safe, there are ethical concerns with exposing patients to any adverse effects to prevent a disease they were not going to develop. Safety remains an important topic for RA patients and providers, and research delineating patients most likely to develop certain adverse effects is proving valuable. Another key recent topic is 'difficult to treat' RA.

### TS-4

**Review of Spondyloarthritis Abstracts at the November 2023 American College of Rheumatology Meeting**

Christopher Ritchlin
Allergy, Immunology and Rheumatology Division, University of Rochester Medical Center, Rochester, USA

Conflict of interest: None

Oral and poster presentations centered on spondyloarthritis were delivered at the American College of Rheumatology (ACR) Meeting in San Diego in November 2023. Topics presented included SPARTAN Referral Recommendations for axial spondyloarthritis and efficacy and safety data for intravenous secukinumab in separate axial spondyloarthritis and psoriatic arthritis phase III trials. In addition, one abstract examined the efficacy and safety of apremilast for treatment of oligoarticular psoriatic arthritis. Other abstracts were devoted to comorbidities including inflammatory bowel disease, uveitis and cardiovascular disease. Finally, several abstracts reported on social determinants of health, biomarkers in the transition from psoriasis to psoriatic arthritis and predictors of treatment response in psoriatic arthritis. The top fifteen abstracts from these sessions will be reviewed and discussed.

# Symposium

## S1-1

**Realization of Regenerative Medicine for Osteoarthritis of the Knee Using Cell Sheets**

Masato Satoh[1,2,3]
[1]Department of Orthopedic Surgery, Tokai University School of Medicine, Kanagawa, Japan, [2]Center for Musculoskeletal Innovative Research and Advancement (C-MiRA), Tokai University Graduate School, [3]Center for Regenerative Medicine, Tokai University Graduate School

Conflict of interest: Yes

Osteoarthritis of the knee (OAK) is a slow progressive degenerative disease with a high prevalence. Although the long-term results of surgical prostheses are excellent, joint-preserving surgeries that aim for biological cure of the disease are highly expected. In a clinical study, we transplanted autologous chondrocyte sheets into 8 patients with OAK. The course of the patients was good with no serious adverse events (Sato M, et al. npj Regen Med 2019). And all patients have been doing well for more than 10 years. Currently, autologous cell sheet transplantation is approved as an advanced medical care B and performed at Tokai University Hospital, but the indication is limited to medial type OAK patients who are eligible for high tibial osteotomy. Currently, 17 patients have undergone transplantation. On the other hand, the most important feature of cartilage tissue is its immune tolerance. We focused on the surgical waste tissue of polydactyly patients and conducted a clinical study in which allogeneic cell sheets derived from polydactyly tissue collected at our hospital were transplanted into the cartilage defects of 10 patients with OAK to repair and regenerate their cartilage (Hamahashi K, et al. npj Regen Med 2022). All of the patients are currently maintaining good results more than 3 years after the surgery. In addition, allogeneic cell sheets were produced from tissues derived from polydactyly patients collected in the United States, and the efficacy of allogeneic cell sheets was confirmed in a xenotransplantation experiment using immune-deficient animals, proving their reproducibility (Kondo M, et al. npj Regen Med 2021). The allogeneic cell sheet is now ready for the start of corporate clinical trials, with the notification of the clinical trial submitted by CellSeed, Inc. Basic research on cell sheets started in 2004 with graduate students at Tokai University to apply to cartilage regeneration in OAK. After translational research, the autologous cell sheet is now being implemented as an advanced medical care B under the Act on Safety Assurance of Regenerative Medicine, etc., although it took much longer than initially expected. On the other hand, the allogeneic cell sheet has finally reached the stage of company clinical trials under the Pharmaceuticals and Medical Devices Law. So, what will be the outcome of these trials?

## S1-2

**Treatment of articular cartilage damage with allogeneic iPSC-derived cartilage transplantation**

Noriyuki Tsumaki
Department of Tissue Biochemistry, Graduate School of Medicine, Osaka University

Conflict of interest: Yes

Articular cartilage covers the ends of bones and composes joints, providing lubrication between opposing bones during joint motion. Cartilage consists of chondrocytes embedded in abundant extracellular matrix (ECM). Chondrocytes produce and maintain ECM, and ECM is necessary for the chondrocytes to sustain their chondrocytic property including the production of cartilage ECM. Articular cartilage, when damaged through trauma, has only limited capacity for repair, probably because the damage causes a loss of cartilage ECM, disrupting the chondrocytic environment. The continued use of joints with damaged cartilage and poor repair capacity gradually expands the damaged area on the joint surface, resulting in debilitating conditions such as osteoarthritis. Human induced pluripotent stem cells (hiPSCs) are reprogrammed somatic cells that have pluripotency and self-renew capabilities. We have developed a method by which human iPSCs (hiPSCs) are differentiated toward chondrocytes that produce ECM to prepare cartilage (hiPSC-derived cartilage). We are studying the use of hiPSC-derived cartilage as a curative material to be transplanted into the defect of articular cartilage. To reduce the cost of this regenerative medicine, allogeneic transplantation is preferable. hiPSC-derived cartilage shows low immunogenicity like native cartilage, because the cartilage is avascular and chondrocytes are segregated by the extracellular matrix. After performing pre-clinical tests by transplanting iPSC-derived cartilage into defects created in the articular cartilage of model animals, a clinical test is being implemented.

## S1-3

**Scaffold-free tissue engineered construct derived from allogenic synovial stem cells in cartilage repair**

Norimasa Nakamura[1,2]
[1]Osaka Health Science University, Osaka, Japan, [2]Global Center for Medical Engineering and Informatics, Osaka University

Conflict of interest: Yes

Purpose: To investigate the feasibility of tissue engineered construct derived from allogeneic synovial mesenchymal stem cells to repair symptomatic cartilage defects. Methods: A randomized controlled phase 3 clinical trial was conducted for 52 weeks follow-up. Seventy patients with symptpmatic cartilage defects (ICRS grade 3 and 4) were enrolled. The patients were treated either with TEC through mini-arthrotomy or with arthroscopic microfracture. The primary outcome was assessed by change in overall knee injury and osteoarthritis score (KOOS). The secondary outcome was repair quality evaluated by MRI (MOCART 2.0 and 3D MOCART) and arthroscopic observation by ICRS grading score. Results: Among 76 randomized participants (mean age, 39.7 years; 40% female; body mass index, 24.6 kg/m2), 65 completed the phase 3 clinical trial. The mean defect size was 2.5 cm2. At 48 weeks, the mean improvement in overall KOOS was 25.1 in both TEC and Microfracture group (p= 0.971) The mean MOCART 2.0 score was 78.9 in TEC group and 58 in MFx group (P<0.001). By ICRS Arthroscopic evaluation of repair tissue, 19% of TEc group and 5% of MFx group was grade I, 61% of TEC group and 51% of MFx group was Grade III, 8% of TEC group and 20% of MFx group was Grade III and IV (p<0.05). There were no differences between the groups in adverse events. Conclusion: TEC treatment resulted in repair with significantly improved tissue quality even at 1 year followup. There was no significant different detected by overall KOOS.

## S1-4

**Cartilage regeneration using cultured cartilage and minced cartilage**

Nobuo Adachi
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Conflict of interest: None

Articular cartilage has no nerves, blood vessels, or lymphatic vessels and is nourished by joint fluid, but its unique structure prevents normal tissue repair mechanisms once damaged, and its ability to repair itself is extremely poor. Articular cartilage damage is caused by traumatic cartilage injury, osteochondritis dissecans, rheumatoid arthritis, osteoarthritis of the knee, and other factors. Treatment of articular cartilage injuries is selected based on the size and location of the injured area, the age and activity of the patient, and other factors. Treatment options are microfracture or drilling techniques osteochondral transplantation or cultured cartilage transplantation using regenerative medicine technology. Currently, autologous cultured cartilage transplantation (JACC™), which is covered by insurance in Japan, is indicated for the "relief of clinical symptoms of traumatic cartilage defects or osteochondritis dissecans in the knee joint (excluding osteoarthritis of the knee). However, it is only indicated for cartilage defects with a cartilage defect area of 4 cm2 or greater where no other treatment is available. There are criteria for the facility and the physician who performs the procedure. Currently, JACC has been established as an option for cartilage repair, with an increasing number of reports from academic societies. In cell-based articular cartilage regeneration, transplanted cells are isolated from biopsy tissue and cultured, and then transplanted alone or together with scaffold. However, high quality control is required for cell culture, and the two-step procedure of tissue collection and transplantation is a major clinical problem. We have attempted one-stage articular cartilage regeneration using minced cartilage that does not require a culture process. We have confirmed the efficacy of minced artic-

ular slices as a cell source in vitro and in vivo regeneration of articular cartilage in rabbits.

## S1-5

**Regeneration of osteochondral defect of the knee using the 3D bioprinted MSC construct**

Yasuo Niki[1], Shu Kobayashi[2], Kengo Harato[2], Shizuka Akieda[3], Masaya Nakamura[2]
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Conflict of interest: None

The three-dimensional (3D) bioprinter is considered one of the fields where Japan can demonstrate high technological prowess and international competitiveness in healthcare. Regenerative medicine, particularly using 3D bioprinters, has been accelerated both domestically and internationally, yet practical applications have not been achieved so far. Since 2016, we have been conducting research using a 3D bioprinter with the aim of regenerating osteochondral defects, using allogenic adipose-derived mesenchymal stem cells (ADMSC). Success has been achieved in creating scaffold-free ADMSC constructs using autologous or allogenic MSC spheroids through the 3D bioprinting technique. Furthermore, in preclinical trials, we confirmed the temporary regeneration of osteochondral defects by transplanting similar MSC structures into the knee joints of rabbits and mini pigs. In this study, a osteochondral defect (8 mm X 8 mm) was created in the patellofemoral joint of mini pigs. We conducted an experiment by transplanting cylindrical clinical-grade human-derived MSC constructs. As a result, after 6 months post-transplantation, it was observed that cartilage tissue had extended from both ends of the defect, indicating ongoing healing. Additionally, regeneration resembling hyaline cartilage was confirmed through Type-II collagen immunostaining. Based on the results of this non-clinical trial, we are considering the clinical application of allogenic ADMSC construct transplantation in humans in near future.

## S2-1

**Clinical guidelines for pediatric rheumatic diseases update 2024: Overview**

Masaaki Mori
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Conflict of interest: Yes

In Japan, College of Rheumatology (JCR), Pediatric Rheumatology Association of Japan and the Ministry of Health, Labor and Welfare (MHLW)'s research team have jointly published the "Revised Guideline for Initial Treatment of Juvenile Idiopathic Arthritis (JIA)" in 2015 and the "Childhood Systemic Lupus Erythematosus (SLE) Treatment Guide" in 2018 etc. We recognize that these have had a beneficial effect on establishing standardization of diagnosis and treatment of major pediatric rheumatic diseases among general pediatricians and other physicians nationwide. However, all of them consisted of expert opinions, no evidence evaluation was performed, and the main content was explanatory text as well as handbook. On the other hand, in recent years, guidelines from adult clinical departments have undergone sufficient systematic reviews (SR), and there are many products that have a prominent level of evidence at the time of creation. Furthermore, overseas, the number of papers that can be used for evidence building in the field of pediatric rheumatology has increased compared to before, and recommendations and guidelines have been presented one after another, in Europe and the United States. In view of this situation, there is a growing momentum in Japan to formulate guidelines based on the GRADE method that are suitable for daily medical treatment. This study was developed by JCR and the Groups from the MHLW and is currently being prepared for publication. We believe that the current formulation of guidelines in Japan will serve as the important foundation for when European and American guidelines are published in the future. In this symposium, four pediatric rheumatologists will explain Japanese JIA and childhood-onset SLE guidelines as of December 2023, or identify differences and problems by comparing them with European and American guidelines for each disease. From a bird's-eye view of the world situation, we hope to encourage discussion from a global perspective.

## S2-2

**Current status of a guideline for juvenile idiopathic arthritis in Japan**

Nami Okamoto
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Conflict of interest: None

The first clinical guidance for juvenile idiopathic arthritis (JIA) was published in 2007 in Journal of the Japan Pediatric Society (in Japanese) and in Modern Rheumatology (in English). The definition of the International Society of Rheumatology (ILAR) classification, the method of diagnosis, the treatment algorithm, and the management were shown in it. The intention behind this was to develop a manual for clinical practice against the background of "The prevalence rate is one in 10,000 and general pediatricians are not familiar to this rare disease," "Pediatric rheumatologists are scarce nationwide and have regional locations, so adult rheumatologists often involved," "Biologics were approved and the need to prepare a guide for proper use was established," and "In the systemic form, there is a serious condition called macrophage activation syndrome (MAS), which requires careful management." At the time of the major revision in 2015 and the minor revision in 2017, we added details on diagnosis, treatment, and management, and published "Guidance for the Diagnosis and Primary Treatment of Juvenile Idiopathic Arthritis 2015" and "Handbook for the management of Juvenile Idiopathic Arthritis 2017". The latter was translated and published in Modern Rheumatology. In 2018, there were 5 biologics approved for JIA, and the "Guidance to Use Biologics in Juvenile Idiopathic Arthritis " was published in 2020. Uveitis, an extra-articular manifestation requiring special attention, is also covered in the "Guidance for the Initial Care of Non-infectious Uveitis in Children" published in 2020, compiled in collaboration with the Japanese Society of Ocular Inflammation. As a result of a large amount of research data collected in recent years, the demand for the " Guidelines " has increased in Japan. Therefore, a systematic review (SR) based on the GRADE method was conducted by the Health and Labour Sciences Research Group from 2020 to 2022, in which CQs on the treatment of "Systemic JIA, " MAS, " "Articular, JIA " and" Uveitis " were reviewed. The SR team included pediatricians, internists, and ophthalmologists, and the opinion was also sought from patient and parent of the patient association and academic committee member of Pediatric Rheumatology association in Japan as an external committee member. The JIA guidelines are scheduled to be published around the time of this annual meeting, together with the revised version of the Guidance. In this symposium, the contents of the guideline are outlined mainly on the SR result.

## S2-3

**Juvenile idiopathic arthritis: the state of the science overseas**

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Conflict of interest: None

The current status of the science surrounding JIA overseas can be inferred from JIA practice guidelines and guidance, surveys of pediatric rheumatologists, and drug approval status in various nations. As of November 2023, guidelines have been available in English only in Japan (PRAJ), the United States (ACR), and the United Kingdom (NICE). The American guidelines were updated in 2019 for non-systemic polyarthritis, sacroiliitis, and enthesitis and again in 2021 for oligoarthritis, temporomandibular joint arthritis, and systemic JIA. The U.K. developed guidance and policy statements for the use of biologics. EULAR, PReS, and APLAR have yet to follow suit. Australia reported that it was developing guidelines in 2022 but have yet to announce their completion. In terms of JIA-related practices and medications, the U.S. guidelines recommend intra-articular triamcinolone hexaacetonide injections for oligoarthritis. However, this drug has not been approved for use in Japan. Moreover, in the U.S. methotrexate (MTX) is administered at 10-15 mg/m2/week, which is higher than the dosage allowed in Japan. Subcutaneous MTX administration is also recommended by the American guidelines, and even autoinjector formulations are available. The drugs approved in each country also differ. In

some countries, etanercept once weekly, subcutaneous tocilizumab, abatacept, a 10 mg adalimumab formulation, and tofacitinib have been approved for pediatric use. Many nations also use biosimilars. In the U.S., anakinra, an IL-1 inhibitor, is recommended for the treatment of systemic JIA instead of systemic corticosteroids. CARRA has reported several surveys on the actual clinical status of JIA treatment. I plan to introduce these along with other studies published in 2019 or later. Finally, PRINTO proposed new JIA classification criteria in 2019. Validation of these new criteria are currently underway. We will watch future trends closely for further developments.

## S2-4

**Current status of pediatric onset systemic lupus erythematosus in Japan**

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Conflict of interest: None

Clinical course of pediatric onset systemic lupus erythematosus (SLE) is more severe compared to that of adult onset SLE. Previous reports in Japan as well as foreign countries showed prevalence and severity of lupus nephritis were higher in pediatric patients compared to adult patients. Classification criteria which consist of 12 items (11 items of ACR 1997 criteria for SLE and hypocomplementemia) has been widely used for the diagnosis of pediatric SLE in Japan. Sensitivity and specificity of this criteria were higher compared to ACR 1997 criteria and SLICC criteria. Validation of ACR/EULAR 2019 criteria for the diagnosis of pediatric SLE in Japan is underway. Treatment plan is decided according to the risk classification (mild, moderate and severe) based on disease activity and kidney biopsy findings. Currently, belimumab (div) is the only available biologics for pediatric SLE over 5 years old in Japan. In 2018, clinical guidance of pediatric SLE based on experts' consensus was published. The first clinical guideline of pediatric SLE in Japan is in preparation with corporation of pediatric rheumatologists, adult rheumatologists, pediatric nephrologists, dermatologists, neurologists, ophthalmologists and hematologists.

## S2-5

**Current clinical guidelines for childhood-onset systemic lupus erythematosus in overseas countries**

Tomo Nozawa
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Conflict of interest: None

Current clinical guidelines for childhood-onset systemic lupus erythematosus in overseas countries Systemic lupus erythematosus (SLE) is often experienced as difficult to manage due to the simultaneous or sequential involvement of major organs and the varying severity of the disease in each patient. Although treatment of SLE is currently undergoing remarkable change with the emergence of new immunosuppressive drugs, biologics, for the past several decades, treatment strategies for SLE have not been supported by high-quality evidence due to the low prevalence of the disease and the paucity of randomized data. Systemic lupus erythematosus (SLE) is often experienced as difficult to manage due to the simultaneous or sequential involvement of major organs and the varying severity of the disease in each patient. Although treatment of SLE have currently changed with the emergence of new immunosuppressive drugs, biologics, for the past several decades, treatment strategies for SLE have not been supported by high-quality evidence due to the low prevalence of the disease and the paucity of randomized data. Overseas, the first practice guidelines for physicians were published by the United States in 1999, followed by recommendations in Europe in 2008. The European recommendations have been updated twice, and recommendations for SLE have also been published in the United Kingdom, Latin America, and Asia. In particular, the 2023 EULAR recommendations brought together experts from each continent and provided a single direction. Childhood-onset SLE (cSLE) occurs severe organ damage and high disease activity. However, it has rarely been addressed in the recommendations of international societies. Consensus Treatment Plan (CTP) for lupus nephritis from CARRA in 2012, followed by recommendations for SLE, lupus nephritis, and antiphospholipid antibody syndrome from the SHARE initiative in Europe in 2017. Based on these recommendations, pediatric rheumatologists have treated cSLE patients. However, the recommendations of the SHARE initiative have been in publication for several years, and there are few references to new therapeutic agents such as biologics. An international task force has developed overarching principles and points to consider for T2T and lupus low disease activity state (cLLDAS) for cSLE. Until now, evaluation of disease activity in cSLE has been based on assessment for adult. However, we believe that evidence will be established based on the new T2T and assessment of disease activity. We hope that recommendations for cSLE will develop in the future.

## S3-1

**Identification of Age-associated T (ThA) cells that increase with aging and possess both cytotoxic activity and B cell helper function**

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Conflict of interest: Yes

Many rheumatic diseases involve the production of autoantibodies, and it is thought that self-reactive T cells activate B cells. However, the immune cells responsible for autoimmune responses are not well understood, although follicular helper T (TFH) cells and other immune cells have been reported. We analyzed the functional genome database of 28 subsets of peripheral blood immune cells, ImmuNexUT, from 416 cases and identified a CD4+ T cell population, Age-associated helper T (ThA) cells, that increases with age and possesses cytotoxicity. In the eQTL analysis of ImmuNexUT, we identified a series of age-related genes, including TBX21, which were characteristically expressed in ThA cells. Analysis of the T cell receptor in ThA cells revealed highly proliferated clones. Introducing age-related genes into CD4+ T cells induced cytotoxic molecules such as GZMB. In SLE and RA, ThA cells showed expression of genes that help B cells, such as CXCL13 and IL-21, correlating with type I IFN signaling. In vitro co-culture with B cells showed that ThA cells had an antibody production-promoting ability equivalent to Tfh cells. Introducing age-related genes into CD4+ T cells also induced CXCL13 and IL-21. In SLE, the gene expression of ThA cells showed the strongest correlation with disease activity among CD4+ T cells, and was related to cutaneous mucosal symptoms, musculoskeletal symptoms, and nephritis. In terms of gene expression, MMF acted on Th1 cells rather than ThA cells, while calcineurin inhibitors acted on ThA cells rather than Th1, explaining the clinical efficacy of combining immunosuppressants. In relation to autoantibodies, CXCL13 expressed by TFH cells was associated with anti-RNP antibodies, while CXCL13 expressed by ThA cells was associated with total IgG and anti-Sm antibodies. ThA cells were also present in the muscles and bronchoalveolar lavage fluid of ARS antibody-positive idiopathic inflammatory myopathies, suggesting a deep involvement in organ inflammation. These findings suggest that ThA cells are a new cell population that increases with age and possesses both cytotoxic activity and B cell helper capability. Further analysis of ThA cells may advance the understanding of the pathology of rheumatic diseases and inflammation associated with aging.

## S3-2

**Stratification of rheumatic diseases with population, individual, and cell type-resolution by human omics**

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Conflict of interest: Yes

Rheumatic diseases include a wide variety of pathological conditions and that multiple pathological stratifications exist even in the same disease. While the remarkable development of human genomics and omics analysis technology symbolized by large-scale human genetics has ush-

ered in an era in which huge amounts of data can be obtained, there is a growing need for research activities that can interpret large volumes of omics data in a cross-sectional manner to elucidate disease pathology and pathological stratification. From the viewpoint of statistical genetics, a discipline that studies the causal relationship between genetic and trait information from the perspective of statistics, we have shown that the integration of large-scale human disease genetics with multilayered omics information in various biological and medical fields can contribute to the stratification of disease pathologies. The human omics information obtained is often categorized as population, individual, or single-cell resolution. In addition to population-resolution omics information such as genome-wide association analysis and individual-resolution omics information such as immunophenotyping, single-cell-resolution omics information based on single-cell analysis is becoming increasingly popular. Projection of population-, individual-, and single-cell-resolution omics information to each other is expected to elucidate the stratification of rheumatic diseases. Immunophenotypic analysis, which quantifies detailed profiles of peripheral blood immune cells, will enable classification of rheumatic diseases at disease, immune cell, and individual patient resolution. Disease patient clusters stratified by immunophenotype have been found to exhibit distinctive clinical presentations. For example, patients with rheumatoid arthritis with an immunophenotypic picture characteristic of systemic lupus erythematosus showed reduced regulatory T cells and resistance to therapy. Furthermore, projection of polygenic scores based on genome-wide association analysis to individual immunophenotypic information and gene expression information of single cell resolution can reveal the key cellular organization of disease pathogenesis (e.g., dendritic cells in rheumatoid arthritis complicated interstitial pneumonia, COVID-19 severe disease Tanaka H et al. ***Ann Rheum Dis*** 2023). In this presentation, we would like to introduce some practical examples.

## S3-3

**Stratification of rheumatic diseases based on peripheral blood immunophenotype and novel therapeutic approaches**

Satoshi Kubo[1], Yoshiya Tanaka[2]
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Conflict of interest: Yes

Since the early 2000s, several molecular targeted therapies have transformed the treatment landscape for rheumatoid arthritis, marking a paradigm shift in the field. Four classes of molecular targeted therapies-JAK inhibitors, CTLA4-Ig, anti-IL-6 receptor antibodies, and TNF inhibitors-are now available. These successes have spurred the development of molecular targeted therapies for other rheumatic diseases, such as psoriatic arthritis, systemic lupus erythematosus, Takayasu disease, and eosinophilic granulomatosis with polyangiitis. However, challenges persist, with some patients remaining unresponsive to these therapies, requiring drug modifications, and experiencing persistent disease activity. The potential for selecting a therapeutic agent tailored to the pathophysiology and etiology of individual patients with rheumatic diseases holds promise for optimizing the balance between efficacy and side effects. This personalized approach is envisioned to expedite patients' return to society and mitigate the social and economic impact of the disease. While precision medicine has achieved notable success in cancer treatment, its application to autoimmune diseases is still evolving. This endeavor necessitates evaluating patients at the genetic predisposition, gene expression, protein, and cellular levels, along with the identification of appropriate biomarkers. This presentation will showcase ongoing efforts toward achieving precision medicine and outline the conceptual framework and necessary steps for its realization.

## S3-4

**The Role of Cellular Metabolism in Autoimmune Diseases: Focus on T cells**

Michihito Kono
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Conflict of interest: Yes

Immunosuppressive agents and biologics have improved the prognosis of autoimmune diseases such as systemic lupus erythematosus (SLE). New therapeutic agents are desired because many patients with autoimmune diseases are resistant or unresponsive to conventional therapy. Many studies have shown that T cell metabolism is central to their proliferation, survival, differentiation, and function. Since each T cell subset uses a preferred metabolic pathway, T cell metabolism is considered a therapeutic target. We have previously shown that glutaminase 1 (Gls1), the first enzyme of glutaminolysis, was increased in Th17 cells, and Gls1 inhibitors reduced Th17 cell differentiation and disease activity of lupus-prone mice, MRL/*lpr* mice. Another group reported that 2-deoxy-d-glucose (glycolysis inhibitor) and metformin (mitochondrial electron transport chain complex I inhibitor) led to the normalization of T cell metabolism and reversal of disease activity of lupus-prone mice. We have also shown that an intracellular anti-inflammatory metabolite, itaconate, altered epigenetic changes by modifying methionine metabolism. Itaconate inhibited Th17 cell differentiation and promoted Treg differentiation, resulting in amelioration of experimental autoimmune encephalomyelitis. In this symposium, I would like to review the role of cellular metabolism in autoimmune diseases, especially in T cells.

## S3-5

**Visualization and identification of cellular pathogenesis in autoimmune diseases**

Masaru Ishii
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Conflict of interest: None

Intravital imaging of various live tissues and organs is not only a useful method for visualizing in situ behavior of a diversity of living cells within intact tissues and organs, but also for identifying diverse kinds of cell types which are only detectable in vivo. Especially we are focusing on tissue-resident macrophages in several pathological conditions critical for the disease onset and activities. For example, based on the observation of inflammatory bone destruction, we have identified a novel macrophage subset generating pathogenic osteoclast involved in autoimmune bone erosions. The pathogenic osteoclasts and their precursor macrophages are present in human arthritis patients and thus emerging as promising therapeutic targets. In additions, we are identifying unique cell types specifically involved in tissue fibrosis in lung and liver. In addition to the application to animal experimental models, we are currently trying to adapt this technique for evaluating disease status in local foci of human patients. Here we will present the recent updates on imaging-based studies for understanding autoimmune diseases in bench and beds.

## S4-1

**Management options in "difficult to treat" rheumatoid arthritis**

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Conflict of interest: Yes

The present generation has witnessed a remarkable expansion in new, approved, and efficacious therapeutics for the treatment of rheumatoid arthritis (RA). This evolution has been prompted by concurrent advances in understanding the pathobiology of RA and in biologic and small molecule engineering which have permitted the development of so-called "targeted therapies". Despite distinct mechanisms of action, all targeted therapies have demonstrated similar efficacy for improvement in disease activity. International treatment guidelines recommend use of a targeted therapy in subjects exhibiting an inadequate response to initial csDMARD. Furthermore, EULAR recommend that if an ideal disease activity target of remission or low disease activity is not attained with the initial targeted therapy, that treatment should be switched to an alternative targeted therapy which may be of a different class or the same class in the case of biologic TNF or IL6R inhibitors. However, this "treat-to-target" approach is revealing a proportion of patients who are responding inadequately, or even non-responsive, to 2 or more targeted therapies of differing mechanisms of action. This subgroup has been described as having "difficult to treat" RA.

Current practice in the sequential choice of targeted therapy is often informed by cost effectiveness and prescriber familiarity rather than by understanding the driving pathological pathways in each individual and this may exacerbate the problem of refractory disease. In this talk, I will review clinical trial data that informs treatment choice after failure of one or more targeted therapies and recent advances in RA biomarker research that may help to identify non-responders but acknowledge that there are no current *precision medicine* biomarkers that reliably indicate optimal treatment. I will also consider an alternative approach using *personalised medicine* indicators based on clinical history to help make the most appropriate treatment choices.

## S4-2

**Advances in systemic lupus erythematosus**

Yoshiya Tanaka
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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease that affect the skin, joints, heart, kidneys, serosa, nerves and blood vessels, presenting with a variety of clinical symptoms. Glucocorticoids (GCs) and immunosuppressants are widely used, but their targets are non-specific, and induce diverse adverse events, particularly immune dysfunction caused by drugs is a major cause of infection that directly leads to death from infections. Thus, molecular targeted drugs with few adverse reactions are needed. It is pathologically characterized by activation of autoreactive T cells and production of autoantibodies by B cells. B-cell depletion therapy using anti-CD20 rituximab was approved for patients with lupus nephritis refractory to conventional therapy in Japan. An anti-B-cell activating factor antibody belimumab and an anti-type I interferon receptor antibody anifrolumab are used for patients with active SLE who respond poorly to standard of cares. Additionally, as many susceptibility genes for SLE are associated with signal transduction of dendritic and B cells, cytokines and signaling molecules that bridge the innate and adaptive immune systems are the current focus of attention. Promising approaches include the development of a Janus kinase inhibitors targeting tyrosine kinase deucravacitinib, plasmacytoid dendritic cell-targeted drugs, proteasome inhibitors (e.g., iberdomide), type II anti-CD20 antibody Obinutuzumab and many. Based on the advances in the treatments, GCs are positioned as 'bridging therapy' during periods of disease activity; for maintenance treatment, they should be minimized and, when possible, withdrawn in the EULAR recommendations for the management of SLE: 2023 update which we have published. If many molecular target drugs are developed in the future, precision medicine that differentiates their use will attract more attention with lowest dose of or without GCs, similar to rheumatoid arthritis.

## S4-3

**Management of interstitial lung disease associated with systemic autoimmune diseases**

Masataka Kuwana
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Conflict of interest: Yes

Interstitial lung diseases (ILDs) are among the most serious complications associated with connective tissue diseases (CTDs), and lead to significant morbidity and mortality. ILD can be present in virtually all CTDs, including rheumatoid arthritis, systemic sclerosis (SSc), polymyositis or dermatomyositis, Sjögren's syndrome, and mixed connective tissue disease. The management of CTD-ILD is challenging due to extreme variability of clinical course, treatment response, and outcomes. For example, subacute or acute ILD is usually responsive to immunosuppressive treatment, while rapidly progressive ILD, typically found in patients with dermatomyositis, is sometimes treatment-resistant and fetal. On the other hand, in chronic ILD, it is important to predict future progressive pulmonary fibrosis (PPF), which leads to restrictive ventilatory impairment and resultant respiratory insufficiency. Therefore, prediction of future course and outcomes as well as treatment responses are critical to clinical decision making of treatment indication and choices. There has been accumulating evidence of risk factors for ILD progression and poor outcomes and efficacy of treatment in patients with CTD-ILD, mainly in those with SSc-ILD, resulting in development of consensus statements, guidelines, and recommendations. Immunosuppressive regimens have been a mainstay of the treatment of CTD-ILD, but in recent years, there have been accumulating data showing potential efficacy of molecular-targeted drugs, such as tocilizumab and rituximab. On the other hand, the effect of antifibrotic agents such as nintedanib on preventing pulmonary function decline is shown in patients with PPF. However, in clinical practice, there are still many issues to be solved, such as in what cases, at what timing, when to use them properly or in combination, and long-term efficacy and safety profiles. This lecture features how to implement the latest guidelines/recommendations in our daily practice.

## S4-4

**Update on treatment of ANCA-associated vasculitis**

Bernhard Hellmich
Medius Kliniken, University of Tübingen, Kirchheim-Teck, Germany

Conflict of interest: Yes

Granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) are small vessel vasculitides that are linked to the presence of antineutrophil cytoplasmic antibodies (ANCA). Results of several randomized clinical trialshave recently led to significant changes of recommendation fro treatment of these ANCA-associated vaculitides (AAV) by the European Alliance of Associations for Rheumatology (EULAR) and other societies. For remission induction in life- or organ-threatening GPA or MPA, a combination of high-dose glucocorticoids (GC) in combination with either rituximab or cyclophosphamide is recommended. For patients without life- or organ-threatening disease, methotrexate can be used as an alternative to rituximab and lower GC starting doses of 30 mg/day can be considered. Based on the results of the PEXIVAS and LOVAS trials, tapering of the GC dose to a target of 5 mg prednisolone equivalent/day within 4-5 months is advised. Avacopan may be considered as part of a strategy to reduce exposure to GC in GPA or MPA. Plasma exchange may be considered in patients with rapidly progressive glomerulonephritis. For remission maintenance of GPA/MPA the use of rituximab for 24 to 48 months is recommended over azathioprine, methotrexate, or mycophenolate mofetil. Cyclophosphamide should be used for remission induction of life- or organ-threatening EGPA, but rituximab can be considered as an alternative. In patients with non-severe relapsing or refractory EGPA the use the use of mepolizumab is recommended. Mepolizumab can also be used for remission maintenance, while azathioprine or methotrexate are alternatives. The administration of co-trimoxazole is recommended for infection prophylaxis during induction treatment. Despite recent progress, substantial data gaps still exist. Thus, informed decision making between physicians and patients remains of key relevance.

## S4-5

**Still's disease: EULAR / PReS guidelines for the diagnosis and management of Still's disease**

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Conflict of interest: Yes

Systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease are supposed to be counterparts of the same disease, but no consensus has been reached yet on a common approach to diagnosis and management across ages. In May 2022 EULAR and PReS endorsed a proposal for a joint task force (TF) to develop recommendations for the diagnosis and management of sJIA and AOSD. The TF included two convenors, a methodologist, three fellows, 25 medical experts and two patient research partners and agreed during a first meeting in September 2022 to cover for main topics: similarity between sJIA and AOSD, novel diagnostic biomarkers, therapeutic targets and strategies, and complications including macrophage activation syndrome (MAS). The TF based their recommendation on three overarching principles (OPs): 1) SJIA and AOSD are a same disease and should be designated by the same name, Still's disease, 2) A treat-

to-target approach and a shared decision making should be implemented, with a final goal of reaching drug-free remission, and 3) although several innovative therapies are available, MAS should remain a concern for physicians throughout disease evolution. Fourteen specific recommendations were issued and are detailed in the Table. Two therapeutic targets were defined: clinically inactive disease (CID) and remission, i.e., CID maintained for at least 6 months. The optimal therapeutic strategy relies on glucocorticoids (GCs) for a maximal duration of 6 months and initiation of IL-1 or IL-6 inhibitors as early as possible after diagnosis. Life-threatening complications can occur any time during disease course, i.e., at diagnosis, under targeted therapies, and after CID achievement. MAS treatment should rely on high-dose GCs, IL-1 inhibitors, cyclosporin and IFNγ inhibitors, which are now available. A specific concern rose recently with cases of severe lung disease in children with Still's disease. The main characteristics are the following: mild clinical symptoms including clubbing, dry cough or shortness of breath; septas thickening and alveolar proteinosis aspects on CT-scan; eosinophilia and increased serum IL-18, history of MAS, exposure to IL-1 or IL-6 inhibitors, and presence of HLA DRB1*15 allele. Adding T-cell directed immunosuppressant seems to be the most relevant option in this case. Finally, the recommendations emphasized the key role of expert centers, notably those of the RITA European Reference Centers.

## S5-1

**Clinical Features of Familial Mediterranean Fever in Japan and Points to Consider in MEFV Gene Variant Interpretation**

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Conflict of interest: Yes

Familial Mediterranean Fever (FMF) is a typical hereditary autoinflammatory disease with periodic fever, arthritis, and serositis, and variants in the MEFV gene encoding pyrin determine its pathogenesis. Variants in the MEFV gene exon 10 are associated with the severity and prognosis of FMF and have been used as a diagnostic tool in Japan. However, the distribution of MEFV gene variants has been shown to be different in Japanese than in other countries (especially in the Mediterranean region), with a smaller proportion of Japanese having an exon 10 variant, which is restricted to M694I, and a larger proportion having an exon 2 variant. In addition, there are many atypical cases of FMF in Japan that do not have typical fever patterns and respond to colchicine, but their pathogenesis remains unclear and diagnostic and therapeutic methods have not been established. The gold standard for FMF diagnosis is clinical diagnosis; MEFV gene variants should be used as adjuncts and should be interpreted with caution, especially for variants other than exon 10, as most have no established pathologic significance. In essence, it is difficult to explain the pathogenesis of FMF solely in terms of MEFV gene variants, and the diversity in age of onset suggests the involvement of environmental factors. In this lecture, I will explain the clinical features of FMF in Japan from the point of view of a rheumatologist, as well as the significance of MEFV gene variants and points to consider at the time of diagnosis, including the latest findings. Through this lecture, we would like to deepen the discussion on the diagnosis of atypical cases of FMF and the significance of MEFV gene variants.

## S5-2

**Type 1 interferonopathy**

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Conflict of interest: None

Type I interferon (IFN) is a cytokine that primarily plays an important role in defense against viral infections. However, overproduction of type I IFNs can cause disease. In multifactorial diseases such as systemic lupus erythematosus and dermatomyositis, it has long been known that type I IFN is deeply involved in the pathogenesis. Recently, a group of genetic diseases, such as Aicardi-Goutière syndrome, have also been reported in which excess type I IFN plays a central role in pathogenesis; in 2011, Crow et al. described a group of Mendelian genetic diseases in which persistent excess production of type I IFN is central to the etiology, and described a type 1 interferonopathies. Since then, various genetic variants in the type I IFN signaling pathway have been identified, and approximately 40 causative genes have now been identified. In type 1 interferonopathies, molecular mechanisms have been identified, including abnormalities in the nucleic acid metabolic pathway, abnormalities in the downstream pathway of the IFN receptor, proteasome dysfunction, and mitochondrial abnormalities. The efficacy of JAK inhibitors for type 1 interferonopathies has also been reported. In this presentation, the history and recent findings of type 1 interferonopathy will be reported.

## S5-3

**Schnitzler syndrome in Japan**

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Conflict of interest: None

Schnitzler syndrome (SchS) is an acquired autoinflammatory syndrome characterized by a chronic urticarial rash and monoclonal IgM (or rarely IgG), with systemic inflammatory symptoms such as recurrent fevers, bone pain/ arthralgia/ arthritis, neutrophilic dermal infiltration, leukocytosis, and elevated CRP and long-term risk of lymphoproliferative disorders. While the clinically similar Cryopyrin-associated periodic fever syndrome (CAPS) often develops in infancy with the NLRP3 mutations, SchS mainly develops in adulthood, and its etiology, pathogenesis, and causative gene are still unknown. Although treatment for SchS has yet been established, the efficacy of IL-1 inhibitors has recently been reported. We have experienced 4 cases, and in 2008, 7 cases were identified in a patient survey (collection rate 31%) conducted in dermatology departments of large hospitals by Hashimoto's group under the Ministry of Health, Labour, and Welfare. Our literature search in PubMed and Ichushi-Web identified 10 cases from English papers and 17 cases from Japanese papers and presentations. We conducted a follow-up survey by contacting the authors and attending physicians, and identified a total of 36 domestic cases, excluding duplicates (Takimoto-Ito R, et al. Allergol Int. 2022). The mean age of onset in the 27 definitive cases was 55.6 years, the male-to-female ratio was 1:1, and the mean period from onset to diagnosis was 3.3 years. Of the 19 followed patients, colchicine is currently administered to 9 patients, and 4 patients achieved a Physician Global Assessment score of 0, suggesting that colchicine is useful as Step 1 of treatment. NSAIDs and hydroxychloroquine should be added for bone or joint pain as Step 2, and if not controlled, biologic agents should be considered as Step 3. However, even when acute inflammatory symptoms are controlled, blood IgM levels often increase over time, and it remains unclear whether these treatments can prevent the development of lymphoma.

## S5-4

**Still's diseases (Systemic Juvenile Idiopathic Arthritis / Adult-Onset Still's Disease)**

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Conflict of interest: None

Systemic Juvenile Idiopathic Arthritis (s-JIA) is defined as idiopathic arthritis accompanied with spiking fever over 2 weeks and one of the following symptoms including rash, generalized lymphadenopathy, hepatomegaly/splenomegaly and serositis. s-JIA was originally reported as Still's disease in 1897. In 1971, adult patients developing a disease indistinguishable from Still's disease were reported and this disease was named as Adult-Onset Still's Disease (AOSD). Classification criteria for AOSD consisted of fever, arthralgia, typical rash, and leukocytosis as major, and sore throat, lymphadenopathy and/or splenomegaly, liver dysfunction, and

the absence of rheumatoid factor and antinuclear antibody as minor criteria. For the diagnosis of AOSD, >5 criteria must be met, including >2 major. Recent studies revealed s-JIA and AOSD have common pathogenesis which belongs to the group of autoinflammatory diseases and overproduction of innate proinflammatory cytokines including IL-1β, IL-6 and IL-18. From these findings, s-JIA and AOSD are now re-defined as an identical disease, Still's disease. In this presentation, I review clinical manifestations, pathogenesis and treatments for s-JIA and AOSD.

## S5-5

**The Current Status and Challenges of VEXAS Syndrome Management in Japan**

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Conflict of interest: None

VEXAS syndrome (Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is an adult-onset autoinflammatory disease with hematological abnormalities caused by somatic variants of *UBA1* (NM_003334.3). *UBA1* variants cause reduced ubiquitylation by decreasing functional UBA1b expression or inducing the abnormal catalytic activity of UBA1, resulting in the activation of the innate immune system leading to multi-organ inflammation. Since the initial report in October 2020 by Beck et al, numerous worldwide reports have rapidly elucidated the clinical presentation of VEXAS syndrome. Patients with suspected VEXAS syndrome are managed by various departments, including rheumatology, hematology, and dermatology. Consequently, the urgent need has emerged to establish an effective system for the genetic diagnosis and management of VEXAS syndrome. At Yokohama City University, we collected 89 patients with clinically suspected VEXAS syndrome throughout Japan. We employed highly sensitive genetic methods to examine *UBA1* variants, detecting variants in 40 patients. Additionally, we developed a clinical scoring system to identify individuals warranting *UBA1* genetic screening. Prompted by the results of our study, we are currently in the process of developing a diagnostic framework in Japan in collaboration with the Japanese Society for Immunodeficiency and Autoinflammatory Diseases (JSAID). While global statements for the diagnosis of VEXAS syndrome is being finalized, the definition of the disease may change with newly reported *UBA1* variants and early-onset case. In addition, there is limited information about treatment strategies and prognosis of VEXAS syndrome. Many issues remain to be resolved. In this presentation, we review the reality and problems of VEXAS syndrome management in Japan, acquired through our cohort, together with recent new findings on VEXAS syndrome.

## S5-6

**Behçet's syndrome**

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Conflict of interest: None

Behcet's disease is a periodic febrile disease characterized by oral ulcers, genital ulcers, uveitis, and erythema nodosum, and sometimes gastrointestinal lesions, vascular lesions, and neurological symptoms. Pathologically, vasculitis due to the over activation of neutrophils is main cause of disease, and in uveitis, the involvement of IFN-γ-producing cells (Th1) and IL-17-producing cells (Th17) has been suggested. In terms of the treatment, in addition to colchicine, small doses of glucocorticoids, immunosuppressive agents such as calcineurin inhibitors and methotrexate are generally used, and TNF-α inhibitory antibodies in severe cases with uveitis and gastrointestinal lesions, and apremilast, a PDE4 inhibitor, has become available for the treatment of oral ulcer. It is important that effective therapeutic agents are selected according to the disease state. In particular, although the frequency of uveitis is decreasing, it is desirable to diagnose and treat uveitis at an early stage because it causes visual impairment and leads to a significant decline in quality of life. Recently, we have found that mitochondrial DNA (mtDNA) is leaked into the serum of patients with Behcet's syndrome, and that this is responsible for the inflammatory pathogenesis in Behcet's syndrome. That is, in monocytic cells from patients with Behçet's syndrome, inflammasome stimulation easily activates caspase-1, which in turn causes gasdermin-D to puncture the mitochondrial outer membrane and mtDNA to leak into the cytoplasm. Then, mtDNA is encapsulated in exosomes and released extracellularly, which leads to the production of inflammatory cytokines and activation of neutrophils, resulting in the immune cell infiltration and the development of pathological conditions characteristic of Behçet's syndrome. In this talk, we will review our recent findings of the pathogenesis on Behcet's syndrome and recent progress of treatment.

## S6-1

**2023 ACR/EULAR antiphospholipid syndrome classification criteria, Focus on Obstetric APS**

Kayoko Kaneko
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Conflict of interest: None

Patients with antiphospholipid syndrome (APS) are presented with non-thrombotic organ complications such as valvular heart disease, chorea, and epilepsy, some of which are thought to be explained in part by organ inflammation caused by antiphospholipid antibodies. In the obstetric complications of APS, recent studies have shown that the pathogenesis is not thrombus formation in the placenta but instead increased production of inflammatory cytokines and complement activation induced by the direct action of antiphospholipid antibodies on β2GP1 expressed on the cell surface of the placental nutrient cell layer, resulting in placental dysfunction and pregnancy-induced hypertension Nephropathy is thought to be the primary pathogenesis. Last year, the APS classification criteria were revised for the first time in approximately 20 years. Unlike the previous criteria (modified from the 2006 Sapporo criteria, Sydney), clinical symptoms and laboratory results are scored as six clinical domains and two laboratory domains, respectively. APS is classified when the sum of the clinical and laboratory scores is three or more points in each domain. In a cohort-based validation, the specificity of the new APS classification criteria versus the old criteria was 99% vs. 86%, and sensitivity was 84% vs. 99%. The new criteria are more specific, especially in the perinatal area, in that they give less weight to habitual abortion, which was considered nonspecific, and more weight to the presence of severe placental insufficiency and gestational hypertension nephropathy, which are highly specific for the action of antiphospholipid antibodies. This presentation will outline the new classification criteria for APS focus on obstetric complications.

## S6-2

**Pregnancy with Takayasu Arteritis**

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Conflict of interest: Yes

Takayasu arteritis is a disease that primarily affects women of childbearing age. As with other connective tissue diseases, it is essential to plan pregnancies during periods of remission or low disease activity in order to reduce the risk of pregnancy complications and disease flare. Beyond a planned pregnancy, it is of utmost importance to implement preconception care that takes into account the impact of treatment and Takayasu arteritis on pregnancy. With regard to treatment, it is important to use safe medications both preconception and during pregnancy to address vasculitis, and stabilization of disease activity is an important factor. Once pregnancy is confirmed, it is important to provide adequate explanations so that patients do not discontinue drug therapy out of concern for fetal effects. If morning sickness in early pregnancy interferes with oral corticosteroid or if the patient has been taking corticosteroids for an extended period of time, it is important to provide information regarding the application of steroids at delivery. The rheumatologist evaluating the impact of vasculitis on pregnancy should assess preconception organ damage due to vasculitis, particularly kidney and heart function and blood pressure. In cases with pulmonary arterial involvement, the degree of pulmonary hypertension should be

assessed simultaneously. Pregnancy increases circulating plasma volume approximately 1.4 times more than in nonpregnant women, placing an increased burden on the kidneys and heart. Takayasu arteritis disturbs adaptation and may lead to the exacerbation of hypertension and the development of gestational hypertension. Patients should have their home blood pressure measured, and early detection of fluctuations is important. Continuous use of low-dose aspirin is essential for patients with stenotic lesions or a history of cerebrovascular disease and plays a crucial role in determining mode of delivery. For previous reports of gestational hypertension, miscarriage, and fetal growth restriction, a collaborative effort with the obstetrician is essential to provide support for achieving better pregnancy outcomes.

## S6-3

**Management of pregnancy in patients with kidney disease**

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Conflict of interest: None

Some patients wonder if they can give birth in the future. Although many nephrologists have advised their patients to avoid pregnancy in the past, this approach is paternalistic and not patient-centered. These days, because of the development of an approach of shared decision-making, "Clinical Practice Guidelines for the Management of Pregnancy in Kidney Disease Patients 2017" does not use expressions like "permission of pregnancy" or "we do not recommend pregnancy." Women with chronic kidney disease (CKD) have a higher risk for maternal and fetal morbidities, including preeclampsia (PE), preterm birth, and fetal growth restriction than the general population. Recent studies revealed the risk of complications to increase, even in earlier stages of CKD. Pregnancy in women with end-stage renal failure (ESKD) is relatively rare and challenging. Women treated with dialysis have reduced fertility, and their prognosis of pregnancy is poor. However, successful pregnancies on hemodialysis are slightly increasing. Kidney transplantation improves infertility in patients with CKD. The number of pregnancies and deliveries in kidney transplant recipients is also growing. In Japan, it is reported that approximately 10% of female kidney transplant recipients of reproductive age experience pregnancy. Nephrologists need to tell their patients the risks of pregnancy and its complications which can be happened. It is essential to diagnose and treat CKD primary disease before conception, give information about the medicine they must stop during the pregnancy period, and share the necessity of pregnancy planning. Ideally, informed consent should be started in the young generation. There were 52 cases of pregnancy with CKD in our hospital from April 2015 to February 2023. Many of the primary diseases of CKD were IgA nephropathy and nephrotic syndrome. Seven of them were kidney transplant recipients. In this symposium, I will talk about pregnancy with kidney disease, showing our cases.

## S6-4

**Sexual Health of MZ Generation Patients with Rheumatic Disease**

Yuzaburo Inoue
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Conflict of interest: Yes

MZ generation is an umbrella term for millennials (Generation Y) and Generation Z. It refers to the generation born between the 1980s and the 2010s. Millennials have grown with the development of the Internet and are said to be highly respectful of diversity in terms of gender and race. In addition, Generation Z, for whom the Internet and digital devices have existed since birth, is considered a generation of digital natives and smartphone natives who use social networking services more frequently, communicate openly, and share information online more generally. The generation of MZ rheumatic disease patients is reaching adolescence to young adulthood, and maintaining their sexual health has become an important clinical issue. Sexual dysfunction, such as painful intercourse and erectile dysfunction, greatly affects quality of life, but it is often difficult to discuss with the primary care physician, and appropriate intervention is not provided. In adolescent patients, physicians need to be "perceptive" because they are more likely to discuss sexual health with their physicians during office visits when they are not accompanied by a parent or guardian or when the patients themselves have concerns. However, it has been pointed out that Generation Z may have more sexual partners and engage in more high-risk sexual behavior than millennials in Western countries because of the widespread use of SNS communication and the ability to have sexual relationships with an unspecified number of people of different ages and genders. Among sexually transmitted diseases, human papillomavirus (HPV) causes cervical cancer and other diseases that can be prevented by vaccination. The risk of cervical squamous intraepithelial lesions caused by HPV in women with SLE is six times higher than that in healthy women, and the risk is expected to be higher in women with other rheumatic diseases. An active recommendation for the HPV vaccine for rheumatic disease MZ generation is desirable.

## S6-5

**Protection of mothers and children from vaccine preventable diseases by live-attenuated vaccine**

Ichiro Kobayashi
Center for Pediatric Allergy and Rheumatology, KKR Sapporo Medical Center, Sapporo, Japan

Conflict of interest: None

Patients with rheumatic diseases are susceptible to infection because of their underlying diseases themselves or immunosuppressive therapy. Although it is important to protect them from vaccine preventable diseases by vaccination, infection of vaccine strain is a medical concern in patients under immunosuppressive therapy. In addition, it is reported that an infant who was born to a mother receiving infliximab for Crohn`s disease during pregnancy died of disseminated infection of BCG. The Pediatric Rheumatology Association of Japan (PRAJ) have published a recommendation for vaccination in pediatric rheumatic disease (PRD) in 2014. Thereafter, efficacy and safety of MMR booster vaccination and primary varicella vaccination has been reported in PRD patients under treatment with low-dose glucocorticoid, MTX, or TNF inhibitor. Recent development of novel bDMARDs and tsDMARDs and world-wide use of live-attenuated rotavirus vaccine have prompted us to revise the guideline. Currently, EULAR and ACR have revised vaccination guidelines in 2019 and 2023, respectively. PRAJ has performed systematic literature review and is revising the guideline for vaccination in pediatric and adolescent rheumatic diseases. The target of the revised guideline included young adults to cover patients in a transitional stage. In this symposium, I would like to focus on the live-attenuated vaccines in young patients with rheumatic disease under immunosuppressive therapy and infants born to mothers receiving bDMARDs.

## S7-1

**Overview of glucocorticoid-induced osteoporosis**

Yoshiya Tanaka
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Conflict of interest: Yes

Synthetic glucocorticoids (GCs) are widely used to treat various diseases, including autoimmune rheumatic diseases, through pharmacological actions. In treating these diseases, synthetic GCs not only exert pharmacological actions by regulating the transcription of proinflammatory mediators through GC receptor, but also cause abnormal metabolism of glucose, lipid, bone, and blood vessels, by the receptors. GC-induced osteoporosis (GIOP) accounts for 25% of the adverse drug reaction to prescribed drugs and causes fractures in 30-50% of patients and markedly decreases their quality of life. Therefore, multiple societies in various countries developed the guidelines for the management and treatment of GIOP. The Japanese Society for Bone and Mineral Research (JSBMR) developed the guidelines for the management in 2004 and intensively revised it in 2014, providing the treatment criteria based on scores of risk factors, including previous fractures, age, GC doses, and bone mineral density, for patients aged older than18 years who are receiving GC therapy or scheduled to receive GC therapy for longer than 3 months. Because evidence of anti-osteoporotic drugs has been accumulated, the JSBMR further revised the guideline in 2023, preparing 17 clinical questions using the GRADE system and conducted systematic reviews to develop the best

management and treatment recommendations based on scientific evidence. As the results, bisphosphonates (oral and injectable formulations), anti-RANKL antibody teriparatide, eldecalcitol, or selective estrogen receptor modulators are recommended for patients who has received or scheduled for GC therapy with risk factor scores of greater than or equal to 3. It is recommended that osteoporosis medication is started concomitantly with the GCs therapy for the prevention of fragility fractures in elderly patients. In this symposium, mechanisms, assessment, fracture-risks and surgical and pharmacological treatment in patients with GIOP will be discussed.

## S7-2

**Fracture-risk in patients with glucocorticoid-induced osteoporosis**

Mary Beth Humphrey
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Conflict of interest: None

Glucocorticoid (GC) treatment is highly prevalent with nearly 3% of adults over the age of 50 receiving them for autoimmune and non-autoimmune conditions. Glucocorticoid-induced osteoporosis and fractures are two of the most important preventable side-effects of GC use. Many factures contribute to GC-induced fracture risk including age, sex, and dose and duration of the GC treatment. High dose daily GC, cumulative GC of > 5 grams in a year, recent fractures, frailty, and falls are associated with a higher risk of GC-induced fracture. GC treatment causes early rapid bone loss and GC-associated fractures often occur at higher bone density than age associated osteoporosis. GC treatment has the strongest negative impact on the vertebrae, with increased fractures occurring at 2.5 mg prednisolone per day for 3 months. GC treatment > 5 mg per day significantly increases risk of vertebral and hip fractures. Medical conditions including rheumatoid arthritis, asthma, COPD, dementia and sleep disorders have the highest rates of GC-induced fractures. Compared to older adults, children and young adults have a high capacity to rebuild bone after GC treatment is stopped.

## S7-3

**New Evidence of Bone Safety of Glucocorticoids in the treatment of Inflammatory Rheumatic Diseases**

Kenneth G Saag
Division of Clinical Immunology and Rheumatology, The University of Alabama at Birmingham, Alabama, USA

Conflict of interest: Yes

Glucocorticoids have been in wide-spread clinical use since the 1950s, and despite the advent of many more targeted therapies they remain in chronic use by approximately one percent of the general population worldwide. Rheumatologic disorders constitute the major source of their utilization. Controversies still persist around their relative bone safety, particular in disorders like rheumatoid arthritis (RA), where they have prominent anti-inflammatory effects that can increase mobility via reduced joint inflammation, which should lead to benefits to bone. Despite this pathophysiologic rationale, newer data continues to implicate even very low dose glucocorticoids (< 7.5 and perhaps even < 5.0 mg prednisone equivalent) in reduced bone mineral density and a heightened risk for fractures, particularly of the spine. New observational analyses using large databases and modern methods in epidemiology better address confounding by indication, whereby glucocorticoid users are at higher risk of fractures independent of their glucocorticoid use. Even well designed randomized controlled clinical trials, such as the GLORIA study, support a higher fracture risk with glucocorticoids. Effects of glucocorticoid dose, duration, disease for which is it used, and disease activity of that disorder are all key factors that must be accounted for when considering glucocorticoid-induced osteoporosis prevention. Many therapies demonstrate proven efficacy and new guidelines, including those from the American College of Physicians support strategies to help manage this serious problem. Does a growing evidence base and new guidelines, the majority of patients taking chronic glucocorticoids do not receive preventive interventions.

## S7-4

**Surgical treatment and management of glucocorticoid-induced osteoporosis**

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Conflict of interest: Yes

According to the 2023 guidelines for the management and treatment of glucocorticoid-induced osteoporosis (GIOP), surgical intervention for fragility fractures associated with GIOP is recommended to follow treatment approaches similar to those for primary osteoporosis. However, in GIOP patients, not only trabecular bone but also cortical bone becomes more fragile, leading to a higher risk of fractures beyond the decrease in bone density. Additionally, even if bone healing is achieved, there is a higher likelihood of sequelae such as malunion. Representative fragility fractures associated with GIOP include vertebral fractures, proximal femoral fractures, distal radius fractures, proximal humeral fractures, pelvic fractures, and rib fractures. While there is no clear evidence regarding the frequency and outcomes of surgical treatment in GIOP patients, the guidelines explicitly state that appropriate surgical intervention, especially for proximal femoral fractures, can improve functionality. Therefore, it is considered crucial to choose treatment strategies in line with these recommendations. However, surgical treatment for fragility fractures associated with GIOP poses challenges due to decreased bone mass and quality, leading to issues such as implant instability, post-fixation dislocation, nonunion at the fracture site, and fractures in adjacent fixed areas. This symposium provides an overview of key points and pitfalls in surgical treatment for fragility fractures associated with GIOP.

## S7-5

**Pharmacological treatment of glucocorticoid-induced osteoporosis**

Kunihiro Yamaoka
Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine

Conflict of interest: Yes

Although treatment with glucocorticoids remains necessary in the realm of autoimmune diseases, there are emerging therapies for these conditions. There have been substantial changes to the concepts of GC dose reduction and initiation. Treatment with GC is recommended with the minimum effective dose, followed by prompt dose reduction and maintenance at the lowest required dose or discontinuation. However, high-dose GC and continuous fixed-dose maintenance therapy are still in use. Additionally, with an aging population in Japan, numerous autoimmune diseases that occur in elderly patients are treated with GC, due to their pathophysiology and age characteristics. Therefore, GC-induced osteoporosis (GIOP) causing socioeconomic burden is an emerging medical issue. Nonetheless, there is insufficient evidence for the management of GIOP, hence conventional treatments for osteoporosis are adopted for the management of GIOP. History of fracture, age, gender, menopause, and glucocorticoid dose and duration are all important factors in determining the appropriate choice of treatment. Bisphosphonates are commonly prescribed due to health economic considerations, but other biologic agents have shown promise in clinical studies. Although therapeutic agents are chosen on a case-by-case basis, discontinuing anti-osteoporotic treatment proves challenging due to the aging of patients with autoimmune diseases and current difficulties in discontinuing GC. Additionally, it's crucial to inform patients about the potential for long-term treatment and the benefits of preventing disabilities related to future fractures when selecting agents. However, there is a shortage of therapeutic evidence for GIOP, and the findings and development of drugs approved for osteoporosis are currently being redirected towards GIOP. This symposium aims to present an overview of osteoporosis treatment for GIOP.

## S8-1

**Characteristics and making process of 2024 Update of the Japan College of Rheumatology clinical practice guidelines for the management of rheumatoid arthritis**

Yutaka Kawahito[1], Yuko Kaneko[2], Eiichi Tanaka[3], Yuzaburo Inoue[4], Kayoko Kaneko[5], Hideto Kameda[6], Mitsumasa Kishimoto[7], Tomohiro Kubota[8], Masataka Kohno[1], Toshihisa Kojima[9], Masayo Kojima[10,11], Takahiko Sugihara[12], Ayako Nakajima[13], Shintaro Hirata[14], Mie Fusama[15], Takako Miyamae[3,16], Akio Morinobu[17], Masayoshi Harigai[3]

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Conflict of interest: Yes

Objective: After the development of the 2020 JCR clinical practice guidelines for the management of RA, novel drug agents have received approval. In addition, the demographics are changing due to the declining birthrate and aging population, necessitating a revision of the guideline. Methods: A research initiative sponsored by the the Ministry of Health, Labour and Welfare conducted a study on the enhancement of medical standards through the revision of RA treatment guidelines (Principal Investigator: Masayoshi Harigai). The GRADE methodology was employed to assess the efficacy of the guidelines. The Systematic Literature Review (SR) group, comprised of 38 medical specialists and 10 SR support committee members, undertook a qualitative evaluation of the evidence for each clinical question. A guideline panel of 20 members, including rheumatologists, nurses, guideline experts, and patient representatives, then determined each recommendation and its strength based on this evidence and reached a consensus using the Delphi method. Results: The 2024 update of RA guidelines include drug treatment of RA, encompassing subcutaneous formulations of MTX, biologic agents including biosimilars and new agents such as JAK inhibitors, and the treatment of RA by life stage, including the elderly, juvenile idiopathic arthritis with oligoarthritis or polyarthritis, pregnancy and lactation. This guideline underwent review by an external evaluation committee members, incorporated public comments, and received approval and publication by the JCR. Conclusion: We have prepared the 2024 Update of the JCR clinical practice guidelines for the management of RA. We hope this guideline will be applied to the daily practice of RA and lead to improvement of prognosis. Acknowledgments: We extend our deepest gratitude to the patient representatives, the SR team, the SR support committee members, and the members of Cochrane Japan for their cooperation in the development of this guideline.

## S8-2

**'JAK inhibitors' in 2024 update of the Japan College of Rheumatology clinical practice guidelines for the management of rheumatoid arthritis**

Akio Morinobu

Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University

Conflict of interest: Yes

In response to the rapid increase in evidence regarding JAK inhibitors in the years since the publication of the Rheumatoid Arthritis Practice Guidelines 2020, it was deemed necessary to revise the recommendations regarding JAK inhibitors in the current 2024 revision. The previous four CQs were updated and two new CQs were added. The content was updated for (1) MTX+JAKi for MTX-IR patients, (2) MTX monotherapy for MTX-IR patients, (3) MTX+JAKi vs. MTX+TNFi for MTX-IR patients (short-term treatment), and (4) MTX+JAKi for bDMARD-IR patients, and (5) MTX+JAKi vs. MTX+TNFi for MTX-IR patients (long-term treatment), and (6) JAKi vs. bDMARD for bDMARD-IR patients. For each CQ, the SR group and supporting committee members systematically reviewed articles on JAK inhibitors in RA patients reported in PubMed, CENTRAL, Embase, and the Central Journal of Medicine. Important outcomes included the percentage of patients achieving ACR50 after 12 weeks of treatment, the percentage achieving DAS28-CRP remission, the amount of change in HAQ, serious adverse events, and serious infections, and both efficacy and safety were evaluated. In addition, patient values and intentions, cost, and panel meeting opinions were synthesized to determine the recommendation, the strength of the recommendation, and a summary and notes were prepared. Finally, panel members voted to determine the level of agreement. Five JAK inhibitors are available in Japan. The results of RCTs of each formulation were presented, and recommendations on efficacy can be made based on the results of many clinical trials. On the other hand, RCTs on the safety of JAK inhibitors were also reported and discussed as a new CQ. In this symposium, each CQ will be briefly introduced. Detailed evidence is provided in the guideline commentary, which we encourage you to read, along with recommendations, strength of recommendations, summaries, and notes.

## S8-3

**Rituximab**

Ayako Nakajima

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Conflict of interest: None

Three years have passed since the 2020 Rheumatoid Arthritis Treatment Guidelines were published. During this time, the treatment of patients with rheumatoid arthritis whose rheumatoid arthritis has become resistant to biologic agents or JAK inhibitors, or who have survived lymphoproliferative disorders, has been recognized as a serious issue. Rituximab, an anti-CD20 monoclonal antibody, is already an option for patients with rheumatoid arthritis who are resistant to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) worldwide, but not in Japan. In particular, rituximab is conditionally recommended for patients with previous lymphoproliferative disorder in the 2021 American College of Rheumatology Guidelines for the treatment of rheumatoid arthritis. In Japan, rituximab is not approved as a treatment for rheumatoid arthritis, but a clinical trial has been implemented currently as of December 2023. As the number of RA patients with lymphoproliferative disorders are increasing, it is mandatory to expand treatment option for rheumatoid arthritis. In the present revision of guidelines, we evaluated treatment with rituximab in terms of efficacy, adverse drug reactions, cost, and patient preference. In this symposium, five recommendations for rituximab in the treatment of patients with RA will be explained.

## S8-4

**2024 Japan College of Rheumatology clinical practice guidelines for the management of Juvenile idiopathic arthritis with oligoarthritis or polyarthritis**

Takako Miyamae

Department of Pediatric Rheumatology, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan

Conflict of interest: Yes

[Objective] Juvenile idiopathic arthritis (JIA) is a diagnosis of exclusion that encompasses all forms of chronic arthritis of unknown origin, starting before 16 years of age. Polyarthritis with Rheumatoid Factor-positive is associated with a higher risk of erosive damage. JIA may last a limited time, such as a few months or years, but in some cases, it is a lifelong disease that requires treatment into adulthood. We have developed

clinical practical guidelines (CPG) for JIA with oligoarthritis or polyarthritis, which are relatively similar to RA in pathophysiology. This is also intended to provide guidelines for transitional medical care to adulthood in JIA. [Methods] As a project of the Ministry of Health, Labor and Welfare's research group (principal investigator, Masayoshi Harigai), using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) method, the CPG including the evidence from Japan was prepared. Clinical questions (CQs) mainly related to the treatment of the disease were drafted for recommendation based on systematic reviews (SRs) and structured abstracts of additional retrieved literature. Recommendations are agreed upon by a panel including patients, pediatric and adult rheumatologists, guideline experts, and health economists using the Delphi method. The guideline is intended for healthcare professionals who are not limited to pediatrics. [Results] For JIA with oligoarthritis or polyarthritis, a CQ on the application of DAS28-ESR was developed in addition to six CQs on medical treatment with MTX, corticosteroids, csDMARDs other than MTX, TNF inhibitors, IL-6 inhibitors, and JAK inhibitors. A narrative review of the CQ on DAS28-ESR was conducted because of limited evidence. Seven recommendations were developed at the panel meeting. [Conclusion] Preliminary recommendations regarding JIA with oligoarthritis or polyarthritis for the guidelines were created.

## S8-5

**Management of older patients with RA (The Japan College of Rheumatology clinical practice guideline for rheumatoid arthritis 2024)**

Takahiko Sugihara
Division of Rheumatology, Department of Internal Medicine, School of Medicine, Faculty of Medicine, Toho University

Conflict of interest: Yes

The Japan College of Rheumatology clinical practice guideline (CPG) for rheumatoid arthritis (RA) 2020 (reference 1) recommended the use of MTX for older patients aged 65 years or older diagnosed with RA and having poor prognostic factors, with careful consideration of safety (strength of recommendation: weak). It was also recommended that bDMARDs and JAK inhibitors can be used in older patients in Phase 2 giving sufficient consideration to safety (strength of recommendation: weak). However, since there were no randomized controlled trials in older patients and the certainty of evidence was very low (reference 2), it is important to continue to examine whether MTX, bDMARDs, and JAK inhibitors are useful in older patients. In addition, the current recommendation for RA in non-elderly patients is to start treatment with MTX and consider short-term concomitant low-dose GC, but no evidence existed for concomitant use of GC in the older population. Therefore, it was considered important to examine whether concomitant use of GC is beneficial when DMARDs, mainly MTX are initiated in older RA patients in order to determine the treatment strategy. Therefore, we conducted a systematic review (SR) of the same clinical questions (CQs) in CPG 2024 as in CPG 2020, which was limited to the period from July 2019 to December 2022. CQ1: Is MTX useful for older patients with RA? CQ2 Are bDMARDs useful for older patients with RA? CQ3: Are JAK inhibitors useful for older RA patients? CQ4: Are corticosteroids useful for older RA patients? In this symposium, we will discuss the SR results, our assessment of the certainty of the evidence, and the reasons for our decision to strengthen our recommendations for older patients in the RA CPG 2024. 1. Kawahito Y, et al. Mod Rheumatol. 2023;33 (1):21-35. 2. Sugihara T, et al. Mod Rheumatol. 2022;32 (2):313-22.

## S8-6

**The 2024 update of the Japan College of Rheumatology clinical practice guidelines for the management of rheumatoid arthritis: treatment during pregnancy and for male patients who had a female partner who attempts to conceive**

Kayoko Kaneko
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Conflict of interest: Yes

Objective: To determine Clinical Questions (CQs), conduct a systematic review (SR), and make recommendations for the treatment of pregnant women and men who have a partner who is a nursing mother or a woman who wishes to have a baby to revise rheumatoid arthritis (RA) guidelines. Methods: CQs were developed for the pharmacological treatment of male patients with partners who are pregnant or lactating women or women who wish to have a baby. The literature search included articles reported in PubMed, Cochrane reviews, and medical journals from January 2019 to December 2022. It included articles on the use of conventional synthetic disease-modifying anti-rheumatic drugs and biological agents in pregnant and lactating RA patients and male RA patients with a female partner who wishes to have a baby. For studies published before 2019, we included the literature evaluated in the "Rheumatoid Arthritis Practice Guidelines 2020" and added them by hand. The following five CQs were developed: 1. Is the administration of TNF inhibitors to pregnant patients with RA acceptable in terms of safety for the child? 2. 2. Are csDMARDs, bDMARDs, and JAK inhibitors acceptable in terms of safety for the child if the partner of a male patient with RA wishes to become pregnant? 3. Are bDMARDs, csDMARDs, and JAK inhibitors other than TNFi safe for pregnant RA patients? 4. Is administering csDMARDs, bDMARDs, and JAK inhibitors to breastfeeding RA patients safe? 5. How should live vaccines (rotavirus vaccine and BCG vaccine) be administered to infants born to mothers who used bDMARDs during pregnancy? Since there were relatively large cohort studies for CQs 1 and 2, quantitative SR, article-by-article certainty assessment, and summary of results were performed to develop a draft recommendation according to the GRADE method. For the remaining CQs, there were not enough studies to conduct SR, so we conducted a narrative review as a Future Question. Conclusion: There is insufficient evidence for the treatment of male RA patients with partners who are pregnant or lactating women or women who wish to have a baby, and further accumulation of evidence is needed. The symposium will present the recommendations the RA Clinical Practice Guideline Subcommittee agreed upon.

## S9-1

**Timing of orthopedic referral: questions from a physician**

Masaru Kato
Hokkaido University Hospital

Conflict of interest: Yes

In recent years, although medications have become dominant in the treatment of rheumatoid arthritis, surgery, rehabilitation, and care still play a role. This symposium will focus on surgery, including synovectomy, joint replacement, arthrodesis (including the atlantoaxial joint), and arthroplasty (particularly the digits), and discuss, through case presentations, when physicians should refer to an orthopedic surgeon. We would also like to discuss the differentiation from osteoarthritis, particularly in the knees, the discrepancy between disease activity and progression of joint destruction, particularly in the large joints, and recent progress in surgical techniques.

## S9-2

**Indications for Hand Surgery in Elderly Rheumatoid Arthritis Patients**

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Department of Orthopaedic Surgery, Keio University School of Medicine, Tokyo, Japan

Conflict of interest: None

Advancements in pharmacotherapy have made it possible to control synovitis in rheumatoid arthritis (RA), leading to a shift in the indications for orthopedic surgery. Surgeries on large joints have decreased, while operations on smaller joints in fingers and toes are rising. Many patients, including the elderly, want to improve the appearance of their hands because they are the part of the body that is constantly exposed to the public. To achieve true remission, treating hand deformities that are not necessarily reflected in the disease activity scores is also important. In terms of treatment for joint deformities, total joint arthroplasty has been established as the standard treatment for major joints such as knee and hip. However, for smaller joints in the fingers, various surgical methods exist depending on the type of deformity and the extent of joint destruction. In cases where

drug therapy adequately controls the disease and joint destruction is minimal, preserving the joint while reconstructing only the soft tissues is ideal. Nonetheless, preventing recurrence while achieving good function requires careful rehabilitation and can be challenging. In treating elderly RA patients, the benefits of joint preservation and the difficulty of treatment must be weighed to determine the best approach. In cases with severe contracture or advanced joint destruction, joint reconstruction using prostheses may be considered, but in some instances, arthrodesis might be a more reliable option. Particularly when multiple adjacent joints are affected, it is challenging to reconstruct all joint functions, and it may be preferable to preserve the function of the MP joints while stabilizing the DIP and PIP joints through arthrodesis. A treatment plan should be formulated based on a thorough understanding of the patient's desired improvements in both cosmetic and functional aspects, considering the realistic outcomes achievable through surgery.

## S9-3

**Foot surgery for elderly RA patients**

Koichiro Yano
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Conflict of interest: None

Currently, there is a trend towards the aging in patients with rheumatoid arthritis (RA). The joints of the foot and ankle are particularly susceptible to RA pathology, with the degeneration of these joints in the elderly being intricately linked to a decline in activities of daily living. Even among the elderly, if a patient expresses a strong desire for autonomous living in their remaining years, surgical intervention for reconstruction is deemed necessary. However, as individuals age, the likelihood of coexisting comorbidities increases, and reserve capacity diminishes, necessitating careful attention to the potential postoperative exacerbation of underlying conditions or the emergence of new systemic complications. Examining the chronological progression of the ages at the time of surgery for the 1,795 cases of RA foot and ankle surgeries performed at our institution since 1993, surgeries in their sixties or older constituted approximately 35% in the 1990s. This percentage experienced a gradual increase, doubling to around 70% in the 2020s. The average age at the time of surgery has also aged about 10 years, from 54.2 years in the 1990s to 64.6 years in the 2020s. It is likely that the number of foot ankle surgeries in elderly RA patients will increasingly increase in the future. The most common chief complaint of foot ankle disorders in elderly RA patients is pain in the plantar callosities. Many elderly RA patients complain that they cannot walk because of the pain of the callosities. Patients who can be treated conservatively are first treated conservatively, but many calluses are caused by severe deformity and require corrective surgery. Bone quality and skin fragility are of particular concern in foot and ankle surgery in elderly RA patients. Bone quality is very important in foot and ankle surgery, as osteotomy, arthrodesis, and arthroplasty are the most common types of foot and ankle surgery. In addition, the foot is a site that is prone to delayed wound healing, so even more attention should be paid to elderly patients.

## S9-4

**Knee surgery for elderly RA patients: Knack and pitfall**

Ken Okazaki
Department of Orthopaedic Surgery, Tokyo Women's Medical University

Conflict of interest: None

Complex rheumatoid knees includes stiff knees, significant valgus knees, bone defects, and significant ligament laxity. Stiff knees without osteophyte formation are sometimes difficult to obtain enough range of motion intraoperatively. Excessive ligament releases or large amount of bone resection might be needed to obtain sufficient gaps to introduce the implant. Significant ligament imbalance could occur. Therefore, a constrained system should be prepared for back-up. Significant valgus deformity is also difficult cases for arthroplasty. Preoperative assessment by stress radiographs are useful to know if the valgus deformity is correctable or not, and MCL insufficiency. If fixed valgus, or MCL deficiency, a constrained system should be prepared as well.

## S9-5

**Total hip arthroplasty in rheumatoid arhtritis**

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Conflict of interest: Yes

Rheumatoid arthritis (RA) can cause systemic joint damage. Although the number of surgeries is decreasing as disease activity becomes well-controlled, but cases that require surgeries remain. Total hip arthroplasty is a common and effective procedure for RA hip disorders, with improved outcomes and a relatively high patient satisfaction rate. Dislocated hips were prevalent previously, but now, osteoarthritis (OA) changes are common as well as knee OA. Our experience has demonstrated postoperative course is faster and better than knee or ankle arthroplasty. The author has experienced planning errors in cup placement, excessive cup medialization due to excessive reaming, and peri-implant fractures due to the presence of RA-specific bone fragility. Preoperative plans included examination of a posterior pelvic tilt due to vertebral fracture, checking of the condition of the reamer during reaming, and measuring the distance to the acetabular floor intraoperatively if bone fragility occurs, Additionally, careful intraoperative checks and soft tissue repair are necessary, because RA is more easily dislocated than OA. Long-term survival rates can be expected for RA and OA. Based on the intraoperative and postoperative perspectives, disease activity control and osteoporosis treatment are important from preoperative to postoperative periods. Postoperative rehabilitation is planned by assessing the status of other joints from the preoperative period and sharing it with the physical therapist. Herein, I would like to introduce some of the points that I pay attention to and my experience with this case, and hope that they will contribute to clinical practice.

## S9-6

**Application of the rehabilitation therapy and care for the elderly patients with rheumatoid arthritis**

Yuya Takakubo[1], Hiromori Sagae[1], Masashi Aso[2], Yoshihiro Wanezaki[2], Suran Yang[2], Hiroshi Orui[2], Aya Narita[1], Akiko Sasaki[3], Michiaki Takagi[2]
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Conflict of interest: None

While advances in drug therapy for rheumatoid arthritis (RA) have led to a worldwide decline in joint fusion and total joint replacement surgeries, there is also a demand for greater functional and cosmetic improvement in surgical treatment. Therefore, rehabilitation treatment for RA surgery has also changed dramatically. It is necessary to be familiar with surgical techniques, characteristics of equipment used, joint reconstruction methods, and soft tissue repair, to share information closely with the surgeon, and to perform rehabilitation as a member of the team supporting the patient with surgeries. Since RA affects multiple joints, it is necessary to plan postoperative rehabilitation while assessing the condition of joints other than the surgical site and the disease activity. In particular, elderly patients are likely to have sarcopenia, frailty, and locomotive syndrome before the surgery, which may be further exacerbated by hospitalization for surgery and bed rest. A comprehensive rehabilitation treatment program is desirable, taking into consideration each patient's pathophysiology, inflammatory status, living environment, family background, and complications, with attention to systemic complications as well as falls, joint contractures, and disuse-related muscle weakness. In this symposium, we would like to deepen the discussion with participants focusing on perioperative rehabilitation therapy for elderly patients with RA.

## S10-1

**Challenges for LORA from the LORIS Study**

Masayo Kojima[1,20], Takahiko Sugihara[2], Toshihisa Kojima[3], Yutaka Kawahito[4], Masayoshi Harigai[5], Hajime Ishikawa[6], Asami Abe[6], Kazuo Matsui[7], Shintaro Hirata[8], Eiichi Tanaka[5], Mitsumasa Kishimoto[9], Akio Morinobu[10], Isao Matsushita[11], Toshihiko Hidaka[12], Toshihiro Matsui[13], Shuji Asai[14], Keiichiro Nishida[15], Ryozo Harada[16], Motomu Hashimoto[17],

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Conflict of interest: None

Pharmacologic treatment of rheumatoid arthritis (RA) has improved dramatically, and early and aggressive treatment with disease-modifying anti-rheumatic drugs (DMARDs) has made a significant number of patients to achieve treatment goals. However, the evidence on the efficacy and safety of DMARDs is mainly based on RCTs in patients under 65 years of age. We established the Late-onset Rheumatoid Arthritis Registry (LORIS) study group to initiate a registry study of late-onset RA (LORA) patients and to develop a consensus statement on the management by DMARDs. The statement consists of three parts: (1) basic concepts that need to be shared between patients, their families, and medical professionals, (2) the current treatment situation in Japan, which is the premise for treatment, and (3) pharmacologic treatment that experts consider desirable, although verification is needed in the future. In preparing the consensus statement, advice was provided by experts in geriatrics, clinical epidemiology, patient groups, and the JCR LORA Research Sub-Committee. During the process of developing the consensus statement, the following issues were raised. First, methotrexate (MTX) is the basic initial treatment even for patients with LORA, but difficulties in risk management due to comorbidities and cognitive decline may preclude the use of MTX. If treatment goals are not met, the addition of molecularly targeted agents to MTX should be considered. The environment surrounding the patient must also be considered in the choice of treatment. Opinions on the use of glucocorticoids (GC) have not reached an international consensus and there is insufficient evidence on the duration of GC use. RA patients are a high-risk group for frailty, but methods of assessment and therapeutic intervention in routine care have not been established. Our ongoing study will examine these issues through the current registry initiated in January 2022.

## S10-2

**Clinical features of late-onset RA**

Takahiko Sugihara[1], Toshihiro Matsui[2], Eiichi Tanaka[3], Toshihisa Kojima[5], Hiromu Ito[4], Masayoshi Harigai[3], Masayo Kojima[6]
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Conflict of interest: Yes

Older rheumatoid arthritis (RA) can be divided into younger-onset older RA with longer disease duration and late-onset RA (late-onset RA). In recent years, the term elderly-onset has tended not to be used, and late-onset RA is increasingly used. Therefore, abbreviation was revised from EORA to LORA in the present symposium. The characteristics of LORA have been reported in cohort studies since the 1980s and in prospective cohorts in the 1990s. The characteristics of LORA include the presence of arthritis in both small and large joints from the onset, and the progression of joint destruction is similar to that of younger-onset RA. Recently, it has been reported that LORA has higher baseline CRP and synovitis activity on echocardiography than young-onset RA. Disease activity improved similarly to that of young-onset RA, but LORA had more progressive joint destruction. On the other hand, compared to younger-onset RA, LORA has been reported to have more rheumatoid factor-negative cases, anti-CCP antibody-negative cases, cases with onset from both shoulder joints that resemble polymyalgia rheumatica, and cases with edema of the dorsal surfaces of the hands and feet that resemble RS3PE syndrome. In the AMED Research Project for late-onset Rheumatoid Arthritis, NinJa (The National Database of Rheumatic Diseases in Japan), IORRA (Institute of Rheumatology, Rheumatoid Arthritis), KURAMA, NICER-J (Nationwide Inception Cohort of Early Rheumatoid arthritis patients in Japan), TBC (Tsurumai Biologics Communication), and CRANE data were used to examine the characteristics of LORA, which will be presented at this symposium.

## S10-3

**The actual situation of LORA treatment in NinJa**

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Conflict of interest: Yes

Approximately 50 facilities nationwide participate in "NinJa" (National Database of Rheumatic Diseases in Japan), which collects data on more than 15,000 rheumatoid arthritis (RA) patients every year. According to NinJa data, the average age, and the average age at onset of RA patients have increased over the past 20 years. When analyzing only patients who recently developed the disease, more than half were 65 years or older, and about a quarter were 75 years or older at onset. LORA has different characteristics from young-onset RA (YORA) and often has various comorbidities from the time of onset, so it is hoped that treatment strategies and treatment goals specific to LORA will be developed. To that end, it is important to first understand the actual situation of LORA treatment. Therefore, using data from NinJa 2010-2019, we compared the actual medical treatment of YORA (onset before the age of 65) and LORA (onset over the age of 65) over time. We also examined the differences between early (onset between 65 and 74 years of age) LORA and late (over 75 years of age) LORA. As a result, disease activity improved over time in all groups, and the remission rate also increased, but although LORA was slightly inferior, there was no significant difference from YORA. Comparing the treatments, the usage rate of MTX and b/tsDMARDs in LORA was lower than in YORA, and lower in late LORA than in early LORA, but over time, the usage rate of both increased year by year, even in LORA. Regarding the selection of bDMARDs, the older the age at onset, the more non-TNF inhibitors were used than TNF inhibitors, and in late LORA, CTLA-4 Ig was particularly prevalent. The rate of glucocorticoid (GCs) use tended to decrease over time in all groups, but the rate was highest in the late LORA group. Furthermore, when considering only those who achieved SDAI remission, the rates of MTX use (61.7% vs 40.9%), b/tsDMARDs use (23.6% vs 12.6%), and GCs use (20.6% vs 30.2%) were lower in early LORA and late LORA. From the above, there was a difference in the treatment content between LORA and YORA, with LORA having a low MTX usage rate and a high GCs usage rate, but this trend was more pronounced in late LORA. Furthermore, since the medical treatment was different between early LORA and late LORA, and there was also diversity in LORA, there is room for reconsideration of the age at onset that defines LORA. In any case, the usage rate of GCs is high in LORA, and we believe this is an issue that needs to be resolved when considering future LORA treatment strategies.

## S10-4

**Pharmacological treatment of LORA - focusing on the results of the JCR survey**

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Conflict of interest: Yes

Rheumatoid arthritis is an autoimmune disease, mainly chronic destructive synovitis, which, if not treated appropriately at an early stage, leads to irreversible deformity and functional decline associated with joint destruction. The advent of methotrexate and molecular-targeted drugs that directly inhibit disease-related molecules has led to marked improvements in the treatment of rheumatoid arthritis, with the aim of achieving remission. The age of onset of rheumatoid arthritis has long been considered to be young to middle-aged, but in recent years the peak incidence has shifted to people in their 60s and 70s, and an increase in the number of elderly-onset rheumatoid arthritis (LORA) has been reported in Japan. The elderly have reduced physiological function, cognitive function and motivation for treatment, which increases the risks of drug treatment, such as drug adherence, changes in blood levels due to reduced renal function and infections due to excessive immunosuppression. However, inadequate arthritis control can lead to rapid ADL decline, particularly in the elderly, and exacerbate the risk of infection and cognitive decline. The treatment of LORA patients with these two conflicting risks is one of the most important challenges in the current management of rheumatoid arthritis. In 2023, we conducted a survey of JCR members and collected the opinions of more than 1000 rheumatologists on their current views on the treatment of older-onset RA, problematic comorbidities and how to deal with specific cases. In this presentation, we will consider the challenges of LORA treatment, focusing on the pharmacological treatment of LORA and the results of the questionnaire survey.

## S10-5

**How to proceed with joint surgery and rehabilitation of LORA**

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Conflict of interest: None

Drug therapy for rheumatoid arthritis (RA) has made great strides. The age structure of RA patients is also aging, with two-thirds of patients aged 65 or older. In addition, the number of patients with late-onset rheumatoid arthritis (LORA) is increasing, and the Guidelines for the Management of RA 2020 proposed the world's first non-pharmacologic treatment algorithm for RA. The fundamentals of this non-pharmacologic treatment strategy remain the same. The basic principles of this non-pharmacologic strategy remain the same: careful functional assessment and intervention with surgery and rehabilitation therapy to complement pharmacotherapy. An important aspect of a careful functional assessment is to recognize that LORA patients have a low base of physical function due to aging and have limited capacity. Frailty and sarcopenia, an assessment of physical and mental frailty due to aging, should be incorporated. Preexisting joint disorders such as osteoarthritis, spondylolisthesis, and compression fractures are also frequent. Early, rehabilitative, and surgical treatment may be used while disuse atrophy due to functional impairment is reversible. In the assessment of frailty and sarcopenia, gait speed and grip strength are representative indicators. We have examined the relationship between HAQ-DI and frailty and sarcopenia using physical function measurements as well as subjective patient assessment. Grip strength is a good indicator to use as a guide, although it may overestimate frailty and sarcopenia in RA patients, as it may deviate from lower limb function in some cases. However, it is a good indicator to use as a rough guide. This presentation will focus on the HAQ-DI as an indicator of frailty and sarcopenia, and will consider how to assess physical function and how to proceed with treatment of LORA.

## S10-6

**Late-onset rheumatoid arthritis treatment from a medical-economic perspective**

Eiichi Tanaka
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Conflict of interest: Yes

In Japan, where the population is aging, not only the number of patients with rheumatoid arthritis (RA) is getting older, but the number of patients with late-onset RA (LORA) is also increasing. In the IORRA (Institute of Rheumatology, Rheumatoid Arthritis), which is a prospective cohort of patients with RA being conducted at Tokyo Women's Medical University, more than half of patients with RA are aged 65 or older. Rising RA care costs have caused concern, placing a heavy burden on society as well as patients with RA. The IORRA study has revealed that annual out-of-pocket costs for patients with RA increase with worsening of disease activity, progression of functional disability, and decline in quality of life (QOL). Although patients with LORA had lower overall average out-of-pocket costs than those with younger RA due to lower out-of-pocket rates, a similar trend of increasing costs with disease activity, functional impairment, and worsening QOL was observed in patients with LORA. The trend of increasing annual RA medical costs with disease activity, functional disability, and worsening QOL was also observed more strongly in patients with LORA when the co-payment was set at 100% of the total medical costs. Although the out-of-pocket costs for patients with LORA were low, the rest was paid by society. Therefore, RA medical costs for patients with LORA are an important issue from a societal perspective. In addition, the number of elderly people working has increased in recent years in Japan, but the impact of RA on employment in patients with LORA has rarely been analyzed. The status of employment among patients with LORA and the impact of RA on the employment of patients with LORA from the results of the IORRA cohort will also be discussed. In this session, I would like to share information on medical-economic issues in patients with LORA.

## S11-1

**Review and update of axial spondyloarthritis imaging**

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Conflict of interest: None

In the imaging of axial spondyloarthritis, MRI is currently the most useful modality for detecting early lesions and monitoring disease activity. A recent meta-analysis reported that ultrasonography also shows good performance in the diagnosis of axial spondyloarthritis, but unlike peripheral joint lesions, monitoring disease activity is more difficult. Although the main principle is that the ASAS classification criteria should not be used for individual diagnosis of spondyloarthritis, the evaluation items "imaging findings of sacroiliitis," "HLA-B27," and "SpA features" are important. In Japan HLA-B27 is not covered by insurance, therefore "imaging findings of sacroiliitis" is vital. When the first definition of MRI findings in sacroiliitis was published in Ann Rheum Dis. in 2009, "bone marrow edema" was thought to be the only lesion associated with active sacroiliitis, but many findings have been accumulated over the years since then. Then in an update 2016, it was stated that structural changes are also important and both active lesions and structural changes should be evaluated. In recent years, there have been scattered reports of imaging findings in other conditions that present with bone marrow edema signal at the sacroiliac joint (e.g., mechanical stress including athletes, osteitis condensans ilii, post-partum). There have also been reports of MRI hardware and software development using artificial intelligence technology and attempts to detect sacroiliitis by MRI using deep learning method. I would like to review the recent knowledge of axial spondyloarthritis imaging with some mention of clinical applications of new sequences such as bone cortical imaging.

## S11-2

**Axial spondyloarthritis**

Toshihide Shuto
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Conflict of interest: None

Axial spondyloarthritis (axSpA) typically manifests in young individ-

uals, with an onset ranging from the teenage years to the 30s. Globally, including reports from Japan, the prevalence of HLA-B27 in ankylosing spondylitis (AS), a global standard, is approximately 75-80% and above. However, recent nationwide epidemiological surveys have shown a lower HLA-B27 positivity rate in cases registered as AS with late-onset after the age of 50, raising concerns about potential misdiagnoses. Ankylosis of SIJ, a characteristic feature of advanced AS, is frequently observed in DISH. DISH typically presents with flowing ossification anterior to the spine, but AS-like thin and flat ossifications are also encountered. A whole spine CT scans revealed DISH in one out of three males and one out of five females aged 40 and above, with an increasing prevalence in the elderly. Recognizing DISH as a common condition in the middle to older age groups is essential. For nr-axSpA, diagnostic guidance has been provided by the Ministry of Health research team, Highly specific MRI findings for axSpA, with high positive predictive value have been reported by the ASAS. In the 2022 update ASAS-EULAR recommendation, NSAIDs are listed as Phase 1 treatment, with b/tsDMARDs as a potential Phase 2 option. Before progressing to Phase 3, they emphasizes the need to reevaluate the accuracy of axSpA diagnosis and consider the presence of comorbidities. As of November 2023, in Japan, two TNF inhibitors, three IL-17 inhibitors, and one JAK inhibitor are covered by insurance for AS treatment, while three IL-17 inhibitors and one JAK inhibitor are covered for nr-axSpA. A case report highlighted the successful remission maintenance of refractory AS using a monoclonal antibody against TCRVβ9, presenting a potential avenue for future treatment (Nat Med 2023). ASAS has also introduced Quality Standards to enhance the quality of care in axSpA management.

## S11-3

**Axial joint lesions in psoriatic arthritis**

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Conflict of interest: None

PsA is characterized by skin symptoms accompanied by peripheral arthritis. Symptoms vary widely, and approximately half of the cases involve some type of axial joint lesion. Spinal lesions in PsA cause relatively mild back pain and limited range of motion compared to AS, a typical disease of axial spondyloarthritis. It has been reported that some patients have asymptomatic axial arthritis who do not complain of inflammatory low back pain, so caution is required. It is sometimes difficult to differentiate between AS and PsA axial joint lesion, and the two may coexist. AS and PsA each have their own characteristics regarding imaging findings. Sacroiliitis is symmetrical in AS, whereas in PsA it is often unilateral or asymmetric and relatively mild. AS is characterized by symmetrical marginal syndesmophytes between spinal vertebral bodies, whereas asymmetrical non-marginal syndesmophytes are common in PsA. Furthermore, in AS, syndesmophytes are characterized by ascending progression from the lumbar vertebrae to the cervical vertebrae, whereas in PsA, syndesmophytes can also develop from the cervical or thoracic vertebrae. It is known that the shape of bone spurs tends to exhibit a change in the horizontal direction called a chunky shape. However, axial joint lesions cannot be diagnosed as PsA based on imaging findings alone, and it is necessary to keep in mind the differentiation not only from AS but also from diffuse idiopathic bone hyperplasia and spondylosis osteoarthritis. Although axial joint lesions in PsA were thought to be less severe than in AS, some studies showed that AS and PsA had similar disease activity, functional impairment, and QOL. The basic treatment for axial joint lesions in PsA is NSAIDs, physical therapy, and steroid injections, and if the effects are insufficient, TNF inhibitors, IL-17 inhibitors, and JAK inhibitors are indicated. Unlike peripheral lesions, IL-12/23 inhibitors were no longer recommended. In addition, patients with highly active PsA sometimes exhibit severe axial joint lesions, which can lead to stiffness of the spine and vertebral fractures due to falls. Internal fixation must be considered because stress is concentrated at the fracture site and instability increases, but the risk of infection due to skin lesions must also be considered. If the fracture can be stabilized by external fixation, conservative treatment is also an option.

## S11-4

**Pustulotic Arthro-Osteitis (PAO)**

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Conflict of interest: None

Palmoplantar pustulosis (PPP) is an intractable disease consisting of aseptic blisters and pustules that occur mainly on the palms and soles of the feet, palmoplantar pustulosis (PAO) is reported to occur in 10-40%. In September 2022, the Japanese Dermatological Association and the Ministry of Health, Labour and Welfare's Large-Scale Multicenter Study Group for the Improvement of Medical Standard and Patient QOL in Spondyloarthritis and Related Diseases published a guide for the treatment of PPP and PAO, respectively. Notably, the PAO diagnostic criteria were revised for the first time in 42 years to provide earlier diagnosis and treatment intervention. In this symposium, we would like to clarify the current evidence on clinical symptoms, examination methods, and treatment of PAO, and to discuss treatment for PAO.

## S11-5

**Differentiation between axial spondyloarthritis and spinal diseases**

Kenji Kishimoto[1,2], Shuji Asai[2], Mochihito Suzuki[2], Ryo Sato[2], Junya Hasegawa[2], Shiro Imagama[2]
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Conflict of interest: None

Axial spondyloarthritis (axSpA) is a group of diseases that cause inflammation of ligamentous attachments on the sacroiliac joints and the spine, including ankylosing spondylitis and non-radiographic axial spondyloarthritis. The main symptom of axSpA is pain and limitation of movement in the low back and buttocks. A characteristic feature of low back pain on axSpA is inflammatory back pain (IBP). The imaging findings of axSpA includes structural changes such as bony erosions and ankylosis on the sacroiliac joint and syndesmophytes on the spine on plain X-ray, and signal changes around the sacroiliac joint and at the vertebral body corners on MRI. HLA-B27 related inflammatory diseases including axSpA have been reported to cause back pain in 0.3% of patients with back pain, and most of the diseases that cause back pain are spinal diseases such as degenerative spondylosis. Differentiating axSpA from spinal disease is important in the diagnosis of axSpA. IBP is also seen in neoplastic lesions such as metastatic bone tumors, and infections such as suppurative discitis and spondylitis on the spine. Degenerative spondylosis and trauma can also present with imaging findings similar to those seen in axSpA. SAPHO syndrome, including palmoplantar osteoarthritis, can present with IBP and imaging findings similar to those seen in axSpA on the sacroiliac joints and the spine. Diagnosis of axSpA based on imaging findings alone may lead to overdiagnosis or misdiagnosis. The rheumatologist should make the diagnosis of axSpA based not only on imaging findings but also on age, history of illness, physical examination, and blood test findings.

## S11-6

**Spondyloarthritis in children**

Nami Okamoto
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Conflict of interest: None

Although the prevalence of spondyloarthritis (SpA) in Japan is approximately 1 in 10,000, 6.7% of SpA occurs before the age of 20. Because time to diagnose is often long, it is not uncommon that child-onset patients were diagnosed in adulthood. It is important to do the appropriate diagnosis and management as early as possible, because if the disease progresses, the impact on life itself is not small due to ankylosis of the axial joint. Reasons for the time required for diagnosis are "Initially, peripheral arthritis predominates and typical axial joint lesions occur lately" "Possession of HLA-B 27 in Japanese population is 0.3%, lower than in other countries, and recognition of disease is low." and "difficulty in evaluating

radiographs and MRI images of the sacroiliac joint necessary for diagnosis," which are equally problematic in pediatric patients or even more than adults. Because the assessment of spondyloarthritis international society (ASAS) classification criteria for axial and peripheral SpA have not been validated in children, the use of the Juvenile Idiopathic Arthritis (JIA) International Rheumatology Association (ILAR) classification criteria (currently updated in Edmonton 2001) further complicates understanding of SpA in children. There are seven forms of JIA, of which "enthesitis-related arthritis" and "psoriatic arthritis" correspond to SpA. However, some are not completely equal and some are included in other forms. Also, the JIA definition of "psoriatic arthritis" is not the same as the classification Criteria for Psoriatic Arthritis (CASPAR). These days, it is often referred to as juvenile SpA (JSpA) in order to seamlessly understand the disease state and manage it smoothly into adulthood. The proposed new PRINTO (The Paediatric Rheumatology INternational Trials Organisation) classification, which is currently under consideration, has a definition that more closely resembles the adult classification. Features of JSpA include more peripheral, unclassifiable forms, a longer time between onset and development of sacroiliitis, a higher incidence in boys, and two subtypes of psoriatic arthritis. However, there are still many issues to be addressed due to the discrepancy between the treatment and medical system in clinical practice and the research field, such as being equivalent to JIA.

## S12-1

**Perspective on glucocorticoid-induced osteoporosis**

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Conflict of interest: Yes

Abnormal bone metabolism induced by glucocorticoids (GCs) is called GC-induced osteoporosis (GIOP). Synthetic GCs are widely used to treat various diseases, including autoimmune rheumatic diseases and not only exert pharmacological actions by regulating the transcription of proinflammatory mediators through GC receptor, but also cause abnormal metabolism of glucose, lipid, bone, and blood vessels, by the receptors. GIOP accounts for 25% of the adverse drug reaction to prescribed drugs and causes fractures in 30-50% of patients and markedly decreases their quality of life. Therefore, multiple societies in various countries developed the guidelines for the management and treatment of GIOP. The Japanese Society for Bone and Mineral Research (JSBMR) developed the guidelines for the management in 2004 and intensively revised it in 2014, providing the treatment criteria based on scores of risk factors, including previous fractures, age, GC doses, and bone mineral density, for patients aged older than 18 years who are receiving GC therapy or scheduled to receive GC therapy for longer than 3 months. Because evidence of anti-osteoporotic drugs has been accumulated, the JSBMR further revised the guideline in 2023, preparing 17 clinical questions using the GRADE system and conducted systematic reviews to develop the best management and treatment recommendations based on scientific evidence. As the results, bisphosphonates (oral and injectable formulations), anti-RANKL antibody teriparatide, eldecalcitol, or selective estrogen receptor modulators are recommended for patients who has received or scheduled for GC therapy with risk factor scores of greater than or equal to 3. It is recommended that osteoporosis medication is started concomitantly with the GCs therapy for the prevention of fragility fractures in elderly patients.

## S12-2

**What are the criteria for initiating drug therapy for GIOP?**

Satoshi Soen
Soen Orthopaedics, Osteoporosis and Rheumatology Clinic

Conflict of interest: Yes

In Japan, the Japanese Society for Bone and Mineral Research (JSBMR) released guidelines on the management and treatment of glucocorticoid-induced osteoporosis (GIOP) in 2004. An approach to determining the pharmacological intervention threshold based on assessment of the absolute risk of fractures was initiated in the mid-2000s and FRAX®, a fracture risk assessment tool supported by WHO, was published in 2007. FRAX® can be used to calculate the 10-year probability of a major osteoporotic fracture and the 10-year probability of hip fracture, and it includes glucocorticoid (GC) therapy as an independent risk factor for fracture. Since then, many guidelines about GIOP have introduced FRAX® as a criterion for initiation of drug treatment. Because of the several limitations as indicated below of FRAX®, a Committee for the 2014 Revision of Guidelines on the Management and Treatment of GIOP of the JSBMR decided not to incorporate FRAX®. FRAX® cannot be used in premenopausal women of men under 40 years old. The dose and duration of GC therapy are not incorporated into the algorithm, so fracture risk is likely to be underestimated in patients on high-dose GC therapy and current GC therapy. FRAX® is mainly useful for predicting for non-vertebral fractures and clinical vertebral fractures, whereas morphometric vertebral fractures are a major problem in patients taking GCs. When the 2014 revised guidelines were prepared, risk factors for fractures were extracted by analyzing three cohort studies on Japanese patients and weighted based on parameter estimated to develop a scoring system and to determine cut-off values for initiating drug therapy. To date, no clear intervention threshold based on FRAX® for initiating drug therapy has been determined in Japan. Thus, using the cut-off scores described in the 2014 revised guidelines as the criteria for initiating drug therapy for GIOP is strongly recommended by 2023 revised guidelines.

## S12-3

**Glucocorticoid-induced osteoporosis: prevention and treatment for children**

Takuo Kubota[1], Keiichi Ozono[2]
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Conflict of interest: None

Children with growth are at the anabolic stage, where bone formation is more than bone resorption. Thus, children recover from osteoporosis/osteopenia due to transient causes after the causes resolve. In fact, many papers that report the spontaneous recovery from multiple vertebral fractures after the treatment with glucocorticoid stops. However, there are a few reports describing the treatment for glucocorticoid-induced osteoporosis (GIOP) in children, resulting in no recommendation in the previous clinical guidelines for GIOP. Recently, a randomized, double-blind, phase 3 trial of zoledronate for GIOP has been reported in children. Together with other reports, weak recommendations for the treatment of GIOP in children have been included in the recent clinical guidelines for GIOP. It is a big step in the treatment of GIOP in children. GIOP may occur in children with chronic inflammatory disease including rheumatoid arthritis, malignant diseases including leukemia, nephrotic disease, bronchial asthma, and inflammatory bowel disease. Clinicians must consider using zoledronate to prevent or treat GIOP. In addition to GIOP, growth retardation is the significant side effect of glucocorticoids in children. To avoid growth retardation and GIOP, dose reduction of glucocorticoid and alternative treatment, including the use of biologics should be considered.

## S12-4

**How is GIOP prevented and treated in elderly patients?**

Hisanori Nakayama
Soshigayaokura-Clinic

Conflict of interest: None

Both aging and glucocorticoid (GC) are the dependent risk of fracture, so the elderly who take GC should tend to fracture. Based on Japanese cohort studies, the hazard ratio of fractures in patients aged ≧65 years is approximately twice higher than that in patients <50 years used as a reference. In older patients, osteoporotic changes are promoted by many factors. Thus, intervention with anti-osteoporotic drugs was strongly recommended for older patients who would receive GC therapy for ≧3 months. The revised GIOP guideline recommends that in elderly patients, intervention with anti-osteoporotic drugs in combination with GC therapy is recommended to prevent fractures. In treatment, evidence-based medicines in GIOP should be administered after consideration of the background and characteristics of individual older patients. Furthermore, because of the increased risk of hip fractures in the elderly, when treating the aged GIOP patients, anti-osteoporotic medicines that have evidence of reducing frac-

tures in primary osteoporosis, especially hip fractures should be considered for administration, even if they don't have enough evidence in GIOP.

## S12-5

**Prevention and management of glucocorticoid-induced osteoporosis in women of reproductive age**

Masakazu Terauchi
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Conflict of interest: Yes

Women of reproductive age are generally at low risk of fragile fractures. Premenopausal women administered glucocorticoid (GC) for a long period, being at substantially higher risk of fractures than those of the same age who are not treated, are advised to maintain healthy lifestyle, and should at the same time be given full consideration for pharmaco-therapy. Cautions are required when prescribing drugs generally used for the treatment of glucocorticoid-induced osteoporosis (GIO), such as bisphosphonates, denosumab, and teriparatide, in women of reproductive age, pregnant and lactating women. With regard to this issue, the updated "Guidelines for the management of glucocorticoid-induced osteoporosis 2023" issued the recommendations shown below. Clinical Question #16-1: What can women of reproductive age do to prevent GIO? Recommendation: We recommend healthcare providers to counsel women of reproductive age who are using or going to use GC about their lifestyle and nutrition according to the "Guideline for the Prevention and Treatment of Osteoporosis (2015)". Clinical Question #16-2: Can women of reproductive age use BPs/DMAb/TPTD to prevent or treat GIO? Recommendation: We recommend healthcare providers NOT to use bisphosphonates, denosumab, or teriparatide in pregnant or lactating women for the purpose of treating GIO. The background and the details of these recommendations will be presented in the symposium.

## S12-6

**What is the surgical treatment of fragility fractures associated with glucocorticoid-induced osteoporosis?**

Sakae Tanaka
Department of Orthopaedic Surgery, School of Medicine, The University of Tokyo, Japan

Conflict of interest: None

Glucocorticoid-induced osteoporosis increases fragility in both trabecular and cortical bone, elevating fracture risk. Elderly patients face complications like pressure ulcers, cognitive decline, and worsened sarcopenia, leading to increased fall and fracture risk. Common fragility fractures from osteoporosis include vertebral and hip fractures. For vertebral fractures, conservative treatment is preferred unless there are neurological deficits or severe pain. Teriparatide is increasingly used for severe vertebral fractures. Surgical options exist for delayed healing or pseudoarthrosis, with percutaneous vertebroplasty and balloon kyphoplasty considered. Caution is crucial to prevent tissue damage and nerve injury from cement leakage. Hip fractures, common in the elderly, may also occur in younger glucocorticoid-induced osteoporosis patients. Surgical intervention is typically preferred, with early treatment showing better outcomes. Extra-articular fractures may undergo osteosynthesis, while intra-articular neck fractures often require hemiarthroplasty or total hip arthroplasty.

## S13-1

**Epidemiology of osteonecrosis of the femoral head**

Wakaba Fukushima
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Conflict of interest: None

For osteonecrosis of the femoral head (ONFH), which is one of the designated intractable diseases in Japan, various epidemiological studies have been conducted by the Japanese Investigation Committee for ONFH funded by the Ministry of Health, Labour and Welfare. This presentation will introduce the epidemiological information that is fundamental to understand the pathology and treatment of ONFH, based on the research findings by the Japanese Investigation Committee.

## S13-2

**Pathology and diagnosis for osteonecrosis of the femoral head**

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Conflict of interest: None

Osteonecrosis of the femoral head (ONFH) poses a significant health concern, that predominantly afflicts middle-aged individuals. Progression of the disease precipitates hip joint dysfunction, markedly limiting the affected individual's daily activities. However, the etiology is unknown, and the Ministry of Health, Labor, and Welfare has designated it as an incurable disease. To address this, the Japanese Investigation Committee (JIC) for ONFH was established. ONFH's onset is characterized by ischemia affecting a specific femoral head segment, resulting in osteonecrosis. A history of systemic steroid administration, habitual drinking, and smoking are associated with osteonecrosis, however, the intricate mechanisms leading to ischemia remain unclear. The JIC introduced the criteria for diagnosis, classification, and staging of ONFH in 2001. Diagnosis required to fulfill more than two diagnostic criteria without exclusion criterion. However, Stage 1, lacking X-ray findings, is diagnosed in practice based on a single criterion. To address this inconsistency, the JIC introduced supplementary provisions in 2022. No appreciable modifications were identified in the staging protocol. The Association Research Circulation Osseous (ARCO), the international academic association, revised its staging classification in 2019. The revision aligned with the 2001 JIC staging system. Various international classifications have been employed for ONFH categorization, predominantly focusing on the assessment of necrotic size. In contrast, the JIC classification is more practical than other classifications, relying on the necrosis localization at the joint surface loading area. The ARCO introduced a novel type classification system and the JIC has subsequently adopted an updated classification that integrates this revised ARCO classification. The 2022 revised criteria for the diagnosis, staging, classification, and etiologic classification of ONFH were proposed by the JIC in December 2022.

## S13-3

**Conservative treatment for osteonecrosis of the femoral head**

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Conflict of interest: None

The strategy for nonoperative treatment of idiopathic osteonecrosis of the femoral head (ONFH) includes three possible targets: 1) preventing the occurrence of the disease, 2) preventing the onset of the disease, and 3) improving symptoms after the onset of the disease. Although the pathogenesis of ONFH remains unknown, a variety of drugs have been investigated for the prevention of its development in response to hypothesized pathogenesis. Statins for lipid metabolism, anticoagulants for intravascular coagulation, vitamin E for oxidative stress, various flavonoids, NF-Kb/IRF7 inhibitors for anti-inflammatory action against innate immunity mediated by toll-like receptors, and proton pump inhibitors are some examples. A clinical trial using a three-drug combination of vitamin E, pitavastatin, and an antiplatelet agent is underway at the beginning of treatment of SLE, and the results are promising. It is believed that pain is caused by femoral head collapse, and prevention or cessation of collapse is the key to preventing the onset of osteoporosis. Bisphosphonates and OPGs have been used to inhibit bone resorption, and osteoporosis drugs such as parathyroid hormone preparations have been used to promote bone formation. Although animal studies and initial clinical studies reported good collapse prevention results for bisphosphonates, two RCTs using alendronate and zoledronate, respectively, showed no significant difference from controls, and the ONFH Clinical Practice Guideline (2019) recommends that bisphosphonate administration to reduce long-term collapse of the femoral

head is unknown. There are scattered reports on symptom control after onset of symptoms, including exercise therapy, bracing therapy, physical therapy such as external shock wave and electromagnetic field stimulation, and hyperbaric oxygen therapy, all of which may contribute to improvement of pain, but the long- term preventive effect of femoral head collapse is unknown.

## S13-4

**Surgical treatment for osteonecrosis of the femoral head**

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Conflict of interest: None

[Introduction] Osteonecrosis of the femoral head (ONFH) becomes symptomatic following collapse (subchondral fracture) of the femoral head. Since most patients come to the hospital after the onset, the femoral head is already collapsed at the time of diagnosis, and the target of surgical treatment is the post-collapse ONFH. Since ONFH often occurs in relatively young patients, a joint-preserving procedure, femoral osteotomy, has been developed in Japan, and it has become an established surgical treatment for ONFH together with artificial replacement surgery. This presentation will provide an overview of femoral osteotomy and total hip arthroplasty (THA). [Femoral osteotomy] The concept of femoral osteotomy is to prevent the progression of collapse and promote the repair process by transposing the necrotic lesion to the non-weight-bearing portion. A necessary condition for osteotomy is the presence of a sufficiently intact articular surface on the anterior, posterior, or lateral portion of the femoral head. When the anterior or the posterior articular surface is intact, transtrochanteric rotational osteotomy is indicated. When the lateral articular surface is intact, transtrochanteric curved varus osteotomy is indicated. The 10-year joint preservation rates have been reported to be around 60-80% and 80-90%, respectively. [THA] The improved durability of THA and its stable long-term results have led to a younger age range for THA, and even in ONFH with the relatively young age range, THA has become the standard surgical procedure for ONFH. Even when osteotomy is indicated, some patients choose THA for its superior pain relief and early return to society. On the other hand, the rate of revision and the risk of complications such as infection and dislocation are reported to be higher than those of osteoarthritis, and easy indications for THA should be avoided.

## S13-5

**Outlook for the treatment of idiopathic osteonecrosis of the femoral head withDrug**

Haruhiko Akiyama
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Conflict of interest: None

Idiopathic femoral head necrosis is a designated intractable disease. In Japan, stage classification from stages 1 to 4 and type classification from type A to C2 are used. The problem with this disease is that if the disease stage progresses, it will lead to the collapse of the femoral head, resulting in a significant decrease in quality of life such as pain and difficulty walking, and that there is no established treatment method to regenerate necrotic bone. In other words, in type C cases where the necrotic area is large, the femoral head collapses within a few years and progresses to stage 3 or 4. There is no drug treatment that is reliably effective, and there are only reports that bisphosphonates are effective. Surgical treatments include vascularized bone grafting, femoral varus osteotomy, and femoral head rotational osteotomy, but these are highly invasive and have limited effectiveness. Therefore, in Japan, femoral head replacement and artificial hip replacement are mainly performed. However, revision surgery remains a problem in a relatively young patient population. As a form of regenerative medicine, bone marrow mononuclear cell transplantation is being practiced both domestically and internationally, but its effectiveness is still limited. Necrotic bone regeneration treatment using growth factors has not yet been successful. We are conducting a phase II study using basic fibroblast growth factor (bFGF) in the hope of angiogenesis in necrotic bone and proliferation of bone marrow mesenchymal stem cells and osteoblasts. A "clinical trial on the safety of necrotic bone regeneration and prevention of femoral head collapse by the body" was conducted at four universities, and preparations for a phase III trial are currently underway. In this lecture, we will introduce the actual practice, results, and problems of investigator-initiated clinical trials for necrotic bone regeneration treatment using pharmaceutical preparations.

## S14-1

**Occupational therapy in elderly rheumatoid arthritis patients**

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Conflict of interest: None

The purpose of rehabilitation treatment in rheumatoid arthritis (RA) is to relieve existing pain, prevent secondary disorders such as deformity, maintain and improve function during drug treatment aiming for low disease activity or remission, and support participation in daily life and social activities. Furthermore, in recent years, life stage has become an important word, and life stage support, which is the same as that for healthy people, has been newly added. In addition to the underlying RA symptoms, elderly RA patients have a wide range of comorbidities and complications, such as geriatric syndrome, cardiovascular disorders, and respiratory disease, which are referred to as the accumulation model of disability in elderly RA patients. Therefore, occupational therapy for elderly patients with RA can be divided into two main categories, taking into account the comorbidities and maintaining and improving their lives, which is their desired stage of life, and promoting their continued participation in social activities such as leisure time and employment. In recent years, RA treatment has been concentrated in specialized hospitals and centers, and opportunities for occupational therapy support for RA patients have been declining. However, according to the Occupational Therapy White Paper 2021, 80% of the occupational therapists' target population in the field of physical disability is over 65 years old, and the top diseases include fractures, respiratory diseases, malignant neoplasms, and heart diseases. These diseases are frequently coexisting and existing in elderly RA patients, and opportunities for occupational therapists to support elderly RA patients in medical and long-term care facilities other than RA-specialized hospitals are increasing, and the importance of occupational therapists who "see" and "closely" relate to the patients' lives is increasing. The importance of occupational therapists who "see" and "closely" interact with patients in their daily lives is expected to increase. In this symposium, we would like to discuss the support and issues for elderly RA patients as occupational therapists.

## S14-2

**Practical Life Support to Promote Independence of Patients Living in Old Age: Examples of Effective Tools for Assessment and Cooperation**

Noriko Mawatari
Honomikodomoen

Conflict of interest: None

The purpose of this presentation is to show the examples of effective assessment tools for interprofessional, multiorganizational, and multirole collaboration based on the "life structure theory," with a focus on patients living in the aging process. The following are the main points and examples of assessment tools and action plan sheets. First, the people who use these should kept in mind "place management" throughout the entire support process. The presentation is to show the examples of the use of a structured genogram and ecomap interview. Second is to grasp the entire life structure of patient viewed as "a person living now in the community". The presentation is to show the examples of the use of the personal and environmental factors sheet, the community map, and the house situation. Third is to grasp the patients considered both as "individuals" or as "whole families". The presentation is the points to consider when thinking about financial support together and examples of the use of weekly, monthly, and yearly schedules. Fourth is to grasp the patient considered as "a person who has continued to lead a life of his/her own in the past". The patient's life history is shown as an example of a timeline. Fifth is to visualize the patient's own social resources, share a common understanding of "the patient's own image of his/her future life," and visualize it on the action plan

sheet. The presentation is show the example of the use of the problem organization and action plan sheet. The significance of using this tool is the following three points. First is that "the leader of the team approach is the patient himself/herself". Second is that "both formal and informal supporters must maintain the value and attitude that the patient himself/herself is the subject of problem solving". Third is that "the supporters selected by the patient must work together with respect for each other's expertise and roles". These three points coincide exactly with the philosophy and goals of T2T. There is no COI to disclose for this content.

## S14-3

**Observations from the Patient's Perspective in Elderly Rheumatoid Arthritis Patients**

Kaoru Nagai
Observations from the Patient's Perspective in Elderly Rheumatoid Arthritis Patients, Kobayakawa Orthopedics & Rheumatology Clinic

Conflict of interest: None

The treatment of RA is tailored to the individual's situation and may include methotrexate (MTX) or biologic agents, even in elderly patients. MTX is not taken on a daily basis and requires special attention in the presence of cognitive decline. The "coming to the clinic with a companion" and "signs of looking back" that require the companion to respond to the physician's questions in the clinic setting are known to be highly sensitive and specific assessments for cognitive decline, respectively. The absence of these signs is a perspective that can be easily observed. When elderly patients self-inject as a treatment for rheumatoid arthritis, it is also necessary to take into account cognitive function. Assess for problems with vision, hearing and comprehension, and whether there is someone to support the patient prior to instruction. Although there are individual differences, elderly patients need more careful follow-up because it is said that their ability to write, analyze, and manipulate their hands and fingers declines. Another problem of elderly rheumatoid arthritis patients is the decline in physical function: RA patients are at high risk of falling, which can lead to loss of mobility, fractures, disability, and hospitalization. In daily medical care, it may be helpful to observe whether the patient has a small stride or takes time to get up from a chair, and to intervene to prevent falls. Although the elderly are in a decline in various functions, we need to remember that they are our seniors and respect them as such. This presentation will focus on these topics and discuss elderly RA nursing.

## S14-4

**Nutrition management in older patients with rheumatoid arthritis**

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Conflict of interest: None

The maintenance of well-nourished state is important for improving the prognosis, healthy life expectancy, and QOL of patients with rheumatoid arthritis (RA). The Global Leadership Initiative on Malnutrition (GLIM) criteria has been proposed in 2018 as a method to assess nutritional status, and it is now determined that patients are undernourished if they have either (1) non-volitional weight loss, low BMI, and reduced muscle mass as a phenotypic criteria, and if they have an etiologic criteria. In RA patients, the majority of patients are "chronically ill and undernourished with inflammation" due to the nature of disease, and controlling inflammation with medication is thought to be an important factor in improving nutritional status. In RA patients, about 30% of the patients were classified as GLIM criteria undernourished, and that in addition to age, factors related to ADL such as grip strength were significantly related to GLIM criteria undernutrition. In addition, the proportion of RA patients with frailty, which is strongly related to nutritional status, increases with age, suggesting the importance of early detection and intervention of undernutrition in older RA patients. Among non-RA subjects, it has been reported that a cumulative addition of about 7500 kcal is needed in addition to energy requirements to gain 1 kg of body weight in undernourished young people, while 8800-22600 kcal is needed in undernourished older people. Since RA patients show increased muscle catabolism due to inflammation, it is necessary to consider not only the amount of energy, but also the source of administered energy and other nutrients to achieve muscle mass-based weight gain. In addition, RA patients have the basic lifestyle characteristics of lower energy intake and physical activity compared to non-RA subjects. In view of these points, I would like to show the nutritional management methods of older RA patients from both theoretical and practical perspectives.

## S14-5

**Pharmacists' Involvement in Measures against Polypharmacy in Elderly Rheumatoid Arthritis Patients**

Noboru Konno
Department of Pharmacy, Yamagata University Hospital, Yamagata, Japan

Conflict of interest: None

Japan, a super-aged society, faces higher adverse drug event (ADE) incidence in the elderly than in younger patients, largely due to age-related changes in pharmacokinetics and drug responsiveness. This issue is exacerbated by polypharmacy, common among the elderly due to a mix of lifestyle diseases and geriatric syndromes. As a university hospital, we receive many patients with comorbidities referred from various medical institutions, often carrying multiple prescriptions. Surgery patients are screened for preoperative medications, including supplements and OTC drugs. Their medication is rechecked upon admission, with particular attention needed for those bringing numerous medications to avoid duplication, drug interactions, and to ensure optimal dosing. Rheumatoid arthritis treatment primarily involves drug therapy, with key medications like MTX, biologics, and JAK inhibitors significantly enhancing efficacy. However, prolonged arthritis can lead to joint destruction and deformity, impairing functionality and reducing QOL. Difficulty in extracting medications from PTP sheets due to finger deformities hinders adherence, potentially worsening QOL. Pharmacists address these challenges by proposing prescription changes like one-dose packaging and formulation alterations, simplifying medication management for both patients and caregivers. Selecting suitable dispensing methods and sharing information among healthcare professionals are crucial to prevent unnecessary drug administration and mitigate ADE risks, patient financial burden, and rising healthcare costs. In acute care hospitals with brief stays, collaboration between hospital and insurance pharmacy pharmacists is vital to sustain medication adherence post-discharge. Hospital pharmacists must accurately evaluate inpatients' conditions and provide relevant information, necessitating strengthened cooperation with both internal medical staff and external entities like insurance pharmacies.

## S14-6

**Characteristics of elderly rheumatoid arthritis patients and their treatment**

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Conflict of interest: None

In recent years, rheumatoid arthritis (RA) patients are aging, and the incidence of late-onset RA (LORA) is also increasing. The goal of RA treatment has shifted from symptom control to remission with the introduction of methotrexate (MTX) in the early stages of disease onset, and the use of biologic agents and Jak inhibitors for treatment-resistant cases. These treatment goals are the same in the elderly. In addition, the aging process is associated with a high incidence and severity of drug adverse effects due to the decline in renal function and other physical functions, as well as a decrease in fluid volume in the body. It is important to understand the characteristics of the elderly in order to safely administer pharmacotherapy. Moreover, physical factors such as muscle weakness due to aging can cause progressive frailty. In order to suppress muscle weakness and maintain quality of life, it is necessary to make an appropriate diagnosis at

an early stage, assess complications promptly, and set treatment goals before therapy is implemented. The incidence of dementia increases with age, but the impact of drug therapy on dementia is controversial: some reports indicate that the incidence of dementia has decreased in RA compared to the general population, and others indicate that the incidence of dementia has decreased with the use of csDMARDs or with treatment with b/tsDMARDs. while others have reported that treatment with csDMARDs increased vascular dementia. Among elderly patients with RA, there are some cases of secondary amyloidosis that developed before MTX or other therapies and were not adequately treated due to complications or disease progression. Long-term survival can now be achieved in these patients with appropriate management centered on bDMARDs. Although RA patients are aging as life expectancy increases, treatment of elderly RA patients should take into account their various characteristics.

## S14-7

**Rehabilitation for older patients with rheumatoid arthritis: experiences using online patient education under and post COVID-19 pandemic**

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Conflict of interest: None

To prevent the spread of the novel coronavirus disease (COVID-19) that occurred in 2019, people were encouraged to refrain from going out, and older people, considered to be at particularly high risk of infection, were forced to stay at home. As a result, older people have developed frailty in a short period of time based on marked inactivity due to prolonged periods of self-isolation. Among the older people, patients with chronic diseases, especially those with rheumatoid arthritis (RA), have been repeatedly reported to be susceptible to infection due to the use of immunosuppressive drugs. Therefore, not a few patients voluntary discontinued taking the drugs or reduced the dose, resulting to escape from a tight control. Insufficient drug treatment made a disease activity worsen, which in turn increased susceptibility to infection and arthralgia, which reduced physical activity and further worsened frailty. For these reasons, during the COVID-19 pandemic, measures to maintain treatment adherence and physical activity levels for older patients with RA have become urgent issues. Since 2003, we have held monthly educational classes for patients with RA in our hospital. However, due to the COVID-19 pandemic, the classes were forced to be canceled from March to May 2020. We have adopted an online conference system to held remote patient education class since June 2020 to maintain treatment adherence and physical activity during the COVID-19 pandemic. In the class, a multidisciplinary team collaborated on themes such as drug therapy, infection prevention, rehabilitation, orthotic therapy, orthopedic surgery, music therapy, oral care, and nutritional therapy. Among the themes, a physical therapist gave a lecture on topics such as physical activity, frailty, and exercises for patients with RA. A survey revealed that patients with RA had not been doing enough exercise due to the COVID-19 pandemic, and that the education encouraged them to understand the importance of maintaining physical activity. Even after COVID-19 was changed to a Class 5 infectious disease, we have continued to hold the classes online. The education for patients with RA is still necessary in today's post-corona era to maintain treatment adherence and physical activity. In this symposium, we report on our experience of multidisciplinary online patient education for the rehabilitation of older patients with RA.

## S15-1

**Synovial Macrophage in Joint Homeostasis and Inflammation**

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Conflict of interest: None

The synovial tissue is an immunologically challenging environment where, under homeostatic conditions, highly specialized subsets of immune-regulatory macrophages and fibroblasts constantly prevent synovial inflammation in response to cartilage- and synovial fluid-derived danger signals that accumulate in response to mechanical stress. During inflammatory joint diseases, this immune-regulatory environment becomes perturbed and activated synovial fibroblasts and infiltrating immune cells start to contribute to synovial inflammation and joint destruction. We currently aim to expand our current understanding of the phenotypic and molecular characteristics of resident synovial macrophages and fibroblasts and to understand their crosstalk during joint homeostasis and joint inflammation, which is increasingly appreciated as vital to understand the molecular basis of prevalent inflammatory joint diseases such as rheumatoid arthritis.

## S15-2

**Immunogenetics to understand the etiology of autoimmunity**

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Conflict of interest: None

Common variants strongly influence the risk of human autoimmunity. Two categories of variants contribute substantially to the risk: i) coding variants of *HLA* genes and ii) non-coding variants at non-*HLA* loci. For example, each of the two categories explains around half of the genetic risk for rheumatoid arthritis (RA), a prototype of autoimmune disease. To understand how *HLA* coding variants contribute to the risk, we recently developed a novel analytic pipeline of T cell receptor (TCR) repertoire. By analyzing the TCR of around 800 donors, we identified genetic evidence supporting that the risk alleles of the coding *HLA* variants substantially influence T cell thymic selection and modify TCR amino acid usage patterns. A notable example is that RA *HLA* risk alleles prefer TCR CDR3 amino acids to possess a negative charge, potentially increasing the T cell reactivity to citrullinated epitopes. In addition, to understand how non-coding variants contribute to the risk, we conducted comprehensive analyses integrating GWAS results with multiple molecular phenotype databases, such as expression quantitative trait loci (eQTL), cytokine pathways, and epigenomic annotations. We identified genetic evidence suggesting that the risk alleles of the non-coding variants dysregulate gene expression, splicing, chromatin structure, cytokine pathways, and transcription factor activities. Moreover, we experimentally validated the molecular effect of fine-mapped risk alleles using the latest genome-editing technology. Recent functional genetics studies have provided novel insight into the immunological consequences of two major genetic risks.

## S15-3

**Fibroblasts as regulators of inflammation and damage in arthritis**

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Conflict of interest: None

The synovial membrane is the primary site of pathology during the effector phase of inflammatory arthritis. The membrane undergoes profound architectural remodelling in response to inflammation, driven by the expansion and differentiation of synovial fibroblasts towards disease-associated phenotypes. We have demonstrated the existence of fibroblast subsets with distinct effector functions that drive either inflammation or damage. This division of labour is anatomically defined and driven by the response of fibroblasts to specific microenvironmental cues and cell-cell interactions that dictate their phenotype and function. Fibroblasts located in the sublining layer of the synovium are activated by the arterial endothelium to drive an immune effector phenotype and the formation of spatially-defined, immune-permissive tissue niches, which function to support the infiltration and retention of inflammatory cells. Furthermore, the identification of specific biomarkers of pathogenic fibroblast subsets, such as fibroblast activation protein-alpha, has allowed us to develop tools to selectively target these cells therapeutically using engineered T cells that directly deplete these fibroblasts from synovial membrane. In contrast, during the resolution phase of murine joint inflammation, we have identified regulatory fibroblasts that receive instructive signals from pro-resolving macrophages and function as negative regulators of inflammation. These 'regulatory' fibroblasts secrete DKK3 (Dickkopf Wnt signalling pathway inhibitor 3) to maintain their pro-resolving state, restoring tissue homeostasis and promoting repair. In summary, fibroblasts are key regula-

tors of joint inflammation and damage and despite their importance are yet to be targeted therapeutically. We are now developing precision approaches to target pathogenic fibroblasts through highly selective cell depletion strategies or by inhibiting the signalling pathways response for fibroblast pathogenicity.

## S15-4

**The immune-stromal-bone interaction in autoimmune arthritis**

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Conflict of interest: None

Immune system closely interacts with stromal cells in health and diseases. Rheumatoid arthritis (RA) is one of the most common autoimmune diseases worldwide. In RA, the activated immune system co-operates with synovial fibroblasts to enhance inflammation and destruction of bone and cartilage in joints. The crucial role of osteoclasts in bone destruction has been demonstrated by basic studies and the clinical efficacy of antibodies targeting RANKL, an important mediator of osteoclastogenesis. New technologies, such as single-cell RNA sequencing, have revealed the heterogeneity of synovial fibroblasts and immune cells. To understand the mechanisms of bone damage in RA, it is important to clarify how the immune system promotes the tissue-destructive properties of synovial fibroblasts and influences bone cells. We recently clarified the key transcription factor ETS1, which governs the pathological tissue-destructive programs in synovial fibroblasts. An improved understanding of the interplay among the immune system, synovial fibroblasts and bone based on the combination of in silico analysis and biological studies will contribute to the identification of novel therapeutic targets in RA. Here, I would like to introduce our recent findings regarding the immune-stromal-bone triad in autoimmune arthritis.

## S15-5

**Fibroblast-driven pathogenic mechanisms in joint/gut axis diseases**

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Conflict of interest: Yes

Previous research in our lab established fibroblasts as dominant stromal cells performing pathogenic functions in chronic inflammation, immunity and cancer (1,2). Fibroblasts have since emerged as a highly heterogeneous population of cells, exhibiting various organ- or tissue-specific identities and functions. I will discuss recent studies dissecting the compositional, transcriptomic and regulatory network changes that drive the transition of fibroblast subpopulations from homeostasis to pathogenesis in models of chronic inflammatory joint and intestinal diseases. For example, single-cell profiling of synovial fibroblasts (SFs) using RNA-sequencing and chromatin accessibility assays revealed distinct fibroblast subsets in the homeostatic synovium and disease-specific subpopulations emerging with TNF-driven arthritis (3). These subpopulations exhibited enhanced inflammatory responses, promigratory behavior, neovascularization, and collagen metabolic processes. Temporal reconstruction of transcriptomic events identified specific sublining cells as progenitors, culminating in a pathogenic sublining and destructive lining identity. Integrated analysis with human RA sc-RNA-seq data indicated key pathogenic transcription factors, including Bach1 and Runx1, which were further validated as key drivers of arthritogenesis. To highlight the potential of discovering novel, subpopulation-specific targeted therapies, I will present an example of successfully targeting a pathogenic synovial fibroblast cluster in modelled arthritis (4). In further translational efforts, I will also discuss a 'fibroblast-de-activation' drug discovery pipeline (5) for the development of novel, more potent and selective compounds against complex chronic diseases, such as inflammation and fibrosis. 1. Mesenchymal cell targeting by TNF as a common pathogenic principle in chronic inflammatory joint and intestinal diseases. M. Armaka et al, J Exp Med. 2008. 2. The mesenchymal context in inflammation, immunity and cancer V Koliaraki, A Prados, M Armaka, G Kollias, Nature immunology, 2020. 3. Single-cell multimodal analysis identifies common regulatory programs in synovial fibroblasts of rheumatoid arthritis patients and modeled TNF-driven arthritis. M. Armaka et al, Genome Med. 2022. 4. miR-221/222 drive synovial fibroblast expansion and pathogenesis of TNF-mediated arthritis. Fani Roumelioti et al., bioRxiv 2022.07.22.500939 5. Repurposing of Amisulpride, a known antipsychotic drug, to target synovial fibroblast activation in arthritis. D. Papadopoulou et al. JCI Insight 2023.

## S16-1

**Evolution and future perspectives of shoulder and elbow joint surgery for rheumatoid arthritis**

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Conflict of interest: Yes

In the shoulder surgery for rheumatoid arthritis (RA), recent topics include the widespread use of reverse shoulder arthroplasty and the introduction of navigation surgery. In particular, surgical indications for the reconstruction of RA shoulders with relatively large glenoid defects and loss of rotator cuff function have been expanded. This has also led to demands for more secure devices for the setting of the glenoid component including intraoperative navigation and custom guide using 3D-CT, as well as the use of augmented baseplates to minimize bone resection. In the elbow surgery, triceps-on approach has also been applied to elbow arthroplasty, with the expectation of early post-operative recovery and reduced complications. However, there are limitations in the elbow implants those can be used and in the possible intraoperative complications, requiring skilled surgical techniques and the ability to troubleshoot complications during surgery. With improved medical control of RA, adjacent joint disorders have been reduced and the bone quality of the relevant joints has become better. It will therefore be interesting to see whether complication rates, survival rates of implant and patients' subjective evaluation can be comparable to TEA for osteoarthritis, THA and TKA. The age for surgery, which is currently generally set at 65 years and over, may be lowered, and there is a possibility of expanding the indications to include younger patients. It should be noted that the long-term results currently available are for implants used between 2000 and 2010. New prostheses designed on the basis of experience with the clinical results of previous implants and technological innovations are reasonably expected to have better performance, lower complication rates and longer durability. The careful follow-up is also required for other new prostheses, such as shoulder prostheses, which are recently being introduced to the market.

## S16-2

**Clinical Outcomes of Total Wrist Arthroplasty after Minimum 10-Year Follow-Up and Future Prospects**

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Conflict of interest: None

We developed a semiconstrained total wrist prosthesis (DARTS Total Wrist System; Teijin Nakashima Medical Co., Ltd.) and conducted a clinical trial of the prosthesis in patients with rheumatoid arthritis (RA). This wrist prosthesis has favorable clinical outcomes for up to 5 years postoperatively. However, the long-term outcomes are unclear. The objective of this study was to evaluate the clinical outcomes of this wrist prosthesis for the treatment of severe wrist RA during a minimum 10-year follow-up. From 2010 through 2012, total wrist arthroplasty using the DARTS Total Wrist System was performed for 20 wrists in 20 patients with RA (5 males, 15 females). The mean patient age was 64 years (range, 50-84 years). Preoperative radiographs showed Larsen grade IV changes in 16 wrists and

grade V changes in four wrists. Patients were evaluated clinically and radiologically preoperatively and at 10 years or more postoperatively. Evaluated parameters were the visual analog scale for pain, range of motion, Figgie score, and DASH score. The minimum 10-year follow-up clinical results (mean, 11.3 years) were available for all 14 surviving patients (3 males, 11 females). The mean visual analog scale for pain at final follow-up was significantly improved compared with preoperatively. There were no significant differences in wrist extension and flexion angles at final follow-up compared with preoperatively. The mean Figgie and DASH scores at final follow-up were significantly improved compared with preoperatively. Radiographic evaluation had already revealed implant loosening in five of the 19 wrists at 5 years postoperatively, but there were no new cases of component loosening identified at final follow-up. Total wrist arthroplasty using the DARTS Total Wrist System achieves favorable clinical outcomes with no serious complications requiring revision for 10 years postoperatively.

## S16-3

**Evolution and Prospects of Hip and Knee Surgery in Patients with Rheumatoid Arthritis**

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Conflict of interest: Yes

Joint destruction of rheumatoid arthritis (RA) has been decreased, but despite strict management, joint destruction may still progress in some RA patients. We have previously reported that if the hip and knee joints show LG III or greater destruction, joint destruction is likely to progress even with intensified pharmacologic therapy. To avoid reducing ADL in RA patients, we must perform a thorough examination and imaging evaluation of symptomatic hip and knee joints, and introduce surgical treatment in a timely manner without adhering to drug therapy. With advances in RA treatment, severe joint destruction and deformity have decreased, and bone quality has improved, leading to OA in RA joints. Although the results of total hip arthroplasty (THA) are expected to improve accordingly, the risk of postoperative THA dislocation in RA patients is higher than in OA patients, so intraoperative accurate implant placement is even more necessary in RA than in OA. We currently perform THA for RA hip disorders using a robotic navigation system, and have achieved accurate implant placement and good postoperative results. In total knee arthroplasty (TKA) for RA, better results have been reported with patella replacement. However, with disease activity under tight control, the possibility of patella preservation should be reevaluated. We currently perform TKA without patellar replacement unless there is a large bone defect or severe deformity of the patella, and have confirmed good postoperative results with no complaints around the patella and no recurrence of knee arthritis. In this symposium, I will discuss the latest surgical treatment of RA hip and knee joint disorders, presenting my experience.

## S16-4

**Evolution and future perspectives of surgery for rheumatoid foot and ankle**

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Conflict of interest: None

The landscape of orthopaedic surgeries for the patients with rheumatoid arthritis (RA) has transformed with the emergence of highly effective drugs. With decreased major joint surgeries, there's a growing focus on smaller joint from the viewpoints of both patients and healthcare providers. The foot, highly susceptible in early RA, remains a common site of manifestation. Even in an era where clinical remission is realistic, foot-related complaints persist, making rheumatic foot surgery relevant. In RA, once the joints are affected, deformation progresses due to mechanical stress, regardless of the presence or absence of disease activity. This phenomenon contributes to the sustained demand for foot surgeries in RA. Advancements in controlling disease activity and improving bone fragility through osteoporosis treatments have shifted towards joint-preserving surgeries, not previously considered for RA feet. The knowledge and techniques from foot surgery for deformities, apart from RA, are now applied to RA feet. Traditional methods like "forefoot reconstruction" and "ankle fixation" are becoming obsolete. Various surgical options in non-RA feet, such as joint-preserving procedures using different osteotomies, deformity correction for midfoot deformities, and total ankle arthroplasty for ankle arthritis, are now considered for RA feet. However, due to the diverse nature of affected areas and deformities in RA feet, directly applying non-RA foot surgical techniques is insufficient. Understanding RA foot destruction patterns, considering each surgical procedure's effects and limitations, and selecting appropriate methods and intervention timing are crucial. Establishing a comprehensive treatment system for RA feet remains a challenge. Recent findings suggest soft tissue lesions preceding arthritis in RA feet. Advancements in understanding early-stage RA foot pathophysiology raise the prospect of preventive surgeries to avert irreversible joint damage and deformities.

## S16-5

**Changes in the treatments of rheumatoid arthritis in orthopedic surgery**

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Conflict of interest: None

Recent spread of the biologics for the treatment of rheumatoid arthritis (RA) dramatically improves the outcome and ameliorates the pain and dysfunction due to joint destruction. According to this trend, the leading player for the treatment of RA seems to change from orthopedic surgeons to physicians. However, there are still patients who developed RA 20 to 30 years ago and need surgery because of the progressive pain and dysfunction in large and small joints. Since the 1st and the 2nd professors of our department majored in RA, many patients with RA undertook surgery at our hospital. Especially surgery was mainly performed for the treatment of pain and paralysis due to cervical lesions such as atlantoaxial subluxation. However, the prevalence of cervical spondylosis decreased and that of lumber spondylosis due to osteoporosis has recently increased in patients with RA. Treatment of hand and finger deformity has changed from arthrotomy or tendon balancing surgery to articulating spacer or artificial joint. Recent introduction of biologics for the treatment of RA has dramatically decreased massive joint destruction but some patients still need surgery such as replacement by artificial joint. The cases have recently increased who had degenerative joints due to the former rheumatic lesions plus age-related changes, leading to artificial joints. In this symposium, we'll present the changes in the target lesions and the therapeutic development for RA in orthopedic surgery based on the data and experience of our department.

## S16-6

**Advances and future perspectives in cervical spine surgery for rheumatoid arthritis: an over 10-year prospective multicenter cohort study**

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Conflict of interest: None

Rheumatoid arthritis (RA) can cause three characteristic cervical spine instabilities: atlantoaxial subluxation (AAS), vertical subluxation (VS) of the axis, and subaxial subluxation (SAS). These should be cautious, possibly inducing serious neurological deficit. An over 10-year prospective multicenter cohort study was thus designed to clarify the incidence and predictive risk factors of cervical spine instabilities in RA. Three types of instability were radiographically categorized into the criteria for ''moderate'' and ''severe''. In 2001-2002, of 634 ''classical'' or "definite'' RA patients, 503 without baseline "severe" instability were enrolled at 21 institutions. In 2006-2008, 228 including 5 undergoing surgery were prospectively followed for >5 years. The >5-year incidence of "severe" instabilities was higher in 33.3% ($p$<0.01), 75.0% ($p$<0.01), and 42.9% ($p$=0.06) with baseline AAS, VS, and SAS, respectively, than in 12.9% without baseline instability. Similarly, the incidence of canal steno-

sis and/or basilar invagination was higher in 17.5% ($p$=0.03), 37.5% ($p$<0.01), and 14.3% ($p$=0.43) with AAS, VS, and SAS, respectively, than in 7.1% without instability. Hence, the development of cervical spine involvement is accelerated in those with instabilities-especially VS. In 2012-2013, 143 including 6 undergoing surgery had consecutive follow-up for >10 years. Multivariable Cox proportional hazards model found that baseline mutilating changes ($p$<0.01), corticosteroid administration ($p$<0.01), and previous joint surgery ($p$=0.048) correlated with ‘’severe’’ instabilities. Therefore, sustained low RA activity without radiographic peripheral joint damage and concomitant corticosteroids is essential to prevent advanced instabilities. In fact, biological therapies can reduce the incidence of cervical spine instabilities in patients without instability, but not the progression in those with instabilities. We will discuss future perspectives in cervical spine surgery for RA.

## S17-1

**Central nervous system involvements in SLE**

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Conflict of interest: None

Central nervous system involvements (CNS) in systemic lupus erythematosus (SLE), a severe complication in lupus patients, is characterized by the CNS lesions of neuropsychiatric manifestations primarily attributed to SLE (NPSLE). The major pathogenesis of NPSLE in the CNS involves immune cells, cytokines, autoantibodies, and local reactions specific to the CNS. The etiology of NPSLE comprises two mechanisms: inflammatory manifestations and cerebrovascular diseases, including anti-phospholipid antibody syndrome (APS), as outlined in the 2023 EULAR recommendations for SLE management. Additionally, the classification of NPSLE into diffuse and focal types, based on the ACR nomenclature published in 1999, proves valuable in describing clinical phenotypes. Understanding the mechanisms underlying each phenotype is crucial for accurate diagnosis and treatment. Recent results, including single-cell analysis from lupus-prone mouse studies, reveal certain mechanisms involved in NPSLE development. In addition to the discovery of autoantibodies against neurons or astrocytes, microglial activation plays a significant role in cytokine production and neuronal remodeling in NPSLE model mice. Furthermore, autoantibody-mediated endothelial cell damage can directly disrupt the blood-brain barrier, contributing to the development of NPSLE. Unfortunately, no specific diagnostic biomarkers for NPSLE have been established. However, autoantibodies related to diffuse NPSLE development, such as anti-neuronal antibodies including anti-glutamate receptor subunit GluN2A/B antibody (anti-GluN2 Ab, previously called anti-NR2 Ab) and anti-ribosomal P antibody, as well as anti-AQP4 antibody causing NMOSD through complement-dependent astrocyte injury, serve as potential pathogenic surrogate markers for NPSLE. The measurement of four types of anti-phospholipid antibodies is meaningful for estimating the potential risk of developing thrombosis, in addition to lupus anticoagulants, including anti-phosphatidylserine/prothrombin antibodies. Moreover, interleukin-6 provides an advantage in detecting diffuse NPSLE based on a retrospective cohort study. Nothing was updated on NPSLE treatment due to lack of evident papers in the past five years according to the EULAR recommendations of 2023. However, many kinds of molecular-targeting therapy has been established for immune-mediated neuronal diseases. Therefore, a comprehensive approach involving specialists in both local and systemic autoimmune disorders is essential to overcome NPSLE.

## S17-2

**ACR/EULAR Antiphospholipid Syndrome Classification Criteria: Applications for Clinical Practice in Japan**

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Conflict of interest: None

Antiphospholipid Syndrome (APS) is an autoimmune disease characterized by thrombosis and obstetric complications with antiphospholipid antibodies (aPL). The classification criteria of APS, established in Sapporo in 1998 and revised in Sydney in 2004, were updated in 2023 to the ACR/EULAR antiphospholipid syndrome classification criteria. This presentation will detail the new criteria and discuss how to apply this criteria in Japan. The new system scores clinical and laboratory criteria. Clinically, six domains are scored, requiring three points for a diagnosis in both clinical and laboratory criteria. Thromboses are categorized as macrovascular (Domains 1 and 2) with risk-based weighting. Microvascular APS (Domain 3) includes livedoid vasculopathy, aPL nephropathy or pulmonary hemorrhage. Pregnancy complications (Domain 4) are scored, with lower weights for fetal-related issues. Cardiac valve disease (Domain 5) and thrombocytopenia (Domain 6) are defined. Laboratory criteria assess lupus anticoagulant by testing twice over 12 weeks. aCL and aβ2GPI require standardized ELISA measurements, with titers weighted. The new criteria were developed for use in observational studies and clinical trials. Understanding the differences between classification and diagnosis for APS is crucial for the proper management of APS in clinical settings.

## S17-3

**Characteristics and Therapeutic Strategies for difficult to treat RA**

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Conflict of interest: Yes

Rheumatoid arthritis stands out as the most prevalent rheumatic disease with the most advanced treatment approaches. For instance, the “EULAR recommendations for the management of rheumatoid arthritis 2022 update” suggest the use of glucocorticoids as symptomatic therapy in phase I, emphasizing a swift reduction in dose and discontinuation within a few months. Recommendations for the treatment of systemic lupus erythematosus now position glucocorticoids as a bridging therapy. However, glucocorticoids still continue to serve as first-line agents for remission induction in various autoimmune diseases. As such, compared to other autoimmune diseases, rheumatoid arthritis treatment has significantly progressed in moving away from glucocorticoid use. Despite these advancements in the treatment of rheumatoid arthritis, there exist cases of rheumatoid arthritis resistant to multiple classes of molecular targeted therapies. Addressing this challenge is a key research focus, particularly in creating an optimal treatment for difficult-to-treat RA (D2TRA). Our efforts have involved exploring a refined treatment strategy based on the data from the First registry of molecular targeted therapies, including over 5,000 RA patients. Notably, around 15% of patients progressed to D2TRA even after the approval of JAK inhibitors for the treatment of rheumatoid arthritis. This presentation will delve into the risk factors associated with D2TRA and discuss corresponding treatment methodologies.

## S17-4

**Interstitial lung disease associated with idiopathic inflammatory myopathy**

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Conflict of interest: None

Idiopathic inflammatory myopathy (IIM) is often accompanied with interstitial lung disease (ILD). ILD is one of the most important prognostic factors in IIM as well as other connective tissue diseases. There are two types of IIM-ILD, a rapidly progressive type and a chronic type, both of which have recalcitrant cases. Rapidly progressive types are often positive for anti-melanoma differentiation-associated gene 5 (MDA5) antibodies, are resistant to immunosuppressive therapy in the early stages of the disease, and have a low 6-month survival rate. Thus, in anti-MDA5-positive patients, the importance of early intervention with triple combination therapy (glucocorticoid (GC), calcineurin inhibitors (CNI) and intravenous cyclophosphamide) as well as early diagnosis has been recognized. However, cases that are refractory to the combination of conventional immunosuppressive therapy are often experienced. In such cases, efficacy of plasma exchange or use of JAK inhibitors have increasingly been suggested.

Chronic types are often positive for anti-aminoacyl tRNA synthetase (ARS) antibodies. ILD with anti-ARS tends to respond well to initial GC therapy but often recur, which results in progressive fibrosing and deterioration of pulmonary function. The main therapeutic goals for the chronic type are to minimize relapse, reduce the total steroid dosage, and control the progression of respiratory failure. Early concomitant use and continuation of immunosuppressive drugs are suggested for this purpose, especially the concomitant use of CNI. However, the relapse rate is still high even when immunosuppressive drugs are used in combination with GC, and such cases often show progressive fibrosis. Therefore, there are growing expectations for the use of antifibrotic agents in combination with immunosuppressive drugs. In this symposium, the management of ILD associated with IIM will be outlined and be discussed on future perspectives.

## S17-5

**Pulmonary hypertension**

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Conflict of interest: None

Pulmonary arterial hypertension (PAH) is one of important organ involvements in connective tissue diseases (CTDs) since this organ involvement can determine the outcome of the patients. However, PAH itself is a rare disease, one third of PAH is explained by complication with CTDs. Furthermore, CTD-PAH, especially Scleroderma (SSc)-PAH, still has worse prognosis compared with other PAH subgroups even the development of the new drugs, suggesting that much more effort is needed to improve this situation. In order to improve these situations including CTDs, a guideline was revised and issued from ESC/ERS in 2022. In this guideline, several new points were raised associated with CTDs. One of important point is “screening”. The importance of the “screening” in high-risk groups including CTDs were clearly stated. The structure of the “diagnosis” has 3 steps, suspicion, detection and identification, and suspicion and detection is the steps of “screening”. “Screening” is start from risk evaluation of having PAH and proceed to detection and identification of PAH. In the new guideline, important update of the change in the threshold of mean pulmonary arterial pressure (mPAP), decreased to 20mmHg, was also proposed. However, evidence is still insufficient to support this concept for patients with 20<mPAP<25 mmHg. The second point is a treatment approach for PAH patients who are complicated with cardiopulmonary comorbidities. Since CTDs are systemic diseases and have various organ involvements which can affect the pulmonary arterial pressure, treatment decision must be considered including this situation. The third is importance of immunosuppressive treatment, which is specific to CTDs, based on the pathogenesis of diseases. I would like to discuss new diagnostic and treatment approaches for CTD-PAH based on the revision of the new ESC/ERS guideline update.

## S17-6

**Thrombotic microangiopathy among patients with systemic autoimmune disease**

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Conflict of interest: None

Thrombotic microangiopathy (TMA) is a syndrome characterized by microangiopathic hemolytic anemia, thrombocytopenia, and end-organ damage (including renal and cranial nerve deficits). The clinical spectrum of TMA includes Shiga toxin-producing Escherichia coli (STEC)-associated hemolytic uremic syndrome (STEC-HUS), thrombotic thrombocytopenic purpura (TTP), caused by decreased ADAMTS13, a specific von Willebrand factor cleaving enzyme, complement-mediated TMA, and secondary TMA caused by infection, drugs, pregnancy, malignant tumors, and systemic autoimmune disease. Systemic lupus erythematosus (SLE) is the leading systemic autoimmune disease that causes secondary TMA, followed by systemic sclerosis, polymyositis, and dermatomyositis. TMA is diagnosed based on the presence of thrombocytopenia, severe anemia, or elevated serum lactate dehydrogenase levels. There are various causes of cytopenia in patients with systemic autoimmune disease, such as hemolysis and autoimmune thrombocytopenia. Moreover, cytopenia may also be caused by hemorrhagic conditions, from the gastrointestinal tract or the alveoli, drug-induced bone marrow suppression and blood cell destruction, and thrombocytopenia secondary to antiphospholipid antibody syndrome and disseminated intravascular coagulation. Furthermore, antiplatelet drugs such as calcineurin inhibitors and ticlopidine can induce TMA, requiring close monitoring to screen for drug-induced TMA. Because patients with SLE also present with fever, central nervous system symptoms, and kidney damage, it may be challenging to differentiate these symptoms from those of TMA. Obtaining an accurate diagnosis is crucial because the management plan among patients with TTP and STEC-HUS varies significantly. In recent years, our understanding of TMA’s pathophysiology has improved, and major advances have been made in its treatment methods. TMA should be considered as a differential diagnosis in patients presenting with hemolytic anemia or thrombocytopenia with an unknown etiology. The appropriate diagnostics for an STEC infection, determination of ADAMTS13 activity, and investigation of other diseases that may cause secondary TMA should be done. This lecture will focus on TMA among patients with systemic autoimmune disease.

## S18-1

**Evidence-practice gap for the treatment in patients with MPA/GPA in Japan**

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Conflict of interest: None

Vasculitis syndromes are classified according to the size of the blood vessels. Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), which damages arterioles and capillaries as ANCA-associated vasculitis (AAV), cause alveolar hemorrhage, interstitial lung disease, and rapid progressive glomerulonephritis. It is, therefore, primarily treated by not only rheumatologists but also pulmologists and nephrologists. It has been previously pointed out a certain gap in the frequency of use of immunosuppressive drugs among these departments, especially in remission induction therapy. In order to standardize treatment between clinical departments, the Japanese Respiratory Society, the Japanese Society of Nephrology, and the Japan Society of Rheumatology jointly published the 2017 Clinical Practice Guidelines (CPG) for AAV. In 2021, the Ministry of Health, Labor and Welfare’s Vasculitis Subcommittee conducted a web survey on the proportion of patients using cyclophosphamide (CY) or rituximab (RTX) during remission induction as the primary endpoint. (Mod Rheumatol, 2023). As a result, 31.5% (95% confidence interval [CI] 25.1-38.5) of physicians answered that they use these immunosuppressive drugs for MPA/GPA more than 60% annually and 35.3% (95% CI 28.4-42.7) of physicians answered for severe kidney disease of MPA/GPA. When we investigated the factors related to this evidence-practice gap, the most relevant factor was the physician’s subspecialty. Actually, compared to other general physicians, rheumatologists had a significantly higher rate. These gaps might be due to the low level of clinical evidence in Japanese AAV patients and/or the facts that clinical manifestations differ even for the same AAV among subspecialities. In 2023, the CPG for AAV was revised and the position of RTX in remission induction treatment is equal to that of CY. In this lecture, I would like to discuss how rheumatologists can be involved the standardization of AAV treatment.

## S18-2

**Advances in MPA/GPA Practice**

Hiroaki Dobashi
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Conflict of interest: Yes

ANCA-associated vasculitis (AAV) is a systemic necrotizing vasculitis mainly involving small blood vessels (small arteries, small arteries, capillaries, and small veins) and is associated with antineutrophil cytoplasmic antibodies (ANCA). ANCA is a useful biomarker for diagnosis, but ANCA-negative AAV cases also exist in a small number, and the positivity rate and types of ANCA in AAV patients in Japan are different from

those in the West. The pathogenesis of AAV has been elucidated, and evidence for the efficacy of various therapies has been established. However, morbidity and mortality are still high in AAV, and the reasons for the poor prognosis of AAV include active disease and infectious complications during the induction phase of remission, and malignant tumor complications and relapse of the underlying disease during the maintenance phase. High-dose glucocorticoid (GC) and cyclophosphamide (CY) therapy has been important for remission induction therapy of AAV. However, recent trials have shown that GC doses can be reduced in remission-induction treatment. In addition, rituximab (RTX) has been proven to be an alternative treatment option to CY. However, there is insufficient evidence for the efficacy and safety of RTX in Japan. For maintenance therapy, azathioprine and methotrexate are recommended, and glucocorticoids are tapered or discontinued. The efficacy of RTX is being demonstrated for maintenance therapy. The introduction of new agents such as biologics in the treatment of AAV is expected to improve the efficacy of treatment, reduce the dose of GC, and decrease the incidence of adverse events. Recently, avacopan, a C5a receptor (C5aR) inhibitor, has been attracting attention as an alternative to GC, which has been the mainstay of treatment. However, there is no clear consensus on the use of avacopan other than in remission induction therapy. In this symposium, we will focus on MPA and GPA of AAV, and discuss the current status and problems of diagnosis and treatment with case examples.

## S18-3

**Remission maintenance treatment for MPA and GPA**

Ken-ei Sada
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Conflict of interest: Yes

In the treatment of ANCA-associated vasculitis (AAV), treatment phases are divided into “remission induction treatment,” performed during periods of high activity at the onset or relapse, and “remission maintenance treatment,” aimed at reducing relapse after remission is achieved. Among AAV, treatment options for microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis are usually considered separately. Since 2020, JPVAS had been revising the AAV clinical practice guidelines (CPGs), resulting in the publication of updated CPGs 2023. These CPGs include various new evidence-based revisions for maintenance therapy. In remission maintenance phase, it’s essential to select treatments considering long-term remission maintenance and relapse prevention, along with reducing adverse events from treatment such as glucocorticoids (GCs). For MPA and GPA, azathioprine (AZA) had long been the first line in combination with GCs. However, two randomized controlled trials (RCTs) comparing AZA have confirmed the superiority of rituximab (RTX) in preventing relapse, leading to its recommendation as the first-line concomitant in the revised CPGs. Subsequently, RCTs have also been conducted on the administration methods and durations for RTX in maintenance therapy. The MAINRITSAN2 trial confirmed non-inferiority between regular administration and tailored administration based on B-cell count and ANCA titer monitoring. In the MAINRITSAN3 trial, extending maintenance therapy with RTX to 36 months, compared to 18 months, confirmed its effectiveness in suppressing relapse, leading to recommendations for longer-term continuation of RTX. In remission induction phase while early reduction of GCs has been confirmed to be non-inferior compared to conventional regimen, there is no clear evidence regarding the optimal reduction or discontinuation strategy of GCs in maintenance of remission.

## S18-4

**Management of Pulmonary Lesions in Patients with AAV**

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Conflict of interest: None

ANCA-associated vasculitis (AAV) includes three types of disease: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA); all of which are designated as an incurable disease in Japan. The pulmonary lesions associated with AAV are diverse; and those are characteristic of each disease. The major pulmonary lesions manifest alveolar hemorrhage and interstitial pneumonia in MPA; nodules or mass lesions with cavities associated with necrotizing vasculitis, tracheal and bronchial lesions (masses and stenoses) in GPA; and bronchial asthma, eosinophilic bronchiolitis, and eosinophilic pneumonia in EGPA. In addition, MPA and MPO-ANCA-positive AAV are more common in East Asian populations, including Japanese, than in Western populations, and interstitial pneumonia is more frequent among MPA than alveolar hemorrhage. However, the mechanisms underlying the development and progression of interstitial pneumonia in AAV patients and the role of ANCA in the pathogenesis of interstitial pneumonia are currently obscure. Management of pulmonary lesions in patients with AAV is performed according to the “2023 Clinical Practice Guidelines for the Management of ANCA-associated Vasculitis”. On the other hand, MPO-ANCA-positive interstitial pneumonia includes not only interstitial pneumonia associated with AAV but also interstitial pneumonia without systemic vasculitis. However, the treatment strategies for MPO-ANCA-positive interstitial pneumonia without AAV have not been established, and further studies are needed to determine the efficacy and safety of early steroid and immunosuppressant therapy, indications for methotrexate, rituximab, avacopan, and antifibrotic agents, duration of therapy and timing of dose reduction or discontinuation. We will present the latest findings on MPO-ANCA-positive interstitial pneumonia as well as discuss the management of pulmonary lesions associated with AAV in this symposium.

## S18-5

**Renal involvement and usefulness of plasma exchange for AAV**

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Conflict of interest: None

MPA/GPA, which belongs to AAV, frequently shows renal lesions, which not only increases a risk of ESKD but worsens life prognosis. It presents clinically with rapidly progressive glomerulonephritis (RPGN), pathologically with a pauci-immune necrotizing GN with crescents. Although the prognosis has improved due to treatment progress, there are still cases resulting in dialysis when it is delayed. As a predictor of renal prognosis, serum Cr and renal pathology has been utilized; typical examples are Berden and Brix scores. The standard treatment is a combination of corticosteroids and rituximab or cyclophosphamide, but recently anti-C5a inhibitor avacopan was added to the regimen. In severe cases, plasma exchange (PE) has been considered to remove the etiological agents. In the MEPEX trial for patients with severe kidney injury (sCr 5.6 mg/dL or more or dialysis-dependent), the superiority of PE to steroid pulse therapy was shown at 3 and 12 months in dialysis prevention, while no difference was found in life prognosis and adverse events, the positive result reflected in the subsequent many clinical practice guidelines. Long-term follow-up of MEPEX trial showed 36% risk reduction of dialysis, but with no significance ($p=0.08$). A recent PEXIVAS trial, a large RCT for severe AAV with eGFR<50 or lung hemorrhage, could not show effectiveness of PE for primary outcome (ESKD and death). There were no significant differences in patients that meet the MEPEX criteria as well, however, subsequent meta-analysis suggest that PE may be effective at least in some cases. There have also been attempts to specify subgroups in which PE may be useful, for example, by scoring renal biopsy findings. Based on such results, the Japanese AAV clinical practice guideline has been published in 2023, including recommendations on PE. Avacopan might be effective in ANCA-related GN. In this symposium, treatment update of ANCA-associated GN will be summarized, focusing on the usefullness of PE.

## S19-1

**A case of adult-onset Still’s disease with tendonitis and tenosynovitis -including ultrasound assessment-**

Sho Sendo, Eriko Yamamoto, Haruka Yasuba, Takumi Yamaoka, Kodai Yamamoto, Katsuhiko Yoneda, Hirotaka Yamada, Keisuke Nishimura, Yo Ueda, Jun Saegusa
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Conflict of interest: None

Adult-onset Still's disease (AOSD) is an uncommon systemic inflammatory disorder of unknown etiology characterized by high spiking fever, salmon-like skin rash, arthralgia/arthritis and elevated serum ferritin. While arthralgia/arthritis is one of the most frequent symptoms, it has not been elucidated what structural changes are associated with the symptoms. A previously healthy 65-year-old female was visited our department because of fever of unknown origin. Four weeks before admission, she noticed linear erythema on her forearms and thighs, and two weeks before, she presented with high fever over 40 °C. As acetaminophen did not relieve the fever and as she had pharyngalgia and polyarthralgia 4 days before, she was admitted to our hospital. On physical examination, she had high fever (39.1°C), enlarged lymph nodes in the left mandible and left supraclavicular fossa, polyarthralgia and erythema on the upper part of her right knee. Laboratory investigation revealed elevated CRP (14.5 mg/dL), ferritin (1941 ng/L), transaminase (AST: 93 U/L, ALT: 63 U/L), while negative rheumatoid factor (RF), anti-cyclic citrullinated peptide (ACPA) and antinuclear antibody (ANA). CBC showed that normal levels of WBC ($4.7 \times 10^3$ /mm$^3$, 87.3% of neutrophils) and anemia (Hb: 8.9 g/dL). Contrast-enhanced CT revealed an enlargement of the left mandible and supraclavicular fossa lymph nodes, and hepatosplenomegaly. MSKUS showed active tendonitis in right quadriceps femoris tendon and left 2PIP extensor tendon, and tenosynovitis in left extensor digitorum longus and tibialis anterior tendons. Biopsy of left supraclavicular fossa lymph nodes was performed to exclude malignancy. Initiation of NSAIDs once resolved the fever for 3 weeks. However, she got high fever, rash and arthralgia again. One month after the admission, histological findings of the lymph node revealed burnt out histocytic reaction with no malignancy, and she was finally diagnosed as AOSD. At that point, she developed macrophage activation syndrome (MAS) and started prednisolone 1 mg/kg and tocilizumab. All the symptoms including MAS were relieved a week after the treatment and MSKUS showed no obvious findings. We experienced a case of AOSD with tendonitis and tenosynovitis. In this session, we would mainly discuss about the characteristics of arthralgia/arthritis in AOSD especially focusing on its MSKUS.

## S19-2

**Developing a EULAR network of early career researchers dedicated to lung diseases in inflammatory rheumatisms**

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Conflict of interest: None

EULAR study groups are european networks of experts dedicated to quality of care or research in a specific field of Rheumatology. To date, more than 30 EULAR study groups are active. The EULAR study group for Lung involvement in Rheumatic Musculoskeletal diseases was recently founded and is currently chaired by Anna-Maria Hoffmann-Vold (Norway), Olivier Distler (Switzerland) and Armando Gabrielli (Italy). It aims to bring together an international group of experts with a special interest in lung involvement and ILDs. The study group includes more than 40 rheumatologists, pulmonologists and more. It partly evolved from the EULAR task force "ERS/EULAR Clinical practice guideline on Connective tissue diseases with ILD". For the first time in a EULAR study group, the chairs decided to develop a network of early career researchers. The objective of this network would be to fulfill unmet educational needs, support and offer collabortive opportunities to its early careers members. The young network was created in May 2023 and is chaired by Puja Mehta (UK), Jens Vikse (Norway) and Pierre-Antoine Juge (France). The first action was to gather early career researchers intersted in participating to the network. A first call gathered more than 40 young european rheumatologists, pulmonologists and radiologists. Then, a survey was sent to these members to understand their expectations from the network. According to the answers, educational offers and projects will be created starting 2024. This young network has received support from the EMerging EUlar Network (EMEUNET) to develop their projects. If the network is a success, this could be further developped in other EULAR study groups that wish to builsd a netzork for their young members.

## S19-3

**Modifications of T cell phenotype with TYK2 Inhibitor and its implications for the treatment of Systemic lupus erythematosus (SLE)**

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Conflict of interest: None

Objective: SLE is characterized by an "immune imbalance" with increased Tfh and decreased Treg cells. Since T cell differentiation is cytokine-dependent, Jakinibs may correct the immune imbalance in SLE. We investigated the relationship between T cell phenotypes and SLE pathogenesis, and the effect of differential JAK selectivity on T cell subset using various Jakinibs. Methods: PBMC from 82 untreated SLE and 62 healthy donor (HD) were analyzed by flowcytometry. T cells in nephritis tissues were evaluated. Naive B and T cells were co-cultured to examine the effect on B cell, and IC50 were evaluated by STAT phosphorylation assay using various Jakinibs. To evaluate the differential inhibition by Jakinibs on Tfh and Treg differentiation, naive T cells were promoted into Tfh and Treg cells under each Jakinibs. Results: CXCR3+CXCR5+ICOS+CD3+CD4+-cells (Tfh1 cells) and plasmocytes showed the most significant difference between SLE and HD (p=<0.0001 respectively). Tfh1 positively correlated with SLEDAI and BILAG (r=0.221, p=0.005 and r=0.218, p=0.05) and increased in cases with active nephritis (p=0.015). Immunohistochemistry of nephritis showed infiltration of Tfh1. Co-culture of Tfh1 and naive B cells induced differentiation of T-bet$^+$B cells. All Jakinibs inhibited JAK2/TYK2-dependent IL-12-induced pSTAT1/4 in memory CD4 T cells. However, inhibition of JAK1/3-dependent IL-2-induced STAT5 phosphorylation was about 3.8- to 1000-fold lower in TYK2 inhibitors than others. When various Jakinibs were added under induction of Tfh1 by IL-12 and Treg by IL-2+TGF-β, Tfh1 were significantly inhibited by most Jakinibs, but Treg were retained only by TYK2 inhibitors and inhibited by others. Conclusions: Tfh1 cells have an ability of inducing T-bet$^+$B cell and expanded in active SLE. Unlike other Jakinibs, TYK2 inhibitor suppresses Tfh1 differentiation while preserving Treg differentiation. This suggests TYK2 inhibitor has the potential to efficiently correct the "immune imbalance" in SLE.

## S19-4

**From clinical observation to data analysis: a case report on IgG4-related kidney disease and evaluating infection risks of rituximab in anti-neutrophil cytoplasmic antibody-associated vasculitis through network meta-analysis**

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Conflict of interest: None

**1. IgG4-related tubulointerstitial nephritis;** A 73-year-old male with cerebral infarction, diabetes, and IgG4-related illness history exhibited reduced appetite and bilateral leg edema. Diagnostics included a CT scan revealing kidney, bile duct, and pancreatic abnormalities, and lab tests showing elevated IgG4, low complement levels, non-nephrotic proteinuria, and high creatinine. Kidney biopsy indicated chronic tubulointerstitial nephritis with a 20% IgG4/IgG ratio. The patient improved with glucocorticoid therapy and subsequent low-dose glucocorticoids and mycophenolate mofetil. Diagnosis of IgG4-related kidney disease was confirmed by pathological, serological, radiological data, meeting EULAR

criteria. Treatment mainly involved prednisolone, sometimes combined with mycophenolate mofetil, typically improving kidney function. **2. Rituximab and infection-related risk in anti-neutrophil cytoplasmic antibody-associated vasculitis: a systematic review and pairwise and network meta-analysis;** In this systematic review, incorporating both pairwise and network meta-analyses, we assessed the infection risk associated with rituximab (RTX) in treating anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), which encompasses granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic GPA (EGPA). Our analysis drew upon data from eight randomized controlled trials (RCTs) for the network meta-analysis and five RCTs for the pairwise analysis, spanning January 1998 to December 2023. The objective was to evaluate the relative risk (RR) of serious infections in patients treated with RTX compared to those receiving alternative treatments such as azathioprine (AZA), cyclophosphamide (CYC), and the CYC-AZA combination. The comprehensive analysis involved 800 participants in the network analysis and 623 in the pairwise analysis. Results indicated that the RR of serious infections associated with RTX did not show a significant difference compared to AZA, CYC, CYC-AZA, and placebo. Consequently, RTX appears to be a safe option for managing AAV.

## S19-5

**Omics analysis of severe complications of autoimmune diseases**

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Conflict of interest: Yes

Systemic autoimmune rheumatic diseases (SARD) sometimes complicate severe life-threatening conditions, such as interstitial lung disease (ILD) and secondary hemophagocytic lymphohistiocytosis (sHLH). Both ILD and sHLH are heterogeneous syndrome driven by different diseases and immune cells. This complexity provides a challenging field for elucidating the mechanism of these conditions. Some ILD patients develop progressive fibrosing interstitial lung disease (PF-ILD) despite immunosuppressive treatment, but it is difficult to predict which patients develop PF-ILD. We analyzed comprehensive gene expressions of immune cells in bronchoalveolar lavage fluid (BALF) from ILD, bone marrow (BM) from sHLH, and blood from both patients by using single-cell RNA sequencing, multi-color flow cytometry and ELISA. We found that alveolar macrophages (AMs) are the most abundant cell types in BALF of PF-ILD patients. We further classified AMs and neutrophils into more detailed subsets based on their gene expression patterns. In PF-ILD patients, we found increased $CXCL10^{+}$, $CXCL8^{+}$ AMs and complement activation associated genes were upregulated in AMs. Moreover, we found increased $MMP\text{-}9^{+}$ and immature neutrophils, which were reported to be associated with severe COVID-19 pneumonia, in the blood of PF-ILD patients. Differentially expressed gene analysis revealed high levels of *high mobility group box (HMGB)-2*, *IL-1β*, and complement activation associated genes in AMs in PF-ILD patients. On the other hand, SARD-induced sHLH raised neutrophils while malignancy-induces sHLH raised lymphocytes in BM. We also detected one of monocyte subsets that overexpressed phagocytosis-related genes despite the etiology of sHLH. In conclusion, innate immune abnormality is associated with severe complications of SARD, PF-ILD and sHLH. Innate immune cell subpopulations and differentially expressed genes on BALF or BM immune cells would be potential biomarkers or therapeutic target of PF-ILD or sHLH, respectively.

## S19-6

**EMEUNET- aspirational goals for a harmonised community**

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Conflict of interest: None

Established in 2009, the EMEUNET (Emerging EUropean NEtwork) emerged with a visionary goal: to integrate highly skilled and dynamic young professionals into all activities conducted by EULAR. Our diverse membership comprises clinicians, basic scientists, epidemiologists, and health professionals-welcoming individuals under 40 years old with a keen interest in Rheumatology. Looking ahead, we aspire to forge collaborative initiatives in partnership with JSTAR with shared objectives to synchronize the online digital community, fostering seamless knowledge exchange and promoting academic growth for young rheumatologists and researchers on a global scale.

# Educational Lecture

## EL1

**Pathogenesis and novel management of immune-mediated TTP**

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Conflict of interest: Yes

Thrombotic thrombocytopenic purpura (TTP) is a fatal disease in which platelets and von Willebrand factor (VWF) thrombi in microvessels throughout the body. More than 90% of patients die if untreated, but remission rates have increased to more than 80% since plasma exchange was introduced. The diagnosis of TTP is made by unexplained hemolytic anemia and thrombocytopenia with a marked decrease in ADAMTS13 activity, a VWF-cleaving protease, to less than 10%. Congenital TTP is caused by a mutation in the ADAMTS13 gene, whereas acquired TTP is caused by the production of autoantibodies against ADAMTS13, resulting in a marked decrease in ADAMTS13 activity. Therefore, acquired TTP is also referred to as immune-mediated TTP (iTTP). As iTTP is an autoimmune disease, it has been reported since the early 2010s that the disease-susceptible HLA in Caucasians is DRB1*11. We identified DRB1*08:03 as a genetic risk factor for iTTP in Japanese patients. iTTP has been treated with plasma exchange and steroid therapy since the 1990s, and a new treatment, caplacizumab, will be available even in Japan in 2023. Caplacizmab is an antibody-drug called nanobody against the VWF A1 domain and has been reported to reduce the frequency of plasma exchange and mortality.

## EL2

**Differential diagnosis and treatment of pediatric rheumatic diseases**

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Conflict of interest: None

Rheumatic diseases that manifest in childhood are called pediatric rheumatism. Some of these conditions are called "childhood-onset" diseases since they resemble rheumatic diseases that typically emerge in adulthood, while others are called "juvenile" diseases due to distinct disease concepts compered to their adult manifestations. Juvenile idiopathic arthritis (JIA) is a term conceived at a time when arthritis was difficult to control, and long-term treatment of joint disease was the focus of medical care. It includes adult-onset Still's disease, rheumatoid arthritis, and various types of spondylarthritis. Current treatment protocols vary based on the underlying pathological conditions, making classification of subtypes crucial. However, there are rare cases where accurate subtype diagnosis at onset is difficult, and the patient may be diagnosed with a different subtype until adulthood. In such cases, the subtype should be reevaluated after the transition to adulthood. Furthermore, diagnosing JIA in children is more difficult than in adults due to a lack of ability of children to articulate symptoms in detail. Also, some medications approved for use in adults lack approval for pediatric use due to insufficient efficacy and safety in this cohort. In medical practice, dealing with patients who transition from pediatric rheumatic care to adult care, questions may arise among physicians unfamiliar with pediatric rheumatic diseases. In this lecture, I will discuss the differential diagnosis and treatment of pediatric rheumatic diseases.

## EL3-1

**Optimal Surgical Intervention for RA Upper Limb Surgery ~Considering the Synergistic Effect with Drug Treatment~**

Natsuko Nakagawa
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Conflict of interest: Yes

Recent advances in drug treatment for rheumatoid arthritis (RA) are expected to have the potential to suppress and repair joint destruction. There has also been a change in RA orthopedic surgery, such as the direction of an increase in small joint surgery. In order to bring out the effects of both appropriate surgical intervention and drug treatment and surgical treatment, the understanding and cooperation of internal medicine doctors are indispensable, and the timing of referrals is important. In this study, we will consider the synergistic effect of RA upper limb surgery with optimal surgical intervention and drug treatment. In RA, inflammation may remain in some joints even if the disease activity is good, and in addition to the problem of subjective symptoms such as pain, if left untreated, joint destruction and deformity may occur, which can cause functional impairment. There is also the option of actively considering synovectomy for cases where conservative treatment is ineffective, rather than intensifying drug treatment only for minority joint symptoms. This treatment strategy can not only maintain and improve function, but also prevent future deformities, so the timing of therapeutic intervention is an important point. On the other hand, even if tight control by drug treatment has been achieved, there are still situations where joint destruction or deformity remains in some joints. In addition, even if the inflammation subsides, joint destruction and deformity may progress. It is necessary to deal with destroyed joints by improving their function by arthroplasty and artificial joint replacement. In functional reconstruction surgery, it is necessary to consider the situation of adjacent joints and make a surgical plan. Since the deformity of the hand is often particularly noticeable, surgical treatment may be required not only for functional impairment but also for cosmetic problems. In addition, if the deformity is mild, joint-preserving surgery is also indicated, so early intervention is desirable if possible. Timing is also important in this regard. In cases where appearance is a problem, carefully plan by considering how far you want to go, that is, the needs from the patient's side. RA upper limb surgery is expected to expand and become more sophisticated in the future, but there are still many difficulties that need to be examined. In the future, we would like to actively devise and perform surgeries with higher hurdles.

## EL3-2

**Appropriate Surgical Intervention in the Treatment of Rheumatoid Arthritis - Lower Extremity**

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Conflict of interest: None

Drug therapy for rheumatoid arthritis (RA) has made great strides. Joint destruction is said to be controlled and the incidence of joint surgery is decreasing. On the other hand, not all patients are or can be treated with the so-called T2T treatment strategy. Even when they are implemented, only a limited number of patients achieve remission, and joint destruction is not always completely suppressed. Therefore, there will always be a certain number of patients who will require surgical treatment. In the conventional setting of high disease activity and many joint disorders, the impact of improving a single joint disorder is relatively low. The Guideline for RA 2020 states that surgical and rehabilitative therapies, in addition to thorough drug treatment, should be considered as part of a nonpharmacologic treatment algorithm. indicated in the algorithm for drug therapy. As the effectiveness of RA treatment improves, not only improvement in so-called objective measures but also improvement in patients' subjective assessment of the disease is required. The systematic review of RA orthopedic surgery also showed an improvement in patient subjective evaluation. This has led to the recommendation of surgical therapy in the RA Practice Guidelines 2020. In recent years, we have reported improvements in patient satisfaction with achieving functional remission by HAQ-DI or with eliminating frailty. Timing of surgery is also important to achieve better surgical outcomes. In this educational lecture, I would like to discuss the effectiveness of lower extremity surgery and the timing of surgery to maximize the therapeutic effect.

## EL4

**Unraveling Complexities: Biologics, Treat-to-Target, and the Future of Large Vessel Vasculitis**

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Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Conflict of interest: Yes

Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are classified as large vessel vasculitis (LVV), but these diseases differ in genetic background, pathogenesis, and clinical aspects. Biologics (Bio) are widely used in rheumatoid arthritis and ANCA-associated vasculitis. Since the GiACTA and TAKT trials demonstrated the efficacy of IL-6 inhibitors in LVV, clinicians have incorporated Bio into LVV treatment. However, many questions regarding its use remain unanswered. There is a lack of information on evidence-based medicine (EBM) in the field of LVV. This lecture will discuss the diagnosis, treatment, and treat-to-target (T2T) of LVV based on EBM. In particular, the latest evidence after GiACTA/TAKT will be presented and explained clearly with cartoons. New classification criteria for GCA and TAK have been published by the United States (ACR) and Europe (EULAR) and have attracted much attention, but their utility has not yet been fully confirmed. This talk will address papers validating these classification criteria: while effectiveness has been reported for GCA, specificity for TAK has been noted to be reduced compared to the 1990 version. The ACR and EULAR treatment guidelines include tocilizumab (TCZ), abatacept, and TNF inhibitors (TNFi), but their use has not yet been firmly established. GCA is particularly common in the elderly, and the risk of Bio is also a concern. In this talk, I will present real-world data on TCZ use after GiACTA/TACT; an analysis of TCZ use limited to GCA patients over 80 years of age suggests its efficacy and safety. T2T has been advocated for a variety of diseases. Recently, T2T for GCA has been proposed from Europe, and T2T and treatment algorithms for GCA and TAK have been published in Japan by the MHLW research group. Finally, early diagnosis and effective treatment are essential to improving patients' quality of life. Recent advances in diagnosis and treatment will make this feasible.

## EL5

**Chromosomal and genetic abnormalities that cause joint disorders and pain attacks in autoimmune and rheumatic diseases**

Yasuji Inamo
Teikyo University of Science, Tokyo, Japan

Conflict of interest: None

We review the pathogenesis of rheumatic and collagen diseases and joint disorders from chromosomal abnormalities as chromosomes are carriers of genes. We will also outline pain attacks due to genetic abnormalities in view of hereditary pain-related diseases. In Klinefelter syndrome (47, XXY), and SLE and Sjogren's syndrome which are common in women (46, XX), genes escaped from X chromosome inactivation (XCI), and skewed XCI are present. It is thought to be a factor in the onset of the diseases. Because increased expression of several X-linked immune-related genes is involved in the onset of autoimmune diseases (AD). This is thought to be due to increased expression of X-linked immunity-related genes due to skewed inactivation of the second X chromosome, which is normally inactivated in women. The effect of XCI on self-tolerance in the thymus has also been associated with sex bias in the development of AD. Furthermore, in SLE, abnormal XCI of T and B cells has also been revealed, which may provide new hints for the development of AD. Other chromosomal abnormalities as follows, Turner syndrome (45, X) is rarely causes SLE and complicated by autoimmune thyroid disease and juvenile arthritis. Down syndrome (21-trisomy)-associated arthritis (considered a type 1 interferonopathy), trisomy on the short arm of chromosome 9 (lupus-like disease due to increased type 1 interferon), and juvenile idiopathic arthritis in both 18p- and 18q- syndrome. Regarding pain attacks, we will mainly review hereditary pain-related diseases. Sodium channel abnormalities (Nav 1.7) (erythromelalgia, paroxysmal extreme pain disease), Nav 1.9 abnormalities (familial episodic (limb) pain syndrome, familial episodic pain syndrome), hereditary sensory autonomic neuropathy (HSAN-IV, HSAN-V), Fabry disease, small fiber neuropathy caused by genetic abnormalities, familial cold autoinflammatory syndrome. Chromosomal abnormalities provide hints for elucidating various pathological conditions. Furthermore, we plan to give an educational lecture with content that emphasizes a renewed awareness of pain attacks caused by a wide variety of genetic abnormalities.

## EL6

**Evidence based prevention for surgical site infection on clean surgery**

Koji Yamada[1], Sakae Tanaka[2]
[1]Department of Orthopaedic Surgery, Nakanoshima Orthopaedics, Kanagawa, Japan, [2]Orthopaedic Surgery, Department of Orthopaedic Surgery, The University of Tokyo, Tokyo, Japan

Conflict of interest: None

This talk will cover the update of SSI prevention especially focusing on its economical impact, the recent CDC/WHO/MSIS guidelines, antimicrobial prophylaxis, anti-MRSA agents, decolonization, skin preparation, wound contamination prevention, wound irrigation, local antibiotics, and wound closures. In this talk, I would like to share some information I got from my experience visiting Prof Javad Parvizi during the summer of 2023.

## EL7

**Enhancing Productivity with the Power of Generative AI**

Satoshi Maki
Department of Orthopaedic Surgery, Chiba University, Graduate School of Medicine, Chiba, Japan

Conflict of interest: None

In recent years, the technology known as generative AI has gained significant attention, with the noticeable growth of large language models. Generative AI enables computers to "generate" new information or content based on data, with large language models acting as a good example. Models trained on medical-specific data have shown results that rival or even surpass the diagnostic capabilities of physicians. In this lecture, we will explore how to apply large language models in daily clinical practice and academic activities. We will discuss methods for resolving clinical queries quickly and based on evidence, conducting data analysis using Advanced Data Analysis in natural language, effective techniques for English proofreading and translation of research papers, creating drafts and illustrations for presentation slides efficiently, and managing lengthy texts exceeding 4,000 tokens. Additionally, we will address methods for pre-reviewing one's research papers and the optimal use of search AI. The progress in this domain is impressive, and the lecture will not only cover information available at the time of abstract was written but also introduce the latest topics. A deep understanding of large language models is crucial, and harnessing this innovative technology has the potential to elevate clinical capabilities and optimize research activities. ((Drafted with the assistance of ChatGPT))

## EL8

**Treatment of Rheumatic Diseases from the Perspective of Chronic Pain**

Tomoko Tetsunaga
Locomotive Pain Center, Okayama University Hospital

Conflict of interest: None

The International Association for the Study of Pain defined chronic pain as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage in 2022. In other words, in treating chronic pain, it is necessary to diagnose organic disease based on the patient's pain and distress. However, this can be particularly difficult in practice and sometimes requires a multidisciplinary approach with a multimodal evaluation. We started a consultation-type pain liaison outpatient clinic in 2012 in order to provide multidisciplinary evaluations of pain and to support patients who want to control their own pain. The representative diseases of the musculoskeletal system that cause chronic pain include osteoarthritis, osteoporosis, and rheumatic diseases. These diseases could occur alone or coexist. Therefore, treatment may only be given to a single disease with symptoms, and other co-morbid diseases may not be treated. To avoid such diagnostic delays, we evaluate the presence or absence of risk factors that affect musculoskeletal diseases that cause chronic pain, including not only physical aspects, but also psychological factors, lifestyle, and working conditions. In this lecture, we would like to introduce the diagnosis and treatment of rheumatic diseases from the perspective of chronic pain. We hope that it will be of some help for medical treatment starting tomorrow.

## EL9

**Understanding muscle MR images in idiopathic inflammatory myopathies**

Ken Yoshida
Division of Rheumatology, Department of Internal Medicine, The Jikei University School of Medicine, Tokyo, Japan

Conflict of interest: None

Idiopathic inflammatory myopathies (IIMs) are an autoimmune disorder with diverse phenotypes characterized by chronic inflammation of the skin, fascia, muscle, and lung. Recent advances in imaging technology have allowed MRI and ultrasonography to diagnose IIMs and to evaluate the disease activity. In this educational training lecture, I will focus on skeletal muscle MR images and explain how to read MR images in general, to distinguish fasciitis from chemical shift artifacts, and to differentiate myositis from other diseases including vasculitis syndrome that target skeletal muscle. Next, I will describe the evaluation methods for skeletal muscle MRI findings in IIMs. Although no evaluation methods for classification of a disease subtypes and prediction of clinical characteristics using skeletal muscle MRI have been established in IIMs, I will show the characteristics of skeletal muscle MRI findings corresponding to myositis-specific autoantibodies and the clinical presentation that can be predicted from skeletal muscle MRI findings based on the data analyzed at our institution. Finally, I would like to describe the relationship between skeletal muscle MRI findings and prognosis of rapidly progressive interstitial lung disease (RP-ILD) in anti-MDA5 antibody-positive dermatomyositis. Patients with anti-MDA5 antibody-positive dermatomyositis and RP-ILD must be treated with aggressive immunosuppressive therapy because of the poor prognosis. However, some patients have a good response to therapy and have a good prognosis. Prediction of such a favorable population would be beneficial from the perspective of avoiding the side effects of intense immunosuppressive therapy by reducing the intensity of treatment. I will also discuss the potential of skeletal muscle MRI findings as prognostic favorable and unfavorable factors for RP-ILD in anti-MDA5 antibody-positive dermatomyositis.

## EL10

**Multidisciplinary discussion in the management of connective tissue disease-associated interstitial lung disease**

Tomoyuki Fujisawa
Second Division, Department of Internal Medicine, Hamamatsu University School of Medicine, Hamamatsu, Japan

Conflict of interest: None

Interstitial lung diseases (ILDs) are a group of diseases that cause inflammation and fibrosis in the interstitium of the lungs, and encompass an extremely wide variety of diseases, including idiopathic interstitial pneumonias (IIPs) of unknown cause, connective tissue disease-associated ILD (CTD-ILD), pneumoconiosis, hypersensitivity pneumonitis, and radiation and drug-related ILD. ILDs are broadly classified into IIPs and ILD with a known underlying disease or cause (secondary ILD). CTD-ILD is as frequent as hypersensitivity pneumonitis in secondary ILD, and their proper diagnosis is extremely important to provide appropriate treatment. IIPs are classified into 9 major diseases, including idiopathic pulmonary fibrosis, and each disease has a different treatment strategy and prognosis, thus accurate diagnosis is important in clinical settings. The accuracy of diagnosis can be improved by multidisciplinary discussion (MDD), which includes respiratory physicians, radiologists, and pathologists. Currently, MDD is considered as the gold standard for the diagnosis of IIPs in international IIPs guidelines. Recently, the significance of MDD is recognized in the diagnosis of ILD, and MDD including rheumatologists is important for the diagnosis of CTD-ILD. In a study of 90 consecutive ILD cases, the frequency of CTD-ILD diagnosis increased from 10% to 21% after MDD performed by a multidisciplinary team consisting of a respiratory physician, a rheumatologist, a radiologist, and a pathologist (Respirology 2016). In addition, there is a type of CTD-ILD that develops CTD after the initial IIPs diagnosis during their clinical course. IPAF is a concept that encompasses ILD that does not meet the diagnostic criteria for a specific CTD but has some features suggestive of CTD. It will also be important to perform MDD repeatedly if necessary to provide appropriate management for patients with ILD.

## EL11

**The History of Rheumatoid Arthritis**

Jinju Nishino
Department of Orthopaedic Surgery, Towa Hospital

Conflict of interest: None

RA is a strange disease. We cannot confirm RA in the ancient texts or Egyptian mummies. RA deformities were found in the paintings of the 16th century. However, the ancient Indian's skeletons in the New World have the bone destructions which were typical in RA. For this reason, there is a hypothesis that RA is endemic in Ohio, and that Vector arrived in Europe during the Age of Discovery after 1492 and then spread throughout the world. Bacteria, viruses, smoking, etc. have been proposed as vectors, but it is not clear. The first scientific description of RA was by Augustine-Jacob Landre Beauvais in 1800, but it took 60 years for the disease to be named "Rheumatoid Arthritis." We could not distinguish among RA, osteoarthritis, Gout, tuberculosis. The first academic descriptions in Japan were found in the 1930s. The Disease classification criteria were proposed by ARA in 1956. There were no causative drugs and symptomatic treatments such as physical therapy, analgesics drugs, Opium, and corticosteroids had long been the mainstream. The dramatic effects of corticosteroid led to the developers winning the Nobel Prize in a short period of time, but their side effects caused tragedy for them. Gold sodium, the oldest csDMARDs, were originally used to treat tuberculosis due to their bacteriostatic properties. Other csDMARDs are also often diverted from drugs to treat other diseases. This reflects the struggle of the medical staffs who treat RA as they searched for a cure. Methotrexate, the mainstay of anti-RA drugs, is also a repurposed treatment protocol for psoriasis from the dermatology. As the analysis of the mechanism of inflammation in RA progressed, Infliximab was finally reported in 1993. It was a major step in modern RA treatment. Although many efforts have been made in orthopedic treatment of RA over the past 100 years, but there are still exist unmet needs. I describe the overview of RA focusing on history.

## EL12

**Health Economics**

Hideo Kunitoh
Department of Medical Oncology, Japanese Red Cross Medical Center, Tokyo, Japan

Conflict of interest: None

Article 25 of the Constitution of Japan says, "All people shall have the right to maintain the minimum standards of wholesome and cultured living". What is guaranteed here is "minimum" standards of living. As for medical services/medical care, however, we have never thought about "minimum". We have tried to, and successfully did so far, provide "optimal" medical care for everybody, since (we think) everybody's life is equally priceless. It is not for us health care providers to think about cost. It is a shame for us physicians to think about money, in treating our patients before us. With the advent of highly effective, but exorbitant-priced drugs, both in oncology, rheumatology and everywhere, our patients enjoy far better outcomes as compared to, say, only a decade ago. But it is also associated with skyrocketing, unsustainable cost. At ASCO (American Society of Clinical Oncology) 2012 Educational lecture, Dr. Ian Tannock of Princess Margaret Hospital, Toronto, pointed out that progress in colon cancer therapy achieved 2-fold prolongation of median survival, with 340-fold cost. And that is even before we know immune-checkpoint inhibitors! Now we know that. But we did little, if any, for that. Increase of medical cost results from 1) progress of (medical) science and 2) aging population. Nobody is to blame for them, and nobody can stop them. Dr. Leonard Saltz of Memorial Sloan Kettering Cancer Center, New York, says "we all know we are in an inflating bubble that can't last forever. Whenever I say that oncology care costs are unsustainable, no one disagrees, but no one wants to do anything about it, because none of the solutions are easy." Also in rheumatology, right? We cannot go on with what we are currently doing, because it is unsustainable. We have to think about the money we spend. Otherwise, we will make ourselves Francisco Goya's "Saturn devouring his son". Do you want to become such a monster?

## EL13

**How to evaluate disease activity in patients with systemic sclerosis?**

Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine

Conflict of interest: Yes

Systemic sclerosis (SSc) remains a refractory condition with poor functional and survival outcomes. A number of therapeutic options that have been proven to be effective in preventing progression of the disease are now available in SSc patients, but treatment strategy has not yet been established. The pathogenesis of SSc includes microangiopathy and chronic inflammation, leading to accumulation of extracellular matrix and resultant irreversible fibrosis resulting in distortion of the normal tissue architecture. This pathogenic process is analogous to that observed in rheumatoid arthritis, in which persistent synovitis leads to articular cartilage and bone destruction, resulting in functional impairment due to joint deformity. Therefore, successful experiences in developing treatment strategy in patients with rheumatoid arthritis can be applied to SSc. These include early diagnosis and intervention, treat-to-target strategy, and disease modification. For this purpose, it is necessary to establish concept and definition of "disease activity", "low disease activity", and "clinical remission". A major challenge of development of these indices is diverse clinical course and distribution of organ manifestations, which makes it difficult to predict future progression early in the disease course. In this lecture, we introduce the global efforts for the development disease activity indices and treatment goals in SSc patients.

## EL14

**Dermatological perspectives on cutaneous manifestations of connective tissue diseases and vasculitis**

Tamihiro Kawakami
Division of Dermatology, Tohoku Medical and Pharmaceutical University

Conflict of interest: None

This lecture will provide rheumatologists, orthopedic surgeons, specialists, and dermatologists a better understanding of the cutaneous findings in patients with various connective tissue diseases, including vasculitis. We will review rheumatoid arthritis, pyoderma gangrenosum, vasculitis, dermatomyositis, systemic lupus erythematosus, scleroderma, Sjögren's syndrome, and adult-onset Still's disease, among others. We will note, in particular, the unique cutaneous manifestations that dermatologists may encounter. It is important for the rheumatologist and orthopedic surgeon to be familiar with the spectrum of cutaneous manifestations in these diseases to help prognosticate the likelihood of systemic disease and to ensure patients receive timely dermatologic care with the goal of controlling disease activity to prevent damage. Understanding these cutaneous expressions may lead to early diagnosis, prompt treatment, and lower morbidity and mortality for the affected patients.

## EL15-1

**What cybersecurity countermeasures medical institutions should consider? -IT governance and its medical safety-**

Atsuo Inomata
Cybermedia Center, Osaka University

Conflict of interest: None

The speaker was the chairman of the Cyber Attack Incident Investigation Committee at Osaka General Medical Center, and this committee released a report in order to reduce damage caused by future cyber attacks to whole of medical institutions. The important task of the cyber-attacks which such as ransomware and other malware to medical institutions are not technological, it's risk management for a organization. So the cause of this incident is the lack of IT governance within the organization itself. Therefore, in this my talk, I would like to address and mention what we should and can do now from the perspective of IT governance in the medical safety.

## EL15-2

**Medical safety starts with familiar security measures -First, know thyself**

Kenta Hagihara
Software Association of Japan (IntervaLink Co.,)

Conflict of interest: None

Cybersecurity feels difficult because it is invisible. However, cybersecurity is no different in concept from cold prevention or familiar safety measures. It starts with knowing yourself, and if you know your enemy, you can defend against most cyber attacks. It is important to maintain a vulnerability-free (Cyber hygiene) environment, like washing your hands, and to properly use antivirus functions as well as vaccines. On the other hand, there are more demands on organizations than ever before, including government guidelines. Learning from the cases of Tsurugi municipal handa hospital and Osaka General Medical Center, what security measures can be taken by individuals and organizations that are close at hand?What measures should medical institutions take to comply with the guidelines? And how far should they go? Focusing on security measures that can be implemented from tomorrow, this session will explain familiar and easy-to-understand security measures.

## EL16

**Rehabilitation medicine as infrastructure for medicine care, and social welfare service**

Toshikazu Kubo
Kyoto Prefectural University of Medicine

Conflict of interest: None

In Japan, which has become a super-aging society, it is no exaggeration to say that rehabilitation medicine has become an area that deals with diseases, disorders, and pathological conditions related to almost all clinical fields. On this background, in 2017, the Japanese Society of Rehabilitation Medicine redefined rehabilitation medicine as medicine that grow human activities. In other words, based on the conventional interpretation of restoring physical and mental functions that have deteriorated due to illness or trauma and overcoming disabilities, activities of human life are focused on. Thease are combinations of daily activities such as getting up, sitting, standing, walking, using hands, seeing, listening, speaking, thinking, getting dressed, eating, defecating, sleeping, etc. By promoting daily activies, it leads to activities at home and activities in society at school, work, sports, etc. In recent years, there has been a demand for enhancement of rehabilitation medicine in the acute phase, recovery phase, and maintenance phase. Therefore, rehabilitation medicine is now a field that is positioned as the infrastructure for medicine, care, and social welfare service. It is important to accurately understand these trends.

## EL17

**Osteoarthritis: Current Knowledge and Treatment from the Orthopaedic Surgeon's Perspective**

Stuart B Goodman
Department of Orthopaedic Surgery, Stanford University, Stanford, CA, USA

Conflict of interest: None

Osteoarthritis (OA) is a "wear and tear" disease of diarthrodial joints that affects many middle aged and elderly individuals worldwide. According to one source (Lancet Rheumatology 2023; 5: e508-22), 595 million individuals or 7.6% of the global population had OA in 2020. The age-standardized value for "Years Lived with Disability" (YLD) globally was determined to be 255 per 100,000 in 2020, an increase of almost 10% over the last 30 years. These numbers will rise substantially as the population continues to grow in number and ages in general, resulting in a major financial and social health care burden worldwide. Patients with OA are generally treated first by their primary care physicians, but rheumatologists and orthopaedic surgeons often bear the brunt of treating patients with chronic, recalcitrant, and debilitating OA. This lecture will address 3 questions from the perspective of one orthopaedic surgeon who has treated patients with OA of the hip and knee for over 30 years. 1. Which *non-op-*

*erative* interventions for the treatment of OA are evidence-based? 2. Which *operative* interventions for the treatment of OA are evidence-based? 3. For advanced OA of the knee, which patients should be included or excluded from undergoing knee arthroplasty, based on risks, benefits and outcomes? I will then discuss some of the unmet clinical and research opportunities for diagnosing and treating OA in the future. Finally, I will describe our laboratory's ongoing work using an engineered "Joint-on-a-Chip" model for performing experiments using human cells to further understand the biological mechanisms and critical pathways involved in OA. The model is also capable of being used for high throughput screening of potential disease modifying drugs for the treatment of OA. Currently, no such drugs exist. This model will provide detailed preclinical information on potential drugs and other interventions that could be tested subsequently in appropriate animal models and human clinical trials.

## EL18

**Perioperative Risk Mitigation: Guideline for Perioperative Care of the Rheumatic Disease Patient**

Susan M Goodman
Hospital for Special Surgery, Weill Cornell Medicine, NYC, USA

Conflict of interest: Yes

The majority of rheumatic disease patients undergoing orthopedic surgery are receiving potent medications to control their illness, and many of these medications such as biologics or glucocorticoids increase the risk of infection or may affect wound healing, such as glucocorticoids. In addition, most patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) have active disease which may also increase the risk of surgical complications. This talk will focus on patients with RA and SLE undergoing arthroplasty, as most available published research including observational studies describes these patients, but will include other rheumatic disease populations where data is available. I will first discuss the 1. Ongoing demand for arthroplasty despite improvements in the status of these patients due to more effective treatments, and the changes in the characteristics of these patients when they undergo surgery attributable to these effective therapies. Next, we'll discuss 2. The adverse events that are reported in patients with rheumatic diseases, and the risk factors - some potentially modifiable- for these adverse events. We will include information informing American College of Rheumatology/ American Association of Orthopedic Surgeons (ACR/AAHKS) recent guideline regarding timing of surgery and modifiable risk factors where there is applicability to patients with rheumatic diseases. Finally, we'll review 3. The current ACR/AAHKS guideline for management of anti-rheumatic medications in the perioperative period and the rationale for the updated recommendations. These recommendations provide a template to begin a shared decision-making process with our high risk patients as they approach surgery, so an appropriate decision can be made for each patient, aligning their expectations and optimizing their outcomes.

## EL19

**Application and creation of clinical guidelines, especially in the area of rheumatoid collagen disease**

Norio Watanabe[1,2]
[1]Cochrane Japan, [2]Soseikai General Hospital

Conflict of interest: None

Clinical practice guidelines provide recommendations that are considered optimal for treating a certain disease or subgroup of patients within that. This requires a systematic review that assesses the quality of evidence obtained from existing research in the area and synthesizes it. Furthermore, even if there is a good systematic review, the results do not necessarily translate into recommendations. It is necessary to ensure applicability and fairness in the places and times in which the guidelines are used. It is also necessary to consider how limited medical resources can be used fairly and to the maximum extent possible. In this presentation, we will introduce how to create clinical guidelines and their limitations from the user's perspective, including their significance and how to use them. In particular, the presenter has been indirectly involved in the creation of guidelines in the area of rheumatoid collagen disease, and will also discuss the actual development stage.

## EL20

**Pathophysiology of IgG4-Related Disease and Potential New Treatment Options**

Motohisa Yamamoto
Department of Rheumatology and Allergy, IMSUT Hospital, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan

Conflict of interest: None

It has been nearly two decades since the concept of IgG4-related disease was first established. Diagnostic and classification criteria have been defined in Japan, Europe, and the United States, making the diagnosis of IgG4-related diseases more straightforward in everyday clinical practice. However, despite the disease's positive response to glucocorticoids, it remains prone to relapses and challenging to cure. To address this issue, it is imperative to comprehend the underlying pathogenesis of the disease. Although some disease-related genes, such as HLA-DRB1 and FCGR2B, have been identified through nationwide genome-wide association analyses, numerous questions about the pathophysiology persist, given the disease's association with various immune irregularities. Nevertheless, ongoing analysis of affected organ tissues continues to unveil crucial insights. It has long been recognized that IgG4-related disease involves elements of allergic inflammation, specifically type 2 helper (Th2) inflammation. Follicular helper T cells (Tfh) contribute to the formation of germinal centers in secondary lymphoid tissues and the selection of high-affinity B cells, leading to their differentiation into memory B cells and plasma cells. Meanwhile, peripheral helper T cells (Tph) play a role in the formation of ectopic germinal centers, which are characteristic of this disease. Furthermore, CD4-positive cytotoxic T cells (CD4+CTLs) are implicated in fibrosis, and a recently identified T-cell subset is presumed to be significant in the disease's pathogenesis. B-cell lineage also plays a crucial role, with several autoantigens identified, and the discovery of oligoclonally proliferating plasma cells producing IgG4 in peripheral blood. In this presentation, we will review the existing reports on the pathogenesis of IgG4-related disease, categorizing them into acquired and innate immune systems. Additionally, we will explore the potential for novel treatment options for this disease.

## EL21

**Renal pathology of ANCA-associated vasculitis and its management**

Hironari Hanaoka
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: None

Anti-neutrophil cytoplasmic antibody-related vasculitis, also known as ANCA-associated vasculitis, is a type of vasculitis in which ANCA plays a role in the pathogenesis. This disease primarily affects small blood vessels, particularly capillaries, causing necrotizing vasculitis. Kidneys, being rich in blood vessels, are one of the major target organs affected by ANCA-associated vasculitis. ANCA-associated vasculitis includes three conditions: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Each of these conditions presents distinct renal manifestations. In the early stages, necrotic lesions are segmented, and in severe cases during the acute phase, they result in diffuse crescentic glomerulonephritis. Crescentic glomerulonephritis can evolve from cellular to fibrocellular crescents, and ultimately, fibrous crescents, leading to glomerular sclerosis. Not only glomeruli but also arterioles, interlobular arteries, and arcuate arteries may exhibit necrotizing vasculitis. In 2010, a renal pathology subanalysis of a preceding clinical trial proposed four pathological classifications: Sclerotic, Focal, Crescentic, and Mixed class. These classifications are widely used in clinical practice as they correlate with renal outcomes. Presently, the mainstay of induction therapy for remission includes a combination of glucocorticoid and either cyclophosphamide or rituximab. The effectiveness of azathioprine and rituximab has been demonstrated for maintenance therapy. Additionally, selective C5a receptor antagonist, avacopan, has received insurance approval, supporting glucocorticoid reduction. Furthermore, recent studies have shown the usefulness of protocols with reduced initial glucocorticoid doses, leading to the development of safer treatment strategies. In this context, we will discuss the pathology and management of ANCA-related nephropathy.

## EL22-1

**Advances in surgical treatment for rheumatic diseases in the digital age**

Yutaka Inaba, Hyonmin Choe, Hiroyuki Ike, Koki Abe
Department of Orthopaedic Surgery, Yokohama City University, Yokohama, Japan

Conflict of interest: Yes

Advances in drug treatment for rheumatoid arthritis (RA) have been dramatic, with new drugs being developed, increasing treatment options, and reporting better outcomes. These advances in drug treatment have made it possible to control arthritis, and the number of cases that progress to significant joint destruction is decreasing. As a result, the ADL and QOL of RA patients have improved, and large joint surgeries have decreased. However, a certain number of cases still require surgery, and as the ADL of all RA patients has improved, good surgical outcomes are expected. Orthopedic surgery has greatly advanced with the introduction of advanced computer technology. Surgery, which has developed greatly through the accumulation of anatomical knowledge, has made further progress through improvements in surgical equipment and less invasive techniques and is now entering the era of digitalization. Digitalization of surgery refers to the replacement of decision-making with digital information, which is traditionally based on the surgeon's senses and experience. Although we have not yet reached this point, it is true that this is a future trend. Preoperative planning for total hip arthroplasty, a typical lower extremity joint surgery, has made it possible to plan component placement locations that are less likely to dislocate during activities of daily living. CT-based navigation is useful for accurately carrying out these preoperative plans, and surgery can be performed with an accuracy of 2 to 3 degrees in angle and 2 to 3 mm in distance. In recent years, robotic surgery has been introduced, making it possible to perform more precise and safer surgeries. Similarly, navigation and robots can be used in knee replacement and spine surgery, making them safer and more accurate. Surgical treatment has also progressed dramatically, making it possible to achieve good ADL and QOL after surgery. In this lecture, we will introduce advances in the surgical treatment of rheumatic diseases in the digital age.

## EL22-2

**Current Status and Future Perspectives of Computer Technologies in Joint Surgery**

Masaki Takao
Department of Orthopaedic Surgery, Ehime University Graduate School of Medicine

Conflict of interest: Yes

Computer-assisted orthopedic surgery (CAOS) has been developed since 1990 with the aim of reducing surgeons' human errors, increasing surgical accuracy, and improving clinical outcomes. Current trends include: 1. robots, 2. compact navigation 3. surgical training using augmented virtual reality (VR) technology and augmented reality (AR) technology; 4. clinical use of artificial intelligence (AI). The development of robots in hip surgery has a long history, dating back to 1986 when IBM developed ROBODOC, an active robot that automatically implanted a femoral component of THA. In recent years, a semi-active robot that controls acetabular reamer and acetabular component implantation has been developed, acquired by Stryker in 2013, and is now popular worldwide as MAKO Smart Robotics. In Japan, its use in THA was approved by the Pharmaceutical and Medical Device Agency in 2017. The number of hospitals that have introduced MAKO Smart Robotics is increasing. In 2012, CT-based navigation surgery became covered by Japanese medical insurance for artificial joint replacement, and its introduction has progressed. Since the late 2010s, cameras and sensors have become smaller and more precise, and the development of compact navigation systems has progressed. The usefulness of CAOS in surgeon education has been widely reported, but in recent years, the importance of virtual practical training using VR and AR technologies has been attracting attention. This level of surgical training using VR and AR technologies is limited to the novice's level, and it is expected to develop in the future. Reports of AI in hip surgery have been increasing since 2019. AI that predicts function after artificial joint replacement surgery, short-term complications, and length of hospital stay is being reported one after another. Evaluation of its usefulness in actual clinical practice and social implementation are future issues. Applying AI technology to clinical research and automatically analyzing large amounts of medical databases to obtain new knowledge is also attracting attention.

## EL23

**Basic Immunology**

Sachiko Miyake
Department of Immunology, Juntendo University Graduate School of Medicine

Conflict of interest: None

Immunology is characterised by the early application of new discoveries to treatment, so it is important to update our knowledge from time to time. In rheumatology in particular, the development of various molecularly targeted drugs related to immunology has led to dramatic advances in the treatment of rheumatoid arthritis. Targeted molecules include and auxiliary stimulatory molecules on the cell surface of immune cells and cytokines such as TNFalpha, IL-6. Moreover, tyrosine kinase (JAK), a molecule that transduces stimuli from its receptors into cells, has also attracted attention. To use them effectively, it is important to understand the role of these molecules in the immune response. This lecture will provide an overview of the basics of immunology. Characteristics of innate and acquired immunity; pattern recognition receptors, cytokines and their signaling and function of different helper T cells, regulation of T cell activation by co-stimulatory molecules will be discussed.

## EL24

**Practices for infection control based on the JCR COVID-19 registry**

Yasutaka Kimoto
Department of Clinical Immunology Rheumatology, and Infectious Disease, Kyushu University Hospital

Conflict of interest: None

The COVID-19 pandemic drastically changed our social life. At first, there were no established treatments or therapies, and medical resources were lacking. However, after nine expansions, an understanding of the pathogenesis, laboratory, and therapeutic and preventive methods have been actively developed and adopted quite promptly. As a result, the latest COVID-19 infection control strategies are changing constantly. The Japan College of Rheumatology has been conducting efforts on COVID-19 since the early stages of the pandemic, and information on COVID-19 cases was collected from rheumatology teaching hospitals all over Japan. (JCR COVID-19 Registry) Cases were collected from the Wuhan strain to the omicron period. As a result, risk factors for severe disease were extracted and prognosis was improved by changes in strains and expansion of vaccination for SARS-CoV-2. As in the general population, the frequency of severe cases has decreased due to changes in the prevalent virus strains. However, a certain number of severe cases are seen due to an increase in the number of infections. Therefore, annual vaccination with the SARS-CoV-2 vaccine, which is expected to reduce severe cases, may be useful. The use of antiviral drugs should be considered in cases considered to be at high risk of severe disease due to the presence of rheumatic diseases, unvaccinated patients, and coexisting diseases. Although it has been reclassified as Class 5 under the Infectious Disease Control Law and is regaining its usual status, patients with rheumatic diseases need to continue to maintain appropriate protection against contact infections. For these reasons, continuous patient education on infection control is necessary. Medical institutions that manage patients also need to continue to maintain appropriate standard precautions and other hospital infection control practices.

## EL25-1

**Scaffold-free Bio-3D Printing for Solid organ fabrication**

Koichi Nakayama
Center for Regenerative Medicine Research, Saga University, School of Medicine, Saga, Japan

Conflict of interest: Yes

Fabrication of transplantable 3D tissue or organ in vitro is one of the major goals in regenerative medicine. Several scaffold-free systems have been developed to avoid potential side effects caused by scaffold mainly used to build three-dimensional tissue construct. They seemed to be still unable to produce fine structures without contamination from exogenous biochemical materials. Inspired from bone fracture treatments in orthopedic surgery, we established a simple method to fabricate 3D scaffold-free cell construct. This method use spheroids and temporal fixator which enable placement of various types of three-dimensional cells into desired xyz positions without need of hydrogels or biochemical reactive materials. We also developed a robotic system for scaffold-free cell construction. By using this "Bio 3D printer", we successfully fabricated cartilage, blood vessels, liver, and so on. In addition, some of pipe-lines are already start clinical study and clinical trial. Near future, we may be able to build living organs for autologous transplantation by using this scaffold free Biofabrication system. This multi-cell construct may be useful research tools for drug development.

## EL25-2

**Frontiers in Regenerative Medicine for Rheumatologists: Pathology of Osteoarthritis of the Knee and Cell Therapy for Meniscal Lesions**

Ichiro Sekiya
Center for Stem Cell and Regenerative Medicine, Tokyo Medical and Dental University, Tokyo, Japan

Conflict of interest: Yes

Osteoarthritis of the knee is a multifactorial disease that causes knee pain and walking disabilities due to the wear of joint cartilage. 3D MRI image analysis has revealed that in medial osteoarthritis, the medial meniscus extruded, and cartilage damage extends from the inner edge of the medial meniscus. This extrusion plays a direct role in the progression of the disease. One of the causes on is meniscal injury. Degenerative meniscal tears, which are particularly common in middle-aged and older individuals, occur due to repeated stress and are characterized by flap and horizontal tears at the boundary between the middle and posterior segments of the meniscus. For degenerative meniscal tears accompanied by mechanical symptoms such as instability, surgery is selected. In Japan, meniscus surgery for those over the age of 40 consists of 80% meniscectomy, with 32,000 cases performed annually. However, many comparative studies report that the clinical scores one year after meniscectomy do not differ from those of sham surgery. Furthermore, removing the meniscus reduces the load distribution function and irreversibly accelerates the progression of osteoarthritis. Meniscal repair surgery carries a high risk of re-operation. We are focusing on the high proliferation and cartilage differentiation abilities of synovium-derived mesenchymal stem cells (synovial stem cells) to develop cell therapies that preserve the damaged meniscus. We started a clinical study in 2014 targeting patients with meniscal flap tears. In five patients, autologous synovial stem cells were locally administered to the suture site after meniscal repair. After two years of observation, no serious adverse events were reported, and clinical scores improved in all five patients. Furthermore, a physician-initiated trial was conducted in 2017 for patients with meniscal injuries such as flap tears, radial tears, and horizontal tears, transplanting autologous synovial stem cells after meniscal repair. Clinical scores significantly improved after one year. In February 2023, we initiated a multi-center clinical trial to examine whether the proposed cell therapy can be effectively implemented in a wide range of medical institutions. This trial targets patients with flap tears, and we are verifying whether the improvement in clinical scores after treatment is actually due to the healing of the meniscus. To achieve this, we are collecting data that can objectively quantify arthroscopic findings. Our ultimate goal is to have this therapy covered by insurance and to spread its use.

## EL26

**Current and future of genome analysis for clinical application**

Chikashi Terao
Laboratory for Statistical and Translational Genetics, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan

Conflict of interest: None

Genome analysis has unveiled the genetically defined causes of diseases, and substantial progress has been made in elucidating the pathogenesis of complex traits, such as rheumatic diseases. However, efforts to integrate the findings of genome analysis with individual genomes and apply them to individuals are still evolving, marked by varying objectives and approaches. One challenge lies in the fact that genetic polymorphism associations typically exhibit small effect sizes, necessitating large sample sizes to identify factors associated with these small effect sizes for prediction and the construction of association models. Goals of the clinical application may vary, including predicting diseases, differentiating diseases, and forecasting the course of diseases post-onset. Disease prevalence significantly impacts prediction accuracy in disease prediction scenarios. For those aiming to predict disease courses, intra-case analysis with a specific sample size becomes essential. In terms of clinical application approaches, some focus on strongly related factors, while others explore a broad range of polymorphisms, with HLA being a representative and strongly associated region in autoimmune diseases. Additionally, structural variations, rare variants, and copy number variations can have substantial effect sizes. The Polygenic risk score is a representative approach when considering a broad range of genetic variations. It is crucial to recognize that heritability defines the upper predictive limit of genomic analysis using germline variations. In other words, if the proportion of disease onset or progression explained by genetic factors is minimal, the upper limit of feasible genomic predictions will be low. This underscores the need for modeling that incorporates dynamic factors not explained by germline genetic factors. Dynamic factors encompass gene expression, protein levels, and acquired genomic changes such as somatic mosaicism. Understanding that innate genomic information represents the body's predisposition, while acquired factors signify current physiological states, emphasizes the importance of incorporating dynamic factors in constructing models. As dynamic factors vary from cell to cell, obtaining dynamic factors, such as gene expression, more easily and with higher precision poses a future challenge. Machine learning, capable of capturing non-linear relationships, is also considered effective for modeling in this context.

# Meet the Expert

## MTE1

**Management of the antiphospholipid syndrome: AtoZ**

Tatsuya Atsumi
Department of Rheumatology and Nephrology, Hokkaido University Hospital

Conflict of interest: Yes

Antiphospholipid syndrome (APS) is known as an autoimmune thrombosis and/or autoimmune pregnancy morbidity. A group of antiphospholipid antibodies present in patient blood has been recognised as pathogenic autoantibodies. In vitro, however, antiphospholipid antibodies are 'lupus anticoagulants', i.e. they have anticoagulant effects, and it has been a mystery why they correlate specifically with thrombotic tendencies. Antiphospholipid antibodies have diverse antigen specificities, but the main corresponding antigens are the phospholipid-bound beta2-glycoprotein I and prothrombin. These antiphospholipid antibodies have a procoagulant effect in the liquid phase under certain conditions. They also activate prothrombotic cells and induce tissue factor, an initiator of exogenous coagulation factors, to promote thrombin production. Treatment of APS is mainly secondary prophylaxis against thrombosis. In European Caucasians, deep vein thrombosis is the most common manifestation of APS, thus anticoagulation is the mainstay of treatment. We have shown that arterial thrombosis is more common in Japanese patients compared with venous events, therefore platelet-aggregation inhibitors are also recommended in Japan. Antiphospholipid antibody testing is not only diagnostic, but also attempts to predict the risk of recurrent thrombosis from the antiphospholipid antibody profile. If the intensity of treatment can be adjusted according to risk, thromboprophylaxis will be more effective.

## MTE2

**History taking and physical examination in the patient with arthralgia and arthritis**

Mitsumasa Kishimoto
Department of Nephrology and Rheumatology, Kyorin University School of Medicine

Conflict of interest: None

In primary care, patients with rheumatic diseases, such as rheumatoid arthritis (RA), are often encountered. In the case of musculoskeletal symptoms such as joint pain, it is said that most of the information necessary for diagnosis can be obtained through history taking and physical examination. Only then can the usefulness of tests be recognized. In 2010, the criteria for the new classification of RA were changed for the first time in 23 years, and the new criteria include "exclusion of other diseases causing arthritis. In other words, it is imperative for primary rheumatologist to become familiar with the identification of other autoimmune diseases that cause arthritis in order to treat RA, one of the most common autoimmune diseases encountered in daily practice. In this session, I will review the different diseases that can cause arthralgia and arthritis, and the methods and approaches to identify them. If time permits, we will also cover the basics of joint examination in a hands-on session.

## MTE3

**Essential knowledge for accurate diagnosis and treatment of axial spondyloarthritis**

Naoto Tamura
Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine

Conflict of interest: Yes

Axial spondyloarthritis (axSpA) is a group of SpA in which arthritis is predominantly seen in sacroiliac joints and spine. axSpA often develops in young men with inflammatory back pain, and strongly associated with *HLA-B27* gene. Primary site of the inflammation is enthesis at the attachment of the ligaments. Over the course of the years, bone erosion and its repair with fat tissue are followed by new bone formation, seen as syndesmophytes leading to spinal ankylosis. Non-radiographic axSpA (nr-axSpA), which has no apparent radiographic changes in sacroiliac joints, progresses to ankylosing spondylitis (AS). Although nr-axSpA often does not progress to radiographic axSpA, the patient's disease burden is the same as that of AS. Early diagnosis and intervention are required for axSpA to improve the patient's QOL, however, early diagnosis of axSpA is frequently challenging. Most important in the diagnosis of axSpA is the presence of non-infectious sacroiliitis. ASAS (Ankylosing SpondyloArthritis International Society) criteria must be used for cases already diagnosed with axSpA, and it should not be applied to the initial diagnosis. It is necessary to familiarize yourself with the characteristics of axSpA, and careful observation is needed before making a diagnosis. In the treatment of axSpA, patient education, including smoking cessation and encouragement of exercise, is important. In drug therapy, non-steroidal anti-inflammatory drugs (NSAIDs) are used at first. There is no evidence of efficacy of methotrexate for both axial and peripheral symptoms. In addition, systemic glucocorticoid is not normally used. If NSAIDs are inadequate, TNF inhibitors or IL-17 inhibitors are used. A JAK inhibitor is also a choice of treatment in cases of inadequate response to these biologics. These drugs are expected to have an inhibitory effect on new bone formation, although it has not been clearly proven yet. In this MTE, I would like to outline and discuss diagnosis and management of axSpA.

## MTE4

**Applying 2024 update of Japan College of Rheumatology Clinical Practice Guidelines for the management of rheumatoid arthritis to clinical settings**

Masayoshi Harigai
Division of Rheumatology, Department of Internal Medicine, Tokyo Women's Medical University

Conflict of interest: Yes

The points of 2024 update of Japan College of Rheumatology Clinical Practice Guidelines for the management of rheumatoid arthritis (hereafter, 2024 edition) will be discussed in this Meet the Expert. The previous edition of this guidelines has been used by many medical professionals since its publication in 2020 as a guideline showing standard treatment for rheumatoid arthritis (RA) in Japan. In the 2020 edition, drug treatment algorithms and 55 recommendations were developed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system, along with several review articles to correspond to patients with various backgrounds in clinical settings, as well as Q&A on RA treatment and pregnancy/childbirth and on the treatment of juvenile idiopathic arthritis (JIA) during transition to adults. In the 2024 revision, we developed or revised recommendations for MTX subcutaneous injection formulation, tumor necrosis factor (TNF) inhibitors (ozoralizumab), Janus kinase (JAK) inhibitors (upadacitinib, peficitinib, and filgotinib), and biosimilars that have been approved for RA in Japan since the development of the 2020 edition. In addition, we developed recommendations for rituximab, which is already widely used for RA overseas and is expected to be approved for use in Japan in the coming years. Considering the particular attention to long-term safety of JAK inhibitors after the results of Oral surveillance JAK inhibitors being published, we developed recommendations separately for short-term and long-term treatments with JAK inhibitors. For rituximab, we developed recommendations for use in Phase II and Phase III of the drug treatment algorithm. With the 2024 revised edition, it is expected that understanding of the effectiveness and safety of new antirheumatic drugs will deepen, and shared decision-making between medical professionals and patients will be put into practice.

## MTE5

**Pitfalls of management of systemic sclerosis: case-based study**

Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine

Conflict of interest: Yes

Systemic sclerosis (SSc) remains an intractable condition with poor functional and survival outcomes. This is primarily due to high variability of clinical course and irreversibility of pathogenic process, but the physicians' misunderstandings play a major role. Specifically, some patients are

left untreated without being referred to specialized centers, and others receive unnecessary, inappropriate treatment without risk assessment. It is meaningless to discuss the treatment indication and its efficacy without a full understanding of the unique features of this disease. A number of global randomized controlled trials have been conducted or are ongoing, and many disease-modifying treatment options are now available in clinical practice. Fundamental knowledge of SSc management required for introduction of 'appropriate' treatment for 'appropriate' cases at 'appropriate' timing will be discussed in this session through a case-based study.

## MTE6

**Preparing for Rheumatology Care in Disasters**

Hiroaki Umebayashi
Department of Rheumatism, Infectious Disease, Miyagi Children's Hospital, Sendai, Japan

Conflict of interest: None

Natural disasters such as earthquakes, typhoons, and heavy rains can occur anywhere in Japan. A cyber attack on a hospital that results in its loss of function is also a human disaster, and social dysfunction caused by a pandemic of COVID-19 can be considered a type of social disaster. Disasters occur equally regardless of the position of the people involved, but their effects vary widely. The impact varies depending on whether the disaster is localized or widespread. From the standpoint of patients with rheumatic diseases who receive treatment as outpatients, the response will differ depending on whether they themselves are affected by the disaster or the medical facilities where they go to receive treatment. When patients themselves are affected by a disaster, they must consider how to respond depending on their situation. In addition, if the medical providers are affected by the disaster, their response to patients will depend on the extent to which they can provide medical care, including access to medical facilities. In other words, it is necessary to consider measures to cope with various situations, such as whether it is possible to see a doctor, whether it is possible to prescribe or administer intravenous infusions, and whether it is possible to contact a medical facility that can provide immediate medical care on behalf of the patient. When considering disaster countermeasures, it is important to take measures based on all possible scenarios. Needless to say, however, disasters can occur beyond these assumptions. In such a situation, it may be necessary to respond with measures that do not exist in the manuals, but are devised on the spot. In order to demonstrate such adaptability, it is important to be aware of basic situational measures on a regular basis, and to communicate with individual patients from time to time about how to respond to disasters. I would like to exchange opinions with the participants of this session on disaster preparedness in rheumatology practice in the future.

## MTE7

**Antinuclear antibody up-to-date in connective tissue diseases**

Takao Fujii
Rheumatology and Clinical Immunology, Wakayama Medical University, Wakayama, Japan

Conflict of interest: None

Connective tissue disease (CTD) is described as a systemic autoimmune disease and one of the reasons is the presence of high frequency and/or high titer anti-nuclear antibodies (ANA) in serum. ANA is used as autoantibodies (auto Abs) to cellular antigens, not only to the nuclear components of cells, but also to the cytoplasm and cell membrane (*Ann Rheum Dis,* 2014). ANA is included in the classification criteria for many CTD and is an essential test when CTD is suspected in clinical practice. The ACR/EULAR classification criteria for systemic lupus erythematosus (SLE) requires that ANA is detected even if patient serum is diluted 80 times or more when using HEp-2 cells as a substrate (*Ann Rheum Dis,* 2019). It is also known that some ANA are associated with CTD-related serious organ damage and provide important information for predicting mortality Particularly, in dermatomyositis (DM) and systemic sclerosis (SSc), it is usual that only one type of disease-specific ANA is detected in a single patient. Knowing the disease-specific ANA detected in patient, therefore, give a useful information regarding the future management. In DM, anti-MDA5 Ab suggests the onset of serious interstitial lung disease and anti-TIF1-γ Ab suggests the presence of malignancy. In SSc, anti-RNA polymerase III Ab-positive patients may develop heart and/or renal disorders and increase rate of malignancy (*J Rheumatol,* 2017). Recently, anti-SMN (survival motor neuron) complex Ab has been reported to be associated with pulmonary arterial hypertension and severe interstitial lung disease in patients with mixed connective tissue disease (*Rheumatology,* 2023). Furthermore, there is ANA associated with disease activity, such as anti-dsDNA Abs in SLE. The pathogenicity of these disease-specific ANA, however, is not clear. In this seminar, we would like to introduce the latest information on ANA, including not only its clinical but also pathological significance.

## MTE8

**Seeing is believing for understating rheumatic diseases**

Masaru Ishii
Department of Immunology and Cell Biology, Osaka University Graduate School of Medicine

Conflict of interest: None

As the saying goes, a picture is worth a thousand words, and the information gained from seeing is rich in both qualitative and quantitative terms. In order to understand the enigmatic rheumatic diseases, I have originally elaborated a microscope system and developed an imaging system to visualize living organisms *in vivo* and has succeeded in analyzing immune and inflammatory processes in real time. In addition to basic research on bone destruction by osteoclasts in arthritis and the identification of their progenitor cells, and the pathogenesis of interstitial pneumonia and pulmonary fibrosis, I have recently been working on the development of opto-biopsy, *i.e.* diagnosis without biopsy, a human diagnostic method using *in vivo* imaging. In this Meet the Expert, we would like to introduce the flow of my research and development to date, with stories of his hardships, and discuss the future perspectives of the trend.

## MTE9

**Diagnosis of arthritis and arthralgia from the view point of manus**

Michiaki Takagi
Department of Orthopaedic Surgery, Yamagata University Faculty of Medicine, Yamagata, Japan

Conflict of interest: Yes

Advance of medical approach, including biologic DMARDs and JAKi, for rheumatoid arthritis (RA) enables the treatment to be more active. The approach aimed for remission comes in sight with great interest. It has been accomplished by recommendation of early treatment lined by effectiveness and safety. Twelve years have passed after introduction of 2010 ACR/EULAR classification criteria. It is characterized by superior diagnostic accuracy, and recognized useful for early diagnosis of RA before appearance of radiographic change. To the contrary, differential diagnosis of arthritis/arthralgia is essential to utilize 2010 ACR/EULAR classification criteria, and to reach preferable therapeutic approach. In this process, basic knowledge of arthritis and arthralgia is required for rheumatologists as well as various type of diseases and disorders relating to their symptom, including pain and swelling. They include so-called collagenous disease except for RA, such as systemic lupus erythematosus, mixed connective tissues, and Sjögren syndrome, osteoarthritis, spondylarthritis, such as psoriatic arthritis, enteropathic arthritis due to inflammatory bowel disease, and reactive arthritis. In addition, arthritis and/or arthralgia associated with microbial and/or viral infection, malignancy, metabolic and endocrine diseases, drug-induced type are another great concern. In the era of super-aging society, patients with musculoskeletal disorders increase and support for elderly RA patients and elderly-onset RA are essential. In this session, I focus the manus/hand, which can be easily taken as macroscopic findings. The diseases presenting arthritis and arthralgia of the manus/hand will be overlooked with great interest of the importance in taking macroscopic findings.

## MTE10

**How to use glucocorticoid - Minimal essence for daily clinical use**

Yutaka Kawahito

Inflammation and Immunology, Kyoto Prefectural University of Medicine

Conflict of interest: Yes

The inception of glucocorticoid (hereafter referred to as “steroid”) development can be traced back to the triumphant isolation of cortisone by Dr. Reichstein in Switzerland and Dr. Kendall in the United States in 1935. This was succeeded by the pioneering application of cortisone, an adrenal hormone, by Dr. Hench in the United States in 1948 for the remediation of rheumatoid arthritis. It is universally acknowledged that this trio of researchers were bestowed with the Nobel Prize in Physiology or Medicine in 1950. Subsequent to this, steroids have been in use for over seven decades and are presently employed in a multitude of areas including but not limited to rheumatic diseases, inflammatory bowel disease, hematologic disorders such as malignant lymphoma, neurological conditions, renal diseases, allergies, among others. Steroids are procurable in an extensive spectrum of clinical doses, with each drug possessing a distinct duration of action, anti-inflammatory action, electrolyte action, and biological half-life. Concurrent with their effects, a plethora of side effects are recognized, with the time of onset and symptoms potentially varying contingent on the dose and duration of administration. The crux lies in determining the dosage, route, and duration of administration by taking into account the severity of each disease and treatment objectives, monitoring side effects and implementing countermeasures to these side effects while effectively manifesting anti-inflammatory immunological effects. What constitutes the conventional wisdom, the insanity, and the truly correct use of steroids? In this seminar, we aim to deliberate on the fundamental essentials of steroid usage and the pivotal points of steroid prescribing from the perspective of a medical specialist, predicated on our erstwhile experience.

## MTE11

**Keys to musculoskeletal physical exam**

Masato Nagao
University of California San Francisco, San Francisco, USA

Conflict of interest: None

The key to a musculoskeletal physical exam is the history and physical examination. For a spinal exam, including spondyloarthritis, the neurologic exam is critical. This session will focus on the basics of the musculoskeletal exam, particularly spine exam. The exam includes motor function, tendon reflexes, sensory test, and neuromechanical testing. Combining the history with physical exam often helps to find out the neurological level. It will include a lecture and practical exam to improve your understanding of spine disorders. We will also discuss injection therapies such as joint injections and trigger point injections that can be done on an outpatient basis.

## MTE12

**Physical examination of an arthritis or spondyloarthritis patient. The Scandinavian way to perform it**

Markku J Kauppi[1,2]
[1]Faculty of Medicine, Clinicum, Helsinki University, Helsinki, Finland, [2]Päijät-Häme Central Hospital, Lahti, Finland

Conflict of interest: None

There are several goals for good physical examination. The doctor usually should find out, what causes the symptoms and/or complaints of the patient. Physical examination is usually more extensive, if the patient has new undiagnosed disease, than if the disease is chronic. When examining an early case, it is very important to find out, whether the patient has arthritis and if so, is the inflammation active. Especially in chronic cases, permanent tissue changes and possible signs and risks of complications should be detected. The ability or limitations in function in daily activities should always be noticed as well as other health problems. The practical implementation of the examination strongly depends on available time and other resources. The doctor should study the available written background information of the patient, before meeting the patient. It makes it possible to optimize the value of anamnesis. Doctor can make a good first impression to the patient only once! A good, appreciative connection with the patient helps to get useful anamnesis. While asking the patient history, the doctor also observes the patient’s essence and activity. After short general examination (including heart, lungs, skin and often lymph nodes), the active function and ranges of joint and back movements can be tested briefly. Based on these findings one can concentrate the further examination to those musculoskeletal areas, where impaired function was detected and/or the patient has symptoms. All the joint areas, even those without symptoms are examined, if there is time for that. Possible swollen and tender joints are looked for and documented, as well as permanent deformities and function disorders. Physical examination can be supplemented by ultrasound evaluation performed by the clinician. It can be called sonopalpation, and often gives extra value to the visit. A purposeful and careful physical examination makes it easier to make correct diagnosis and choose an effective treatment.

## MTE13

**How to diagnose and manage juvenile spondyloarthritis**

Nami Okamoto
Department of Pediatrics, Osaka Rosai Hospital

Conflict of interest: None

Spondyloarthritis (SpA) is a general term for a group of diseases in which axial arthritis, peripheral arthritis and enthesitis occur. The enthesis is where the tendon, ligament, fascia and joint capsule attach to the bone. Ankylosing spondylitis (AS) is included in SpA as a representative disease. It also includes a group with extraarticular manifestations such as ocular, mucocutaneous, gastrointestinal, and genitourinary tract manifestations, and has been associated with HLA-B 27. SpA includes non-radiographic axial SpA, psoriatic arthritis, inflammatory enteritis-related arthritis, reactive arthritis, and unclassified peripheral SpA. The prevalence in Japan is approximately 1 in 10,000 and 6.7% cases occurred before the age of 20. It often takes a long time to make a diagnosis, and the reasons for this are as follows: “It takes several years to obtain a typical disease image,” “In young people and women, axial joint involvement is scarce and peripheral arthritis predominates” “Possession of HLA-B 27 is 0.3%, lower than in other countries, and recognition of disease is low.” and “It is difficult to evaluate X-ray images and MRI images of the sacroiliac joint necessary for diagnosis.” The axial and peripheral classification criteria of assessment of spondyloarthritis international society (ASAS) are broadly used for classification of SpA, but validation has not been established for children. On the other hand, since 1997, there have been internationally unified criteria for the definition and classification of chronic arthritis in children, and chronic arthritis of unknown origin occurring before the age of 16 is called juvenile idiopathic arthritis (JIA). The International Rheumatology Association (ILAR) classification criteria of 2001 Edmonton edition are used at present. There are seven forms of JIA, of which “enthesitis-associated arthritis” and “psoriatic arthritis” correspond to SpA. In recent years, there has been a shift in the field of pediatric rheumatic diseases from the aim of smoothly overcoming the transition from childhood to adulthood to the understanding and management of the disease state, and pediatric patients with SpA are often referred to as juvenile SpA (JSpA). Features of JSpA include more peripheral, unclassifiable forms, a longer time between onset and development of sacroiliitis, a higher incidence in boys, and two subtypes of psoriatic arthritis. The characteristics of the management of children will be introduced, including that the treatment and medical system will be equivalent to JIA.

## MTE14

**Synthetic anti-rheumatic drugs and biologics that can be used for juvenile idiopathic arthritis in Japan - what is the difference between adults?**

Masaaki Mori
Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University

Conflict of interest: Yes

As of December 2023, there are 13 synthetic anti-rheumatic drugs, including 5 JAK inhibitors, and 8 biologics that can be used for rheumatoid arthritis in Japan. is doing. On the other hand, in juvenile idiopathic arthritis (JIA), the former has only methotrexate and the latter only 5 agents, and the disparity is extremely large. The common causative factors of the inflammatory pathology of arthritis are inflammatory cytokines, and

recently monoclonal antibodies, specific receptors directed against individual inflammatory cytokines, have been formulated as therapeutic agents to inhibit the function of single inflammatory cytokines. In JIA, various inflammatory cytokines are produced, and the mutual induction mechanism has also been clarified, but there is actually a leading cytokine specific to the disease, and blocking that cytokine can end inflammation. Systemic JIA requires long-term, high-dose steroid use for strong systemic inflammation, and suffers from side effects. Tocilizumab (TCZ), an anti-IL-6 inhibitor, was the first in the world to be approved as an anti-IL-6 inhibitor in biologic therapy after undergoing clinical trials. Canakinumab, which has a proven anti-IL-1 inhibitory effect in Europe and the United States, was also approved in Japan, demonstrating efficacy for TCZ-ineffective patients. In addition, anti-TNF therapeutic agents such as etanercept (ETN) and adalimumab (ADA) are used for the type in which arthritis persists even after systemic symptoms have improved. On the other hand, for articular JIA, in addition to ETN, ADA and TCZ, abatacept, which inhibits co-stimulatory signals between antigen-presenting cells and T cells, is also approved in Japan. Recently, it obtained indication approval as a result of clinical trials. In this presentation, I will outline the drugs that can be used in JIA, their dosage forms, and how to use them in clinical settings, focusing on the differences from RA.

## MTE15

**Evaluation of the skin thickening in patients with scleroderma**

Hidekata Yasuoka
Department of Internal Medicine, Division of Rheumatology, Fujita Health University School of Medicine

Conflict of interest: None

Scleroderma (SSc) is one of the connective tissue diseases (CTDs) that is characterized by excessive remodeling, microvascular abnormalities, and autoimmunity. The disease process of CTDs is common, which starts from the various triggers and infiltration of the immune cells. These are followed by the inflammatory process and cause tissue damage, which results in the loss of organ function and poor prognosis. Non-SSc CTDs can be captured at an inflammatory phase, and modification of the disease process is possible using anti-inflammatory drugs, however, SSc is difficult to find at an inflammatory phase, treatment approach must be different from other CTDs. For the development of new drugs, identification of the new pathways or mechanisms of the diseases is quite important to determine the targets for the treatment. However, the development of the outcome measures to “sense” the treatment effect which is associated with clinical conditions such as disease activity is simultaneously needed for the development. However, in SSc, it was difficult for us to develop new treatment agents because direct regulation of fibrosis/remodeling was quite difficult compared with inflammation. Also, the development of new outcome measures has also been delayed in this field so far. To overcome this situation, the revision of classification criteria, the proposal of the concept of very early diagnosis of SSc (VEDOSS), early intervention at the inflammatory phase, and the establishment of novel composite measures including revised ACR CRISS were attempted extensively. Now we are in front of the entrance of the development of novel treatments for SSc. However, even in the new era, evaluation of skin thickening is still one of the important and basic procedures for physicians for CTDs. If you would like to use this procedure for clinical trials, certification or standardization is needed to minimize the variability. In this session, we would like to explain the outline of this evaluation.

## MTE16

**The essential techniques to evaluate the bone and joint radiographs in rheumatoid arthritis for rheumatologists**

Yuichi Mochida
Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan

Conflict of interest: Yes

Due to the introduction of the effective drugs such as conventional synthetic disease modifying anti rheumatic drugs (DMARDs), biological DMARDs, and JAK inhibitors, the disease activity of rheumatoid arthritis (RA) patients was improved. Whereas there are the cases with multiple joint destruction, even receiving appropriate medical care. In such patients, the information to be obtained from X-ray photogram (Xp) in judging a diagnosis and effect of treatment is yet important. The skills for Xp evaluation are still the essential in the clinical settings. In this session, we will reconfirm about judgments of the Larsen grade on Xp, bone erosion, joint space narrowing, local osteoporosis, and findings of MRI and ultrasonography of the joint. For upper arms joints, such as shoulder, elbow, hand, and finger joints, we will discuss which part does the orthopaedic rheumatologist focus on it. Also, the buttonhole deformity, swan neck deformity, the developmental mechanism of the ulnar deviation of the 2-5 finger, and the evaluation for the carpometacarpal joint will be discussed. Then, the surgical indication for the synovectomy and the joint replacement will be explained. For lower limb joints, such as hip, knee, and toes, we will discuss about recent trend of joint destruction, recent trend of surgery. For rheumatologists, it will be a good opportunity to understand how to evaluate the Xp findings in real world setting through this session.

## MTE17

**RQ Brush-up Workshop for Medical Staff**

Nobuyuki Yajima
Division of Rheumatology, Department of Medicine, Showa University School of Medicine

Conflict of interest: None

A workshop for medical staff will be held for those who “want to start a clinical research project but don’t know how to go about it.” In this MTE, you will learn the concept of the Research Question (RQ), or “research question,” which is an important first step in research, and how to brush up on it. You will experience the sequence of how an actual clinical question is transformed into a concrete research question. You will also gain a deeper understanding of research through discussions with other participants. This is a great opportunity to share research ideas and make new research connections. Networking with other researchers is very important in advancing your research. In addition, we will provide you with tools and methods for studying clinical research. Don’t miss this opportunity. We look forward to seeing you there.

## MTE18

**Hands-on seminar for systematic reviews using RevMan and GRADEpro**

Takashi Kida
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

Conflict of interest: None

In recent years, the volume of research literature has continued to grow, making it increasingly difficult for healthcare providers and users to evaluate all of the vast amount of primary research and make optimal decisions based on a balance of benefits and harms. A systematic review (SR) aims to support medical decision-making by adequately summarising the empirical evidence on a specific clinical question (CQ) and consists of a series of processes that comprehensively collect, systematically assess and synthesise the literature on the topic. The following are the key elements of SR. -Formulating the clinical question (PICO) -Determination of eligibility criteria and outcomes -Conducting literature search -Screening and reviewing literature -Data extraction -Assessing risk of bias -Meta-analysis -Assessment of the certainty of the evidence While it may initially appear challenging, the workshops for SR have been consistently and openly recruiting participants through the Japan College of Rheumatology since 2020. This initiative aims to train SR personnel to actively contribute to the development of practice guidelines with supervision from instructors dispatched by Cochrane Japan and individuals experienced in SR. The presenter also participated in this project, despite having no experience, and actually took part in the SR for the ANCA-associated vasculitis practice guideline 2023. Similar workshops are currently underway for revising guidelines related to the treatment of rheumatoid arthritis and large vessel vasculitis; opportunities for beginners in SR will continue to expand in the future. This session will provide a hands-on seminar for beginners to learn what SR is all about and to make it easier to approach SR when trying it out in the future. This session will focus on the final processes of SR:

'Meta-analysis using RevMan' and 'Assessing the certainty of evidence using GRADEpro GDT'. I will explain how to integrate the results of multiple studies and assess the quality of evidence, as well as the basic usage of the software.

## MTE19

**Conservative and surgical treatment of RA hand joints and finger joints**

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Conflict of interest: Yes

In recent years, rheumatoid arthritis (RA) drug treatment has changed dramatically and made significant progress. These changes have highlighted the importance of RA strict control toward the goal of achieving remission or reduced disease activity and have been widely recognized. As a result, destruction of joints associated with RA can be suppressed and even repaired, so there is a growing interest in treating small joints, such as hand joints and finger joints, in conservative, and surgical treatments. At this time, I would like to consider conservative and surgical treatments when presenting cases of hand joints and finger joints. Even if the disease activity of RA is controlled, inflammation can persist in some joints, and if such inflammation is left untreated, it will lead to joint destruction and the progression of deformity. For residual joint synovitis in the hand joints and finger joints, intra-articular injections are first performed, and orthotics are also considered. If the effect of these conservative treatments is insufficient, a synovectomy is considered before abnormalities and combined destruction appear. This is important from a joint protection perspective, and it can also prevent tendon rupture in the wrist joint, so the timing of surgical intervention is important. In addition, although inflammation appears to decrease, joint destruction may progress. In such cases, it is important to determine the indications for surgical treatment. If RA finger deformity has already occurred, the cause should be understood and surgical procedures will be considered depending on the situation. Given the impact of joint destruction and repair, joint-protection surgery will be performed if possible. It is important to actively consider whether joint-preserving surgery is indicated, especially if joint destruction has not yet progressed and the rate of deformity is mild. In the future, the importance of surgery on RA hands is expected to increase, but while it is important to do it under strict control, caution about infection is needed due to the increasing use of immunosuppressive drugs. In any case, since RA often affects hand surgery, it is expected that the scope of its content will increase and become more sophisticated, and that is likely to change with rehabilitation. However, there are still many problems left. In the future, we will continue to treat patients with medications as aggressively as possible, and we will treat RA hand surgery with an "aggressive" attitude.

## MTE20

**Essentials of basic and clinical aspects of methotrexate**

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Conflict of interest: None

Methotrexate is an anchor drug for treatment against rheumatoid arthritis even in this era when potent various biologic disease modifying antirheumatic drugs (DMARDs) and JAK inhibitors are available. The reason is that methotrexate has the balanced effectiveness and safety and advantage of cost effectiveness. In the daily practice, methotrexate is used about 60% of rheumatoid arthritis patients all over Japan who are treated with any DMARDs. Methotrexate was developed as anti-folate metabolic agent against leukemia in 1940´s and it inhibits strongly proliferation of cells by binding to dihydrofolate reductase in S phase of cell cycle. Methotrexate also exhibits various effects in suppressing cell proliferation by inhibiting thymidylate synthetase, in suppressing of neutrophil inflammation by increasing adenosine release though inhibiting AICAR transformylase, and in generating reactive oxygen species. As a results, MTX reduces interleukin 6, interleukin 1β, and tumor necrosis factor α and increase interleukin 4 and interleukin 10. In recent years, there has been increasing knowledge regarding differences in efficacy and side effects due to differences in methotrexate polyglutamate formation. While using methotrexate, physicians should be pay attention to the occurrence of adverse events such as lymphoproliferative disorders, drug induced interstitial lung disease, myeloid suppression, infection and liver dysfunction by following guidance of methotrexate 2023. In this lecture, the basic knowledge and clinical knowledge of methotrexate will be explained, which is the core drug of Phase I treatment for rheumatoid arthritis for aiming to conduct the optimal use of methotrexate.

## MTE21

**Update on the Adaptive Immune Response to Rheumatic Diseases Not Covered in Textbooks**

Keishi Fujio
Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Conflict of interest: Yes

The understanding of human immunity has greatly advanced the treatment of rheumatic diseases. In particular, the effectiveness of CD19 CAR-T cell therapy in refractory SLE, recently reported, clearly demonstrates the efficacy of treatment development based on the understanding of human immunity. CD19 CAR-T cell therapy has also been reported to be effective in systemic sclerosis and idiopathic inflammatory myopathies, and B cell-targeted therapy is expected to become an important pillar in the treatment of rheumatic diseases. Therefore, understanding the adaptive immune response is essential for evaluating the indications for B cell-targeted therapy and predicting relapse after remission. In this seminar, focusing on SLE, we would like to discuss (1) what modifications occur in the B cell lineage, and (2) what T cell subsets are associated with such modifications. The genetic predisposition of SLE enhances the action of type I IFN and reduces the risk of severe COVID-19. Type I IFN not only activates the innate immune system but also the adaptive immune response. Recent clinical studies have shown that the IFN signature of adaptive immune cells correlates more with disease activity than the IFN signature of innate immune cells, highlighting the importance of IFN signaling to T and B cells. Type I IFN is thought to promote the differentiation of naive B cells with autoreactive B cell receptors into memory B cells, triggering an autoimmune response. Interestingly, severe COVID-19 infection with enhanced type I IFN shows a similar B cell repertoire to SLE and also produces autoantibodies. Age-associated B cells (ABC) are being focused on as the B cell subset involved in actual autoantibody production. ABC differentiates in the follicular outer region through TLR signaling, and the T cells involved in this differentiation are thought to be peripheral helper T (TPH) cells. The differentiation of TPH cells and the expression of CXCL13 and IL-21 are promoted by type I IFN. However, it has been pointed out that TPH cells are a heterogeneous group, including those with cytotoxicity, as PD-1, a marker of TPH cells, is an activation marker. By understanding the details of the B cell repertoire, ABC, and TPH-like cells, the current topic, it is expected to enable the evaluation of the adaptive immune response in rheumatic diseases, leading to more appropriate treatment choices.

## MTE22

**Discerning Joint Disorders in the Aging Population: A Focus on Distinguishing Rheumatoid Arthritis**

Shigeki Momohara
Hakkeikai Incorporated Medical Institution, Shizuoka, Japan / Endowed Course for Advanced Therapy for Musculoskeletal Disorders, Keio University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

The elderly population commonly experiences primary joint-related ailments such as Osteoarthritis (OA), polymyalgia rheumatica (PMR), pseudogout (CPPD), and rheumatoid arthritis (RA). Distinguishing among these conditions proves challenging due to overlapping symptoms and clinical features. To address this challenge, a thorough understanding of symptom patterns, physical manifestations, and nuanced diagnostic differences becomes essential for precise diagnosis and personalized treatment. OA results from joint cartilage degeneration, identifiable through X-ray indicators and limited joint mobility. PMR manifests as systemic muscle

discomfort, tenderness, often accompanied by fatigue and sleep disruptions. CPPD arises from calcium deposits within joints, leading to sudden episodes of joint inflammation. On the other hand, RA, an autoimmune disorder, exhibits multi-joint inflammations, morning stiffness, and positive blood markers like rheumatoid factor (RF) and ACPA. However, accurately differentiating among these prevalent conditions in the elderly is challenging. To discern between these disorders, a meticulous assessment of patient symptoms and clinical observations serves as a cornerstone. Localized joint pain and swelling may suggest OA or CPPD, while widespread muscle discomfort and tenderness could indicate PMR. RA typically involves multiple joint inflammations and positive autoimmune markers, though cases with negative autoantibodies are not uncommon among the elderly. Diagnostic tools such as X-rays, MRI, and ultrasound aid in observing joint changes and inflammation. Blood tests confirm inflammatory reactions, RF presence, and anti-CCP antibodies. Analyzing joint fluid helps in CPPD diagnosis. A comprehensive review of symptoms and diagnostic findings leads to a precise diagnosis, guiding treatment choices. While medication forms the core treatment, OA often requires exercise regimens, pain management, orthotic interventions, and sometimes surgical procedures. In addressing PMR, alongside exercise and medication, investigating malignancy presence becomes crucial. Acute CPPD episodes find relief in non-steroidal anti-inflammatory drugs, while disease-modifying anti-rheumatic drugs (DMARDs) are preferred for managing RA progression. Thus, a meticulous evaluation of symptoms, clinical findings, and appropriate investigations is pivotal in distinguishing joint-related ailments among the elderly. This systematic approach facilitates accurate diagnoses and the selection of optimal treatments, ultimately enhancing the quality of life for these individuals.

## MTE23

**Pregnancy in patients with collagen disease**

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Conflict of interest: Yes

For pregnancies complicated by collagen disease, there were many problems in the outcome for both mother and babies. Concerned about the negative outcome of pregnancy, we medical professionals did not strongly encourage patients with collagen disease to become pregnant. In the past, patients with collagen disease who had the desire to become mothers tended to avoid raising a baby for a variety of reasons. The high frequency of negative pregnancy outcomes such as miscarriage and premature birth, as well as problems such as infertility, were major reasons for this. Recently, the development of numerous therapeutic agents and the establishment of evidence for their safety have brought about significant changes. Health care provider are now able to face the issue of collagen disease complicated pregnancy, and many patients with collagen disease can now hope to become mothers. However, due to the specificity of the various diseases and individual peculiarities of patients with rheumatic diseases, enough attention should be paid for determining treatment strategies before conception, during pregnancy, and in the postpartum period. Preconception care should be practiced in all patients, not only in female collagen disease patients who plan to become pregnant soon, especially before pregnancy. Treatment strategies should be developed and practiced with future life events in mind. Furthermore, even rheumatologists need to consider the contraceptive methods that should be proposed and the need for infertility treatment. In this seminar, we will present a model case and discuss the specificities of each disease and treatment strategies for patients with collagen diseases who want to become mothers.

## MTE24

**Synovial cells and immuno-abnormality in RA**

Isao Matsumoto
Department of Rheumatology, Institute of Medicine, University of Tsukuba

Conflict of interest: None

Rheumatoid arthritis (RA) is a highly diverse autoimmune disease that involves complex interactions between various genetic and environmental factors, as well as many cells and proteins. Recently, precision medicine has been proposed, in which targeted treatments are selected based on findings obtained from local needle biopsies of joints. In the joint region, which is the epicenter of the disease, single-cell RNA sequencing analysis of synovial cells has led to an understanding of what types of cell groups produce what types of proteins, such as cytokines and chemokines, as well as the connections between cells. In this session 1) Joint local cell groups obtained from human immunology analysis 2) Joint local cells changed by biologics or JAK inhibitors 3) Recent topics on immune cells and autoantibodies in RA We will summarize and discuss the latest theories. In addition, I would like to discuss future developments in clinical pathological analysis of RA and its animal models, as well as hints that can be helpful in doing so, with the participants, including examples from our own experiments.

## MTE25

**Rheumatoid foot surgery**

Makoto Hirao
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Conflict of interest: None

With the development of drug treatment for rheumatoid arthritis (RA), we as an orthopedic surgeon would like to provide surgical techniques to reconstruct lower limb function so that RA patients can regain a more normal bipedal gait in this age of longevity. As we look at advances in technology and improved outcomes in spinal surgery, hip and knee joint arthroplasty, and reconstructive surgery, it has become clear that if problems remain in the part of the foot that makes contact with the ground, the two feet are generally normal. Since this does not mean that walking has been regained, we need to focus on foot problems from an early stage of RA management, perform conservative treatment, and have a mindset and a collaborative system that allows us to perform the necessary surgical treatment at the appropriate stage. Currently, we are learning from cases every day in order to maintain and improve the walking ability of RA patients.

## MTE26

**How to Understad Physical Function in Patients with Rheumatoid Arthritis**

Toshihisa Kojima
Orthopedic Surgery, NHO Nagoya Medical Center, Nagoya, Japan

Conflict of interest: None

Rheumatoid arthritis (RA) is a chronic inflammatory disease with arthritis as its main symptom. Assessment of physical function is essential to evaluate treatment efficacy and prognosis, and one of the key therapeutic goals of the T2T treatment strategy is functional remission. The most commonly used assessment of physical function in daily practice is the patient's subjective assessment (Health Assessment Questionnaire-disability index: HAQ-DI). First, it is necessary to ascertain whether any physical dysfunction has occurred or progressed as a result of treatment. If so, we need to know what type of impairment has occurred. Then, we must consider the cause of the impairment, and whether or not we can intervene, and whether or not it is the right time to intervene. The most important steps in determining the cause are to identify arthritis and joint destruction. Arthritis can be easily identified not only by physical examination but also by arthrography. X-rays are the standard method of identifying joint destruction. It is extremely important to observe changes over time. First, if arthritis remains, intensification of drug therapy should be considered. Objective measures facilitate information sharing with the patient. They are important along with the patient's subjective assessment. The most routine objective measure of dysfunction is range of motion. We examined the range of motion of the major joints that are considered to be free of difficulty on the HAQ-DI. For example, the elbow joint must be able to flex at least 120 degrees to reach the face and wash the face. Speed of movement is also important as a physical function. It is also included in the assessment of frailty and sarcopenia. Even during outpatient consultations, it is possible to have an image of the speed of movement, and it is possible to get a rough idea of the speed of movement without measurement. In this lecture, I would like to consider how to diagnose physical disability, focusing on physical measurements that should be kept in mind in daily prac-

tice.

## MTE27

**Clinical epidemiology research on rheumatic diseases using medical big data**

Ryoko Sakai
Department of Public Health and Epidemiology, Meiji Pharmaceutical University, Tokyo, Japan

Conflict of interest: None

In recent years, the medical treatment of rheumatic diseases such as rheumatoid arthritis (RA) has improved by advances in diagnostic technology and the launch of new therapeutic drugs. In particular, for RA, aggressive treatment from an early stage is recommended, and since 2000, biologic drugs have been introduced, making it possible to treat the disease with achieving clinical remission. Although these drugs are highly effective, there are concerns about adverse events, but data obtained from clinical trials is not always sufficient due to strict eligibility criteria, limited target population, and relatively short observation periods. Therefore, in order to know the effectiveness and safety of drugs in clinical settings, it is essential to evaluate the effectiveness and safety of drugs during medium- to long-term use in clinical settings. Medical big data is one of the data sources used to examine the effectiveness and safety of drugs in clinical practice. Among medical big data, administrative claims data has been actively used in epidemiological research in recent years. This data includes data on medical expenses, such as diagnoses, medications, and medical procedures, so by combining this information, it is possible to show what kind of medical care was provided in actual clinical practice. In general, claims data has better generalizability than data obtained from small number of facilities because it includes data from multiple medical facilities. On the other hand, there are some limitations that clinical variables such as laboratory data are insufficient in the claims data. In this lecture, I will focus on the characteristics of claims data that can be used for research in Japan, handling methods, and limitations of medical big data, and will provide the basic knowledge necessary to use medical big data in clinical epidemiology research. I would also like to discuss the barriers to investigate clinical questions using medical big data and how to solve them.

## MTE28

**A primer of statistical analysis for clinical researches using EZR**

Hisashi Noma
The Institute of Statistical Mathematics

Conflict of interest: Yes

I guess many clinicians are still suffering with “statistics” of clinical research papers. However, in modern medical researches, many advanced statistical techniques, e.g., significance tests, confidence intervals, logistic regression, Cox regression, have been commonly used, and we cannot understand clinical evidence from these research articles precisely if we do not have sufficient knowledge about them. In addition, we cannot write a clinical research article if we can use statistical software actually. It is said that the software cannot be used if the user is not familiar with programming skills and most of these software are expensive. In this session, I conduct a hands-on seminar about a free statistical software R (R Foundation for Statistical Computing, Vienna, Austria) and its add-in EZR for statistical analysis for clinical researches, which resolve all of the problems mentioned above. R is a well-known statistical software that has been widely adopted in clinical researches published in international medical journals, and has rich and reliable functions for data analyses. R itself is difficult to use if the user acquires programming skills for the R language, but EZR enables easy-to-conduct statistical computations like as spreadsheet software, e.g., Microsoft Excel. In this seminar, you can experience statistical computations of p-values, confidence interval, and multivariate analyses that are widely used in international medical journals actually.

## MTE29

**Imaging of axial spondyloarthritis**

Yuho Kadono
Orthopaedic Surgery, Saitama Medical University, Saitama Medical University

Conflict of interest: Yes

Recently, it becomes well known that spondyloarthritis (SpA) is a kind of umbrella inflammatory disease concept including ankylosing spondylitis (AS) and psoriatic arthritis. SpA exhibits not only arthritis or spondylitis but also enthesitis. SpA which shows sacroiliac joint or spine involvement like AS, is roughly classified into axial SpA (AxSpA). We use ASAS criteria to classify AxSpA, and call it a ‘non-radiographic AxSpA’ when we can detect too small radiographic change to classify as AS. Although there is the classification criterion, we sometimes have a difficulty to diagnose. When we find spinal fusion or hyper ossification, we should distinguish AxSpA from degeneration of spine, diffuse idiopathic skeletal hyperostosis, psoriatic arthritis, pustulotic arthro-osteitis, or osteitis condensans illi. In AxSpA, we can find out STIR high lesions, though we should three-dimensionally think where the lesion is. In this session, we discuss how to take and diagnose imaging of AxSpA.

## MTE30

**Autoinflammation and pathophysiology and therapy of connective tissue diseases**

Atsushi Kawakami[1], Yoshika Tsuji[1,2], Remi Sumiyoshi[1,3], Mizuna Otsuka[1], Ayaka Umetsu[1], Shoichi Fukui[1], Tomohiro Koga[1]
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Conflict of interest: Yes

Autoinflammatory diseases are a group of diseases induced by abnormalities of innate immunity, and classically defined as the presence of (1) seemingly untriggered inflammation, (2) the absence of high-titer autoantibodies and autoreactive T cells, and (3) detection of mutations of the genes involving in innate immunity. Recently, autoinflammatory diseases are classified into Inflammasonopathies, Endogenous antagonist mutations, Actinopathies, Type I interferonopathies, ADA2 deficiency, NF-kappaB-related disorders, ER stress, etc. according to the inflammation-inducing mechanism. On the other hand, adult-onset Still’s disease, Behcet’s disease, periodic fever, aphthous, stomatitis, pharyngitis and cervical adenitis syndrome (PFAPAsyndrome), Castleman’s disease, etc., specific disease genes not being found, can also be regarded as autoinflammatory diseases in a broad sense. Cytokine storm, a widely established concept during COVID-19 era, triggered by a large amount of inflammatory cytokines, induces an excessive inflammatory response. In this regard, autoinflammatory diseases are also included in this concept. In addition, innate immune response contributes to pathophysiology of rheumatoid arthritis, disease-specific autoantibodies anti-citrullinated protein antibodies being established. Diseases by genetic mutations generally develop in childhood, but adult-onset familial Mediterranean fever (FMF) caused by mutations in the Mediterranean fever gene (MEFV gene) is not uncommon. In addition, VEXAS syndrome, induced by accumulation of somatic mutations in the UBA1 gene (UBA1 gene somatic mosaicism), occurs in adult (even late adult) males. Thus, it should be borne in mind that autoinflammatory diseases are sometimes encountered in adult clinical departments including rheumatology. Toward the appropriate clinical work of autoinflammatory diseases, it becomes to be crucial to understand the utilization of gene panel testing and its application to diagnosis, for which insurance coverage is expanding in recent years. In this Meet the Expert, we will discuss the significance of autoinflammation and disease concept of autoinflammatory diseases in relation to the pathophysiology and therapy of connective tissue diseases.

# International Concurrent Workshop

## ICW1-1

**MicroRNAs as circulating biomarkers for distinguishing early rheumatoid arthritis**

Madhu Baghel[1], Thomas Wilson[1], Vasilios Moutzouros[2], Michelle Ormseth[4], Alireza Meysami[2], Jason Davis[2], Shabana A Ali[1,3]
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Conflict of interest: None

**Objectives:** Rheumatoid arthritis (RA), the most common type of autoimmune arthritis, can be challenging to identify in early stages due to overlapping symptoms with early stages of osteoarthritis (OA). As such, there is a need for novel biomarkers that can reliably distinguish early RA to avoid delays in diagnosis and management. MicroRNAs (miRNAs) are a promising class of circulating biomarkers due to their specificity, stability, and ease of detection in liquid biopsies. We aim to identify circulating miRNAs that distinguish early RA patients from early OA patients and non-RA/OA controls using miRNA-sequencing (miRNA-seq). **Methods:** Plasma samples for miRNA-seq were obtained from our Henry Ford Health Arthritis Biobank, the Osteoarthritis Initiative, and Nashville VA Medical Center, matched across 3 groups by sex, race, age, and BMI. We defined early RA as treatment-naïve patients with <6 months of symptoms and anti-citrullinated protein antibodies within 24-2613.5 U/mL; early OA as patients with knee joint pain and radiographic Kellgren-Lawrence grade 0 or 1; and control non-RA/OA as individuals with no joint disease history. **Results:** We are currently performing miRNA-seq on N=6 early RA [2 female, 4 white, 56 years (SD 8), BMI 27 kg/m² (SD 5)], N=12 early OA [6 female, 12 white, 49 years (SD 11), BMI 28 kg/m² (SD 5)], and N=50 non-RA/OA control [25 female, 48 white, 57 years (SD 8), BMI 26 kg/m² (SD 3)] to identify differentially expressed (DE) miRNAs in early RA versus early OA and non-RA/OA controls, filtered by false discovery rate <0.05. These DE miRNAs will be validated along with 12 other miRNAs identified from literature (1 for early RA and 11 for early OA). Prioritized miRNAs will be used to construct a predictive model for determining their accuracy in distinguishing early RA. **Conclusion:** We expect to discover a miRNA signature that can be further developed into a diagnostic blood test to reliably distinguish early RA patients in primary care settings.

## ICW1-2

**Soluble tumor necrosis factor receptor 1 as a predictive biomarker of relapse after discontinuation of biological agents and response to re-treatment in rheumatoid arthritis**

Yuto Takakura, Takehisa Ogura, Takaharu Katagiri, Chihiro Imaizumi, Yasuto Minegishi, Reina Maezawa, Hideto Kameda
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Conflict of interest: None

[Background] We reported that circulating soluble tumor necrosis factor receptor 1 (sTNFR1) is useful in predicting disease relapse after discontinuation of biological disease-modifying antirheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA) in remission. [Objective] In this post-hoc analysis, we examined the significance of sTNFR1 level in the response to re-treatment with bDMARDs after disease flare subsequent to their discontinuation. [Methods] Patients with RA who maintained a simplified disease activity index ≦ 3.3 for ≧ 3 months during November 2014-January 2018 in our medical center were eligible. The primary endpoint was flare (disease activity score-28 ≧ 3.2 with increase from baseline ≧ 0.6) within 2 years after bDMARD discontinuation. Comprehensive clinical assessments, and blood sampling for 12 biomarkers were performed every 2-3 months for 2 years unless patients experienced flare. [Results] Twenty of 36 registered patients showed disease flare after bDMARDs discontinuation, and 18 patients among them received bDMARDs again. After re-treatment, 15 patients achieved remission or low disease activity (83%). The median sTNFR1 levels at baseline, just before relapse, and at relapse were 1511 pg/ml, 1629 pg/ml, and 1768 pg/ml, respectively (p=0.03 in 3 groups, and p=0.007 for baseline vs. at relapse). Furthermore, the rate of change in sTNFR1 from just before relapse to the time of relapse was significantly higher in patients not achieving remission or low disease activity than in those achieving the above treatment goal. (median +26% vs. +6%, p=0.02). [Conclusion] Our results suggest that sTNFR1 is a useful biomarker not only for predicting disease flare after bDMARDs discontinuation but also for predicting re-treatment response.

## ICW1-3

**Smartphone-acquired patient reported outcomes and smartwatch sensing data in rheumatoid arthritis: a multicenter single-arm prospective study for digital biomarker**

Keisuke Izumi[1,2,3], Misako Higashida-Konishi[1], Shuntaro Saito[2], Satoshi Hama[1], Kazuoto Hiramoto[2], Yasushi Kondo[2], Nobuhiko Kajio[4], Hiroaki Taguchi[4], Yuko Kaneko[2]
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Conflict of interest: Yes

[Background] Symptoms in patients with rheumatoid arthritis (RA) are potentially influenced by exercise load, and often vary from day to day, especially in unstable condition of RA. [Objective] To develop an internet of things (IoT) systems that collects patients' daily condition and activity levels using smartphones and wearable devices, and to elucidate the relationship between smartphone-acquired patient reported outcomes (PRO) and smartwatch-acquired daily sensing data including steps in RA. [Methods] A smartphone (iPhone12) and a wristband-type smartwatch (Fitbit Sense2) were lent to each patient for free. A mobile app was developed and installed into the smartphones to collect patients' daily PRO including patient-pain-visual analogue scale (Pt-P-VAS), patient-general-VAS (Pt-G-VAS), etc. Also, the smartwatch data and physicians' assessment were collected from the same subject. Patients visited the clinic every 4 weeks and were observed for a total of 12 weeks. We conducted a simple linear regression analysis with outcome variables of Pt-P-VAS, Pt-G-VAS, etc. The independent variables included smartwatch-acquired daily steps. [Results] A total of 34 patients (7 men; 27 women) were enrolled. At baseline, mean age was 57.7 years; mean disease duration was 10.3 years; mean SDAI was 10.5; mean DAS28-ESR was 3.58; mean HAQ-DI was 0.5. The total number of PRO data was 53. The difference between the number of steps taken on the day of PRO answer (overall average 11,585 steps) and the average daily number of steps for the last 7 days prior to the day of the PRO answer (overall average 7,788 steps) was associated with Pt-P-VAS (R=0.26, P=0.065) and Pt-G-VAS (R=0.27, P=0.054). [Conclusions] An IoT system that collects patients' daily condition and activity levels was developed. Patients with RA were more likely to feel pain and be in bad health on days when they walked more than usual. Further investigation in larger patient numbers is expected. (This study is funded by AMED.)

## ICW1-5

**Single cell RNA-sequencing analysis reveals quantitative and qualitative alterations of dendritic cells in rheumatoid arthritis**

Yuichi Suwa[1], Saeko Yamada[1], Toshiyuki Ushijima[1], Hideyuki Takahashi[1], Tomohisa Okamura[1,2], Yasuo Nagafuchi[1,2], Keishi Fujio[1]
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Conflict of interest: None

[Objective] Dendritic cells (DC) play pivotal roles in rheumatoid arthritis (RA). In addition to conventional DC (cDC1, cDC2) and plasmacytoid DC (pDC), recent studies revealed the existence of precursor DC (pre-DC), and DC3 in human peripheral blood. We used single-cell RNA sequencing (scRNA-seq) to explore the landscape of human DC in RA. [Methods] We prepared pan-DC scRNA-seq libraries by sorting $CD45^+$ $CD3/16/19/88/89^-$ $HLA\text{-}DR^+$ live cells of blood samples from 20 RA patients (10 active and 10 inactive), 4 systemic lupus erythematosus (SLE) patients, and 4 healthy controls (HCs). Clusters of DC were tested for their association with clinical phenotype and for differential gene expression.

[Results] We identified clusters corresponding to cDC1, pDC, and pre-DC. cDC2-like cells were subdivided into three clusters: a CD5+ cDC2-dominant cluster (cDC2-1), a cluster with a mixture of CD5- cDC2 and DC3 (cDC2-2), and a cluster of DC3. RA showed increased proportion of pre-DC and pDC, and decreased cDC1 proportion compared to HC. SLE also showed an increase in pDC. In differentially expressed gene analysis, RA exhibited a decreased expression of *IL10R* in pre-DC, and an increased expression of activation marker *CD83* in cDC2 clusters. In SLE, there was an upregulation of "inflammatory DC3" markers *CD14* and *CD163* in cDC2-2, and chemokine receptors *CXCR3* and *CXCR4* in pDC. Gene set enrichment analysis revealed upregulation of type 1 and type 2 interferon (IFN) signaling in RA and SLE. Active RA demonstrated a higher proportion of pDC and upregulation of type 1 IFN signaling in cDC2 clusters. Active RA cDC2-1 also exhibited a decrease in the module score of TGF-β signaling. [Conclusions] We revealed a quantitative expansion of pDC in active RA and SLE. In contrast, cDC2 showed activated transcriptome in RA with high disease activity. scRNA-seq analysis of rare DC population holds the potential to elucidate the pathogenesis further and discover new therapeutic targets for RA.

## ICW2-1

**Factors associated with drug retention of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis: the multicenter REVEAL cohort study**

Mayu Shiomi[1], Ryu Watanabe[2], Shogo Matsuda[3], Takuya Kotani[3], Ayana Okazaki[3], Yuichi Masuda[3], Tsuneyasu Yoshida[4], Mikihito Shoji[4], Ryosuke Tsuge[4], Keiichiro Kadoba[4], Ryosuke Hiwa[4], Wataru Yamamoto[5], Motomu Hashimoto[2]

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Conflict of interest: None

[Objective] Real-world evidence of mepolizumab (MPZ) in patients with eosinophilic granulomatosis with polyangiitis (EGPA) has not been fully established in Japan. In this study, we aimed to identify factors affecting drug retention of MPZ in patients with EGPA in the Kansai multicenter cohort (REVEAL cohort). [Methods] We enrolled 60 EGPA patients treated with MPZ from Dec 2016 until June 2023 in the cohort. We retrospectively obtained clinical characteristics, laboratory data, treatments, and outcomes during the disease course. We divided patients into MPZ continuation (n=53) and discontinuation (n=7) groups and compared the drug retention using the log-rank test. [Results] The mean age of 60 patients was 53.8 years, female was 55%, and antineutrophil cytoplasmic antibody (ANCA) was positive in 33% at disease onset. The MPZ retention rate was 94.3% at 1 year and 78.7% at 5 years. The reasons for discontinuation were treatment of coexisting diseases (n=3), inadequate response (n=2), and remission (n=2). Age, sex, eosinophil counts, ANCA positivity, Birmingham Vasculitis Activity Score (BVAS), and initial glucocorticoid (GC) dose at disease onset were comparable between the groups; however, MPZ tended to be continued in patients with higher five-factor score (FFS). At the time of MPZ introduction, ANCA positivity, BVAS, and GC dose did not differ between the groups; however, patients who received immunosuppressants (IS) before the introduction had significantly higher MPZ retention rates than those who did not (5-year retention rate: 92.3% and 49.5%, $P = 0.038$). At the last observation, although disease duration and GC dose did not differ between the groups, the vasculitis damage index (VDI) score was significantly lower in the MPZ continuation group than the discontinuation group (median VDI score: 2 and 3, $P = 0.027$). [Conclusion] Mepolizumab tended to be continued in patients who showed higher FFS scores at onset and required IS before the MPZ introduction.

## ICW2-2

**Real-World Analysis of Avacopan Usage in Patients with Microscopic Polyangiitis: The Multicenter REVEAL Cohort Study**

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Conflict of interest: None

[Objective] Two years after the approval of avacopan (AVA) in Japan, there is still a lack of real-world data on its usage. We conducted a retrospective analysis of real-world clinical data for AVA in cases of microscopic polyangiitis (MPA) using the Kansai multicenter cohort (REVEAL cohort). [Methods] We retrospectively enrolled 221 MPA patients between December 2016 and April 2023, collecting data on clinical characteristics, laboratory findings, treatment regimens, and outcomes. [Results] AVA was used in 19 cases (8 for induction therapy [≦ 3 months], 11 for maintenance therapy). In the induction therapy, the AVA and intravenous cyclophosphamide (IVCY) groups exhibited higher Birmingham Vasculitis Activity Scores compared to prednisolone (PSL) monotherapy and rituximab (RTX) groups (median [IQR]; AVA: 17.5 [14.3, 24]; IVCY: 18 [12, 21.5]; PSL: 12 [6, 16]; RTX: 14 [9.5, 20]). The AVA group showed the lowest six-month relapse and mortality rates (Relapse rate, %; AVA: 0; PSL: 6.7; IVCY: 6.6; RTX: 17.6, Mortality rate, %; AVA: 0; PSL: 5.0; IVCY: 11.8; RTX: 5.9). Though the ANCA reduction rate at three months was similar across groups (mean [SD] %; AVA: 84.4 [15.6]; PSL: 87 [25.6]; IVCY: 86.3 [23.5]; RTX: 85.9 [18.0]), the reduction rate of PSL dose was highest in the AVA group (mean [SD], %; AVA: 74.8 [5.0]; PSL: 53.6 [15.6]; IVCY: 60.3 [15.2]; RTX: 57.4 [18.3]). The same trends were also observed using inverse probability of treatment weighting. In maintenance therapy, AVA was primarily used in patients who had experienced relapses (10/11, 91%). Following the initiation of AVA, PSL gradually decreased (mean [SD], mg; 0 months: 9.0 [8.0]; 1 month: 7.8 [5.8]; 3 months: 6.1 [3.4]; 6 months: 4.8 [3.3]), and the annual relapse rate reduced by 62% (pre-AVA: 1.4% to post-AVA: 0.5%, p=0.046). Only one case discontinued AVA due to infection. [Conclusion] This real-world data revealed a noticeable degree of effectiveness and safety for AVA in the treatment of MPA.

## ICW2-3

**Poor prognostic factors for predicting relapse of interstitial lung disease in microscopic polyangiitis: multicenter study in Japan- the REVEAL cohort study-**

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Conflict of interest: None

[Objective] This study aimed to investigate poor prognostic factors for relapse of interstitial lung disease (ILD) in microscopic polyangiitis (MPA) using clinical characteristics in a multicenter cohort of Japanese patients with MPA (REVEAL cohort). [Methods] Patients diagnosed with MPA according to the Chapel Hill consensus definition were enrolled from 2001 to 2023 in multicenter institutes in the Kansai district of Japan. Among them, patients with MPA complicated with ILD (MPA-ILD) were identified using chest high-resolution CT on admission. We also examined these patients who relapsed ILD after immunosuppressive treatment. We explored the risk factors for predicting relapse of ILD in patients with MPA-ILD by comparing the demographic, clinical, laboratory, and radio-

logical findings and treatments between the relapsed and non-relapsed groups on admission. [Results] Out of the 243 patients with MPA, 134 had ILD. The median age was 75 years and seventy-four (55%) patients were women, and eighty-nine patients (66%) had UIP pattern on HRCT. Among them, 28 relapsed during a mean follow-up of 4.2 years. Serum KL-6 and Sp-D levels and the prevalence of UIP pattern were significantly higher in the relapsed group than in the non-relapsed group ($P$ = 0.0009, 0.001, 0.01, respectively). There were no significant differences in the median dose of prednisolone or ratio of immunosuppressive therapy between the groups. Based on these findings, we determined KL-6≧430 U/mL and Sp-D≧89.5 ng/mL to be the best cut-off values for predicting the relapse of ILD using receiver operating characteristic curve analysis. The 10-year relapse rate was significantly higher in patients with KL-6≧430 U/mL, Sp-D≧89.5 ng/mL, and the presence of UIP pattern than in those without them ($P$< 0.0001, 0.001, and 0.03, respectively). [Conclusions] Our multicenter cohort indicated that higher KL-6 and Sp-D levels and the presence of UIP pattern were useful predictors for relapse of ILD in patients with MPA.

## ICW2-4

**Trans-omics landscape of systemic vasculitis identified matrix metalloproteinase 12 as a novel signature molecule**

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Conflict of interest: Yes

[Objective] Systemic vasculitis involves inflammatory and degenerative changes in vascular structures. Disease progression in asymptomatic patients is important, even under inhibition of interleukin (IL)-6. Here, to identify key molecules involved in the disease pathophysiology of systemic vasculitis, we performed a trans-omics analysis. [Methods] Patients with newly diagnosed or relapsed rheumatic and musculoskeletal diseases from June 2013 until September 2022 were enrolled. We screened vasculitis-specific molecules by combining findings from serum proteome analysis and whole-blood bulk RNA sequencing. We further validated the identified molecules using immunohistochemical staining and spatial transcriptome analysis. [Results] Serum proteome and RNA sequencing identified matrix metalloproteinase (MMP) 12 as a significant molecule for systemic vasculitis: specifically, it distinguished vasculitis from other rheumatic and musculoskeletal diseases, reflected disease activity along with longitudinal change, and predicted relapse in patients with large-vessel vasculitis. MMP12 could also be used to detect insidious disease activity even under treatment with IL-6 inhibition. Immunohistochemical staining of the affected tissues demonstrated that MMP12 was specifically expressed in tissue-infiltrating CD206-positive histiocytes. Spatial transcriptome analysis revealed the characteristic phenotype of MMP12-positive histiocytes and its association with histiocyte maturation and formation of multinucleated giant cells. [Conclusions] MMP12 is a disease-specific molecule that is associated with histiocyte maturation and the formation of multinucleated giant cells and reflects disease activity independently of the interleukin-6 pathway in systemic vasculitis.

## ICW2-5

**Long-term efficacy of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis: a propensity score matching analysis in the multicenter REVEAL cohort study**

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Conflict of interest: None

[Objective] Mepolizumab (MPZ) has been shown to be effective in patients with eosinophilic granulomatosis with polyangiitis (EGPA) in clinical trials; however, there are few studies comparing the disease course between MPZ-treated patients (MPZ group) and those who were not treated with MPZ (non-MPZ group) in a real-world setting. In this study, we aimed to compare the disease course and outcomes between the groups, and assess the long-term efficacy of MPZ in the Kansai multicenter REVEAL cohort. [Methods] We enrolled 113 patients with EGPA who were registered until June 2023 in the cohort. Clinical characteristics, disease activities, organ damage, treatments, and outcomes were retrospectively obtained. Propensity score matching (PSM) was performed to minimize potential confounding factors. [Results] A total of 37 matched pairs of patients were identified after PSM. Clinical characteristics including age at onset, sex, disease duration, antineutrophil cytoplasmic antibody positivity, Birmingham Vasculitis Activity Score (BVAS) at onset, and Five-factor score were comparable between the groups. In the MPZ group, the 5-year survival rates were significantly higher ($P$ = 0.009), and the BVAS at the last observation was significantly lower ($P$ = 0.028) than those in the non-MPZ group. Glucocorticoid (GC) dose at the last observation were significantly lower in the MPZ group ($P$ = 0.011), and the proportion of achieving GC dose ≦ 4 mg/day was significantly higher in the MPZ group ($P$ = 0.027). Multivariate logistic regression analysis revealed that achievement of GC dose ≦ 4 mg/day was positively associated with MPZ administration (OR 3.55, $P$ = 0.028) and inversely associated with wheeze at disease onset (OR 0.103, $P$ = 0.0074). [Conclusion] Mepolizumab contributes not only to controlling the disease activity, but also to sparing the GC dose, which may lead to prolonged survival in patients with EGPA.

## ICW2-6

**Different immunological phenotypes of microscopic polyangiitis identified by single-cell multi-omics analysis**

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Conflict of interest: Yes

[Objective] Patients with autoimmune vasculitis present with a variety of organ-threatening symptoms, but the underlying immunological basis for this clinical heterogeneity remains unclear. The aim of our study is to elucidate the immunological characteristics of autoimmune vasculitis, focusing on microscopic polyangiitis (MPA). [Methods] Patients diagnosed with MPA and age-matched healthy donors were recruited and whole white blood cells were collected. Cells were subjected to single cell transcriptome and proteome analyses. Cell populations were annotated using supervised analysis based on existing single cell data. We then conducted differential abundance analysis using Milo, a statistical framework performing difference-in-presence tests by assigning cells to partially overlapping neighborhoods. To detect interindividual differences among patients, we conducted pathway analysis and differential expression gene analysis. Finally, clinical and laboratory parameters were assessed to determine the potential of single-cell analysis-based classification. [Results] In the context of PBMCs, patient-specific analysis divided MPA into two subgroups: the MPA-MONO group, characterized by a high proportion of activated $CD14^+$ monocytes that persisted before and after immunosuppressive therapy, and the MPA-IFN group, characterized by monocytes with interferon-signature genes that decreased significantly after treatment. The MPA-MONO group had a high relapse rate and increased monocyte to total PBMC ratio. In contrast, the MPA-IFN group showed a favorable response to immunosuppressive therapy and high serum interferon-alpha concentrations (manuscript in press). Similar single-cell analyses have been performed on other cell populations, leading to the identification of pathological cell subsets and novel therapeutic targets. [Conclusions] Our findings provide insight into the immunological phenotypes of MPA and suggest clinical applications based on accurate prognostic predictions.

## ICW3-1

**Factors associated with progression of chronic kidney disease in rheumatoid arthritis patients who treated with methotrexate monotherapy**

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Conflict of interest: None

[Objective] To identify factors associated with progression of chronic kidney disease (CKD) in patients with rheumatoid arthritis treated with methotrexate monotherapy. [Methods] We reviewed consecutive patients with rheumatoid arthritis who underwent continuous methotrexate monotherapy for more than five years from 2018 to 2023 in our hospital retrospectively. Patients who had CKD or who were treated with concomitant other disease-modifying antirheumatic drugs were excluded. We collected information including clinical disease activity index (CDAI), C-reactive protein (CRP) levels, erythrocyte sedimentation rates, estimated glomerular filtration rate, methotrexate dose, and glucocorticoid use. Patients were divided into 2 groups according to CKD progression during 5-years observation period, and their clinical characteristics were compared between patients with and without CKD progression. [Results] Sixty-eight patients were included in the analysis. The mean age was 61 years, and 61 (90%) were female. The mean dose of methotrexate was 8.2 mg/week, and the mean CDAI in 5 years was 2.5. Methotrexate had been administered for the mean duration of 9.9 years. During the 5-year observation period, 10 patients (14.7%) progressed to CKD. Patients in the CKD progression group were older (75 years vs 59 years, p<0.01), were complicated with hypertension more frequently (20% vs 3.4%, p=0.03), and had higher disease activity (the mean CDAI, 5.6 vs 1.9, p=0.02). The dose of methotrexate and the duration of methotrexate use were not different between the two groups (7.7 mg/week vs 8.3 mg/week, p=0.6; 9.9 years vs 9.9 years, p=0.7, respectively). [Conclusions] Older age, complication of hypertension, and sustained high disease activity are factors associated with progression to CKD in patients with rheumatoid arthritis treated with methotrexate monotherapy, while the dose and duration of methotrexate are not relevant.

## ICW3-2

**Frailty is associated with a reduced frequency of vocalization in rheumatoid arthritis patients**

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Conflict of interest: None

[Objective] A lack of opportunities for vocalization can lead to a decline in vocal cord function, and oral function, as well as cognitive function, and a reduction in social connections. As a result, oral/cognitive/social frailty are expected to increase. In this study, we investigated the association between vocalization and frailty in rheumatoid arthritis (RA) patients. [Methods] Among 696 RA patients visited in 2023 (T-FLAG study), 661 patients were available for the investigation of patient backgrounds, including Clinical Disease Activity Index (CDAI) and the Kihon Checklist (KCL), and their responses to a questionnaire regarding vocalization. Frailty was defined as a KCL score of 8 points or higher. Odds ratios associated with frailty were calculated using multivariable logistic regression analysis. [Results] Among 661 RA patients (474 women, 71.8%), 261 (39.5%) patients exhibited frailty. The mean age (± standard deviation) was 73.6 ± 11.9/65.2 ± 13.5 years (frailty group/non-frailty group), disease duration was 14.7 ± 10.8/11.4 ± 9.2 years, and CDAI was 9.1 ± 9.2/4.5 ± 5.9, both of which were higher significantly in the frailty group. Frequency of vocalization (“every day”/”1-5 times a week”/”1-3 times a month”/”almost never”) was 37.2%/25.7%/11.1%/26.1% in the frailty group and 62.5%/20.5%/7.8%/9.2% in the non-frailty group, and frequency of vocalization was lower in the frailty group. Factors significantly associated with frailty were CDAI (odds ratio 1.10, 95% confidence interval 1.07-1.13) and “infrequent vocalization (1-3 times a month, almost never)” (odds ratio 2.81, 95% confidence interval 1.87-4.24). [Conclusions] In this study, frailty was significantly associated with a reduced frequency of vocalization. For patients, oral/cognitive/social frailty are difficult to recognize. These results suggest that, in order to prevent frailty, it is beneficial not only to suppress disease activity in RA patients, but also to support patients in vocalizing.

## ICW3-3

**Thermographic detection of subclinical joint inflammation at the elbow of patients with rheumatoid arthritis: a comparison with ultrasonography**

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Conflict of interest: None

**Objective:** To compare thermal imaging (TI) and ultrasound (US) in detecting subclinical joint inflammation at clinically quiescent (non-tender; non-swollen) elbows in patients with rheumatoid arthritis (RA). **Methods:** TI and US of the right elbow were performed on the same study visit. The minimum (Tmin), maximum (Tmax) and average (Tavg) temperatures per elbow (anterior, medial, lateral and posterior aspects) were summed to obtain the respective TI parameters MIN, MAX and AVG. US grey-scale (GS) and power Doppler (PD) joint inflammation severity scoring (0-3) per elbow (anteriorly and posteriorly) were summed to obtain the respective total GS (TGS) and total PD (TPD) scores. Polyserial correlation and simple linear regression were used to study the relationship between TI (continuous) and US (ordinal) variables. **Results:** This cross-sectional study (35 RA subjects with 35 elbows) included 140 thermograms (4 aspects per elbow) and 70 joint recesses scanned by US. All TI parameters correlated significantly with TPD (MIN: rho=0.60, P<0.001; MAX: rho=0.70, P<0.001; AVG: rho=0.64, P<0.001) and number of joint recess (es) with PD≧1 or GS≧2 (MIN: rho=0.77, p<0.001; MAX: rho=0.95, P<0.001; AVG: rho=0.83, P<0.001). TGS correlated significantly with AVG (rho=0.34, P=0.036) but not with MIN and MAX (both P>0.05). Linear regression demonstrated a statistically significant relationship (all P<0.05) between all TI parameters (MIN, Max and AVG) and US outcomes (TPD, TGS and number of joint recess (es) with PD≧1 or GS≧2) with regression coefficient ranging from 0.08 to 0.15. There was excellent intra-observer reliability (intra-class correlation coefficient ranging from 0.998 to 1.000) when 40 sets each of Tmin, Tmax and Tavg repeated (≧2 weeks apart) readings were obtained from a random subset of baseline thermograms. **Conclusion:** For the first time, our study revealed an association between TI and US detected subclinical joint inflammation at the elbow of patients with RA.

## ICW3-4

**Relationship between types of passive smoking and onset of rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate how passive smoking by parents in childhood and from cohabitants or at work in adulthood affect the development of rheumatoid arthritis. [Methods] The subjects were all outpatients who visited the Department of Rheumatology at JR Hiroshima Hospital between November 2022 and January 2023. Patients’ and parents’/cohabitants’ smoking history, periodontal disease symptoms and onset time were investigated using a questionnaire format, and disease information was extracted from the medical records. [Results] Out of 495 total patients, 379 responded to the questionnaire. One hundred and eighty-eight patients (40%) had rheumatoid arthritis, 40 (11%) polymyalgia rheumatica and 29 (8%) spondyloarthritis, with a median age of 71 years and 72% of the patients were female. In addition, 32% of the patients had a history of smok-

ing, 70% had passive smoking exposure from their parents and 82% had passive smoking exposure at home or at work in adulthood. The rheumatoid arthritis (RA) group was significantly more likely than the non-rheumatoid arthritis (non-RA) group to have a cohabitant smoking in adulthood, although there was no difference in their own smoking history. This was also true for the non-smoker group. [Conclusions] Passive smoking has been reported to be associated with the development of rheumatoid arthritis, and the same trend was observed in the present study. In terms of the pattern of passive smoking, significant differences were found only for smoking by adult cohabitants. The type of passive smoking should also be noted.

## ICW3-5

**Fish consumption influences treatment response in patients with rheumatoid arthritis on molecular targeted therapy**

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Conflict of interest: None

[Objective] Molecular targeted therapies using biologics or Janus kinase inhibitors (JAKi) are widely practiced in patients with rheumatoid arthritis (RA), with good clinical results in many, but not all patients. Intake of fish rich in n-3 polyunsaturated fatty acids (n-3 PUFA) has been shown to have a positive effect on the clinical course of RA. This study aimed to evaluate the impact of fish consumption on treatment response in RA patients receiving molecular targeted therapies. [Methods] This is a cross-sectional retrospective study involving RA patients on treatment with biologics or JAKi who attended Hokkaido University Hospital. Enrolled patients completed a brief-type self-administered diet history questionnaire (BDHQ) and a detailed fish frequency questionnaire (DFFQ) referring to consumption frequency in the previous month. RA disease activity was evaluated by qualified rheumatologists and clinical/laboratory data retrospectively extracted from the medical records. Responder group was defined as disease activity score 28 (DAS28)-ESR <2.6 and DAS28-CRP <2.4. Statistical analysis using chi-square test, Fisher's exact test and logistic regression analysis was performed. [Results] Of the 205 RA patients included, 162 were females and median age was 67 years old. Biologics was on 87% patients, JAKi on 13% and 59% patients were responders. The estimated n-3 PUFA daily intake was higher in the responder group compared to the non-responder group [median grams, 2.49 g/day (IQR 1.82-3.23) vs 1.99 g/day (IQR 1.33-2.94), p=0.04]. Moreover, analysis of DFFQ showed that n-3 PUFA rich fish ≧1 time/week consumption was more frequent in the responder group than in non-responder group (30% vs. 14%, p=0.01) and it was identified as an independent factor for good outcomes in the responder group (OR: 2.50, 95% C. I: 1.06-5.88, p=0.04). [Conclusions] Intake of n-3 PUFA rich fish ≧1 time/week may favorably affect the clinical response of RA patients receiving targeted therapy.

## ICW4-2

**MiDs enhanced mitochondrial fission contributes to proinflammatory characteristics of RASF through activation of mitophagy**

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Conflict of interest: None

[Objective] Rheumatoid arthritis synovial fibroblasts (RASF) are epigenetically imprinted with an aggressive phenotype and are the main effector cells leading to RA pathogenesis. Mitochondrial dynamics proteins of 49 kDa (MiD49) and 51 kDa (MiD51)-mediated mitochondrial dynamics disorder contributes to the aggressive phenotype. Here, we not only explore the regulatory effect but also clarify mechanism of MiD49 and MiD51 in the abnormal functions of RASF. [Methods] Immunohistochemistry and tissue immunofluorescence were used to detect MiD49/51 expression in RASF and endothelial cells from synovial sections of control mice and CIA mice, together with OA and RA patients. shMiD49/51 and siMiD49/51 were used to down-regulate the expression of MiD49/51 in CIA mice and RASF. Western blot was used to detect the expression levels of proliferation, adhesion, angiogenesis, mitophagy and other related proteins after knockdown of MiD49/51in RASF. RASF adhesion, pro-angiogenesis, proliferation and migration were also evaluated after silence MiD49/51. Confocal microscopy was used to detect mitochondrial morphology in RASF. [Results] MiD49/51 expression was elevated on FLS and endothelial cells in the synovium of RA patients and CIA mice. Treatment with sh-MiD49/51 significantly inhibited synovial inflammation. MiD49/51 increased mitochondrial fission in RASF and MiD49/51 silence can restore the RASF mitochondrial network structure. MiDs promote mitochondrial fission and lead to increased mitophagy, which in turn affects the proliferation, adhesion, migration and angiogenesis of RASF. [Conclusions] The overexpression of MiDs in RASF can induce mitochondrial fission and promote mitophagy, thereby affecting RASF function and aggravating the process of RA disease.

## ICW4-3

**Interleukin-26 facilitates hyperplasia of synovium and cartilage destruction in a collagen antibody-induced arthritis model**

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Conflict of interest: None

[Objective] IL-26 is known as a Th17 cytokine, with its gene being absent in rodents. IL-20RA/IL-10RB heterodimer is an IL-26 receptor, and IL-26 binding to this receptor results in functional activation via STAT3 phosphorylation, whereas recent advance in IL-26 research indicates other diverse mechanism of action of IL-26. Although it has been reported that IL-26 levels in the serum and synovial fluids of RA patients are much higher than those in healthy subjects, whether IL-26 is involved in the pathogenesis of RA is not yet well understood. Our objective is to elucidate the role of IL-26 in an animal arthritis model. [Methods] We investigated the role of IL-26 in a collagen antibody-induced arthritis (CAIA) model utilizing human IL-26 BAC transgenic (hIL-26Tg) mice which have been developed in our laboratory. Pathological and flow cytometry analyses of joints and qRT-PCR of synovium were conducted. [Results] Clinical scores of hIL-26Tg mice were higher than control mice. Hyperplasia of synovium, abnormal proliferation of fibroblast-like synoviocytes, and increased levels of neutrophils and macrophages infiltrated into synovium were observed in hIL-26Tg mice. Moreover, we examined safranin-O staining to assess cartilage destruction. A decrease of cartilage over a wide area was markedly observed in hIL-26Tg mice. Inflammatory factors associated with hIL-26 were investigated by qRT-PCR of the synovium in a CAIA model. mRNA expression levels of CXCL10 and MMP-9 in hIL-26Tg mice were significantly higher than those in control mice. [Conclusions] Taken together, our data strongly suggest that IL-26 exacerbates arthritis and that IL-26 may be a novel promising target for the treatment of RA patients who are resistant to current therapies including MTX, JAK inhibitor, or bDMARDs. We are currently investigating the more detailed cellular and molecular mechanism of IL-26-mediated cartilage destruction and hyperplasia of synovium.

## ICW4-4

**Myeloid-derived suppressor cells from the inflamed joints of arthritic SKG mice differentiate into osteoclasts and promote bone resorption**

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Conflict of interest: None

**Background** Myeloid-derived suppressor cells (MDSCs) are heterogeneous immature myeloid cells with suppressive functions. Previous re-

ports indicate that MDSCs are increased in BM and spleen of arthritis model mice, but detailed analysis of MDSCs in inflammatory joints is limited. **Objective** To characterize the MDSCs in the joint of rheumatoid arthritis (RA) model mice. **Methods** We isolated $CD11b^{+}Gr1^{+}$ cells as MDSCs from joints (Jo-MDSCs), bone marrow (BM-MDSCs) and spleen (Sp-MDSCs) of arthritis-induced SKG mice, and investigated differential expressed genes (DEGs) by microarray expression analysis. T cell proliferation and differentiation assays were performed to check the MDSCs suppressive potential. M-CSF and RANKL stimulation was used to analyze the osteoclast differentiation potential of MDSCs. Finally, intra-articular injection of Jo-MDSCs (left paws) or normal saline (right paws) was performed in SKG mice. Joint micro-CT was used to evaluate the degree of damage in the hind paws. **Results** Microarray analysis and qPCR revealed that Jo-MDSCs highly expressed immunosuppressive DEGs (*Pdl1, Arg1, Egr2* and *Egr3*) compared to BM-MDSCs. In addition, Jo-MDSCs highly expressed NF-κB non-canonical pathway DEGs (*Nfkb2* and *Relb*), which are related to osteoclast differentiation, compared to Sp-MDSCs. These results were further confirmed by flow cytometry. BM-MDSCs differentiated into osteoclasts but did not suppress T cell-proliferation, while Sp-MDSCs did the opposite. In contrast, Jo-MDSCs had both functions. Jo-MDSCs decreased Th1 (Cont: 41±12%, Jo-MDSCs: 28±10%, p=0.032) and Th17 (Cont: 40±12%, Jo-MDSCs: 25±8.6%, p=0.046) proportion in vitro. Finally, intra-articular injection of Jo-MDSCs exacerbated the arthritis, and micro-CT images showed more bone erosions (BE) in the Jo-MDSCs injected side (Cont: 0.70±0.28 BE/ankle, Jo-MDSCs: 1.6±0.49 BE/ankle, p=0.03). **Conclusions** Jo-MDSCs exhibit an osteoclast differentiation potential and exacerbate arthritis and bone erosion in a RA model.

## ICW4-5

**Cytosporone B, a Selective Agonist of Nr4a1, Alleviates Experimental Arthritis in SKG mice**

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Conflict of interest: None

[Objective] NR4A family regulates T cell tolerance mechanisms, including thymic-negative selection, Treg generation and function, and anergy/exhaustion. Among the three NR4A nuclear receptors, NUR77, the product of *Nr4a1* gene, is well-characterized in T and B cells. A recent study elucidated that higher expression of *Nr4a1* in $CD4^{+}$ T cells marked their auto-reactivity and arthritogenicity in experimental arthritis mice. This study aimed to assess the impact of cytosporone B (CsnB), a specific agonist targeting *Nr4a1*, on T cells and explore its therapeutic potential in a murine arthritis model. [Methods] In vitro, $CD4^{+}$ T cells were stimulated with anti-CD3/28 in the presence or absence of CsnB, followed by an evaluation employing RNA sequencing. The effect of CsnB on in vitro Th17 differentiation was assessed. In vivo, arthritis was induced in SKG mice by Zymosan A injection. The effect of CsnB (compared to DMSO) on arthritis was assessed, and splenocytes were studied by flowcytometry. [Results] RNA sequencing revealed significant downregulation of inflammatory mediators (including *Csf1*, *Tbx21*, *Gata3*, *Il4*, *Ifng*, *Il21*, *Tnfsf13b*) in CsnB-treated $CD4^{+}$ T cells. Th17 cell differentiation was significantly reduced with CsnB treatment. In vivo, CsnB administration significantly attenuated arthritis development in SKG mice. Notably, effector memory T cells decreased, while naïve T cells increased in the treatment group. Th17 cells decreased, while Th1 and Treg populations remained comparable between groups. The proportion of anergic T cells ($CD4^{+}$ $FoxP3^{-}FR4^{+}CD73^{+}$) significantly increased in the treatment group. No significant changes were detected in B cell subsets, monocytes, or neutrophils. [Conclusions] CsnB mitigates T cell activation and Th17 cell differentiation both in vitro and in vivo experiments. Consequently, CsnB ameliorates experimental arthritis in SKG mice. These findings underscore the potential of Nr4a1 as promising therapeutic target of inflammatory arthritis.

## ICW4-6

**Negative Regulation of Neddylation Reduces RA FLS Inflammatory Responses and Arthritis in Mouse Model**

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Conflict of interest: Yes

[Objective] Fibroblast-like synoviocytes (FLS) contribute to the pathogenesis of rheumatoid arthritis (RA), and display an aggressive phenotype in RA via activation of NF-κB. Neddylation, which conjugates NEDD8 to its substrate, is a post translational modification and regulates ubiquitination by targeting cullin (CUL)-ring E3 ubiquitin ligases (CRL). Our previous epigenetic analysis showed that genes involved with ubiquitination were dysregulated in RA FLS. We hypothesized that dysregulated neddylation in RA FLS contributes to the RA FLS behavior. [Methods] Analysis of ubiquitination pathway epigenetic marks in RA and osteoarthritis (OA) FLS was performed using public ChIP-seq data. NF-κB activation was assessed *in vitro* by stimulating FLS with IL-1β. NUB1 overexpression and MLN4924 (a neddylation inhibitor) was used to evaluate the neddylation status and NF-κB activation in RA FLS. *In vivo* effect of MLN4924 was evaluated in the K/BxN serum transfer arthritis model. [Results] Epigenetic analysis identified a reduced *H3K27ac* peak in the promoter region of *NUB1*, an endogenous inhibitor of neddylation, in RA FLS vs OA FLS. *NUB1* induction by IL-1β was lower in RA FLS than OA FLS. We then explored the neddylation pathway in FLS. The ratio of neddylated CUL1 to non-neddylated CUL1 was lower in OA FLS than RA FLS. NUB1 overexpression (NUB1 OE) decreased the neddylation ratio of CUL1 in non-stimulated RA FLS, decreased NF-κB nuclear translocation, and *IL-6* mRNA in IL-1β stimulated RA FLS. MLN4924 decreased the neddylation ratio of CUL1, NF-κB nuclear translocation and IL-6 mRNA in IL-1β stimulated RA FLS. Administration of MLN4924 decreased the arthritis scores in K/BxN serum-transfer arthritis compared to vehicle alone. [Conclusions] We identified dysregulation of a novel gene, *NUB1*, and upregulated neddylation in RA FLS. These data suggest that neddylation system contributes to the pathogenesis of RA and regulation of neddylation could be a novel therapeutic approach.

## ICW5-1

**Immunological remission, prognosis and smoking impact in rheumatoid arthritis among patients treated with TNF inhibitors**

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Conflict of interest: None

[Objective] evaluate the dynamics of serum titres for RF IgM/A, anti-CCP, anti-MCV under anti-TNFi, identifying pretreatment patients who will/not respond to TNFi, analyze the existence of correlations with the activity scores and evaluate the impact of smoking. [Methods] prospective, observational study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDs. [Results] following the evolution of serum levels, we noticed a reduction almost for all four biomarkers tested as follow RF IgM, (baseline=123.07±126.33,6 months=77.91± 105.670,12 months=50.25± 88.26), IgA (baseline=80.71± 114.84,6 months=44.75± 71.64,12 months=28.78± 65.69), anti-CCP (baseline=101.52± 51.653,6 months=85.14± 50.249,12 months=64.19± 43.669), anti-MCV (baseline=65.66± 132.080,6 months=43.12± 85.368,12 months=17.15± 27.856). Analyzing the possible correlations, between the immunological parameters and the disease activity scores at any visits, they were not observed, but there are strong positive correlations between all these scores. In the case biomarkers, we observe moderate to strong positive correlations for RF isotypes that where maintained throughout the study. Lower baseline titres of RF IgM (51.36±95.359 U/ml, p=0.01629), IgA (22.45±61.256 U/ml, p=0.03336) and anti-CCP (60.82±26.331 ng/ml, p=0.00011) had predictive value for achieving a good EULAR response at 6 months. For anti-MCV baseline titres, there were no differences between groups (p=0.459). For the response at 12 months, lower baseline titres for RF type Ig M (92.93±120.22 U/ml, p=0.0103) and Ig A (49.96±98.08 U/ml, p=0.0024) had predictive value for achieving a good EULAR re-

sponse. Regarding smoking, we noticed that the response to treatment at 6 months is associated with nonsmoker status, and the nonresponder with smoking (p=0.017). [Conclusions] achieving immunological remission does not appear to be an absolute goal. Predicting treatment response remains a major need and finding a solution can begin with the use of common biomarkers.

## ICW5-2

**Immunological remission among new proposed diagnostic biomarkers and their predictive role to TNFi treatment response in rheumatoid arthritis**

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Conflict of interest: None

[Objective] In the era of biologic therapies, at least 2 needs are still being debated: -does immunological remission occur with current TNFi? -diagnosis patients in the early stage, using new biomarkers and the need to identify pre-treatment of patients who will respond to a certain biological agent. We proposed to evaluate two new RA diagnostic biomarkers: 14-3-3eta protein and cartilage oligomeric matrix protein (COMP). We assesed the evolution of serum titres under TNFi, analyzed the existence of correlations with the activity scores and tested their predictive value for treatment response. [Methods] prospective and observational study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDs. Clinical assessment was performed at 0, 6 and 12 months. [Results] following the evolution of serum levels, we noticed a reduction of biomarkers tested as follow: 14-3-3eta protein (baseline=0.43± 0.591, 6 months=0.32± 0.452, 12 months=0.28± 0.499 ng/ml) and COMP (baseline=948.75±215.68,6 months =1044.2±674.67,12 months= 740.88±227.04 ng/ml). Lower baseline titres of 14-3-3 eta protein (0.51±0.580, p=0.045178) and for COMP (746.04±130.095, p=0.00000) had predictive value for achieving a goodnEULAR response at 6 months Grouping patients in 2 categories (responders/nonresponders) for 6 months response we identified significant differences between groups just for baseline titres of 14-3-3eta (responders 0.36±0.515 ng/ml, 0.99±0.888 nonresponders ng/ml, p=0.040) For 12 months reponse, we didn't find significant differences (14-3-3eta p=0.376, COMP, p=0.143). Analyzing the possible correlations, between the immunological parameters and the disease activity scores at any visits, they were not observed, but there are strong positive correlations between all these scores [Conclusions] achieving immunological remission does not appear to be an absolute goal. Predicting treatment response remains a major need and new diagnostic biomarkers could help us in the future.

## ICW5-3

**Effectiveness of the first etanercept biosimilar for Korean patients with rheumatoid arthritis in real-world practice**

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Conflict of interest: None

[Objective] Biosimilars are now widely used in place of their originator, mainly due to their cost-effectiveness and comparable safety profiles. We aimed to compare the drug persistence and adverse events (AEs) of the first etanercept biosimilar approved in Korea with reference etanercept in rheumatoid arthritis (RA), using a nationwide biologic register. [Methods] Data were extracted from the KOBIO-RA registry (NCT01965132) starting from the first registered date of the etanercept biosimilar (September 2014) to April 2023. We analyzed drug retention and efficacy (DAS28-erythrocyte sedimentation rate [ESR] or DAS28-C-reactive protein [CRP], and ACR core set measures) of the biosimilar and its originator, and AEs (grade 1~3) throughout follow-up. [Results] The mean age of the subjects (etanercept biosimilar N=58, originator N= 121) was 54.4 years. Over 80% of patients were on oral glucocorticoids (GC) at baseline (mean 3.8 mg/day of prednisolone or its equivalent). Drug retention of the biosimilar versus the originator was comparable (p = 0.1611). Retention in first-line users (82.1% of subjects) tended to be favorable in biosimilar users but not statistically significant (p = 0.0526). Switching to another agent or discontinuation occurred in 48.5% of patients treated with the biosimilar and 51.0% with its originator. Regarding the two major reasons for switching or discontinuation (lack of efficacy versus (vs.) AEs), data in biosimilar users were 42.4 vs. 6.1%, whereas originator users were 20.6 vs. 18.6%. The etanercept biosimilar showed equivalent improvements in DAS28-ESR, DAS28-CRP, and ACR responses to its originator. Twelve percent (4/33) of biosimilar users and 5.9% (6/102) of originator users developed grade 3 AEs. [Conclusions] Our real-world data corroborate the effectiveness and safety of the etanercept biosimilar for Korean patients with RA. We plan to investigate further biosimilars' utility in reducing oral GC use in Korean patients.

## ICW5-4

**Efficacy of Tocilizumab (TCZ) for skin sclerosis in Systemic sclerosis (SSc) complicated with rheumatoid arthritis (RA)**

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Conflict of interest: None

Objective: To investigate the effect of TCZ on skin sclerosis in SSc complicated RA. Methods: The effect of TCZ on skin sclerosis in 31 patients with SSc complicated RA (TCZ group) and 20 patients with standard of care (SOC) was investigated. Patient background was adjusted for selection bias by PS-IPTW. The primary endpoint was the percentage of improvement in skin sclerosis at 1 year, and the secondary endpoint was the change in mRSS at 1 year (ΔmRSS/year). Improvement in skin sclerosis was defined as a decrease of at least 20% from baseline. Result: The age and disease duration were 59.8 years and 9.4 years in the TCZ group and 61.9 years and 7.1 years in the SoC group, respectively. The activity of rheumatoid arthritis in the TCZ group was CDAI 24.3, and 8 patients (25.8%) had interstitial lung disease (ILD). On the other hand, the proportion of patients with improved skin sclerosis was 8 (25.8%) in the TCZ group, compared to 3 (15%) in the SoC group (p=0.493), and there was no difference in ΔmRSS/year in the TCZ group (-1.4±2.6 vs. -1.8±4.6 in the SoC group (p=0.600). As for treatment predictors, none of the biomarkers (CRP, ESR, RF), RA disease activity, autoantibodies, skin lesions, duration of disease of SSc or RA were associated with changes in skin sclerosis. The results of the nailfold capillary findings showed that patients with severe capillary abnormalities tended to show worse response to TCZ (improvement 14.3%), but there was no statistically significant difference between capillary abnormaliries (p=0.152). The effect of TCZ on ILD was difficult to analyze due to the small number of ILD complications. Conclusion: Overall, improvement of skin sclerosis by TCZ in SSc complicated with RA was poor. Careful selection of cases was considered necessary.

## ICW5-5

**Efficacy of ozoralizumab based on baseline rheumatoid factor titers in patients with rheumatoid arthritis and an inadequate response to methotrexate: Post hoc analysis of a Phase II/III study (OHZORA trial)**

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Conflict of interest: Yes

[Objective] Ozoralizumab (OZR) is a next-generation anti-tumor necrosis factor (TNF) antibody which is a trivalent NANOBODY® compound. The OHZORA trial evaluated the efficacy and safety of OZR at 30 or 80 mg for 52 weeks in patients with active rheumatoid arthritis (RA) despite methotrexate therapy. Generally, the efficacy of anti-TNF antibodies containing the fragment crystallizable (Fc) portion is reduced in patients with high titers of rheumatoid factor (RF); however, that of OZR which lacks the Fc portion for such patients remains unclear. In this post hoc analysis of the OHZORA trial, we aimed to assess whether the efficacy of OZR is influenced by the titers of RF. In addition, we aimed to evaluate changes in RF and anti-CCP antibody titers in patients with RA treated with OZR. [Methods] Patients enrolled in the OHZORA trial were classified into 4 groups according to baseline RF titer quartiles. The sequential disease activity score in 28 joints using erythrocyte sedimentation rate (DAS28-ESR) as well as titers of RF and anti-CCP antibody were monitored in each RF titer group and compared by Wilcoxon matched-pairs signed rank test between baseline and at 52 weeks. [Results] A total of 381 patients were classified into 4 groups (RF1; RF 3-20 IU/mL, RF2; 20-49, RF3; 49-153, RF4; 153-2029). Treatment with 30 mg OZR significantly reduced DAS28-ESR in all RF titer groups ($P<0.001$), and changes in DAS28-ESR between baseline and at 52 weeks were comparable among 4 groups ($P>0.05$). Moreover, the titers of RF significantly decreased in patients treated with 30 mg OZR (median 49 to 21, $P<0.001$), particularly in the RF4 group (median 377 to 20, $P<0.001$). The titers of anti-CCP antibody also significantly decreased in patients treated with 30 mg OZR (median 106 to 64.5, $P<0.001$). [Conclusions] OZR showed effectiveness regardless of baseline RF titers. In addition, it reduced the titers of both RF and anti-CCP antibody, which may be a key feature of this drug.

## ICW5-6

**Comparative effectiveness of subcutaneous sarilumab, subcutaneous tocilizumab and intravenous tocilizumab in patients with rheumatoid arthritis: the ANSWER cohort study**

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Conflict of interest: Yes

[Objectives] Although sarilumab (SAR) and tocilizumab (TCZ) have different forms of antibodies, dosages, routes, affinities to IL-6 receptors (IL-6R), and inhibition of IL-6/STAT3 signaling, direct comparisons of IL-6R inhibitors have not been conducted in patients with rheumatoid arthritis (RA). We aim to examine the real-world comparative effectiveness and the potential effect modifiers of subcutaneous SAR (SAR-SC), TCZ-SC, and intravenous TCZ (TCZ-IV) in patients with RA in a multicentre cohort study. [Methods] Patients with RA initiated with SAR-SC (200 mg once every 2 weeks [q2w]), TCZ-SC (162 mg q2w; may increase to qw based on clinical response), and TCZ-IV (8 mg/kg q4w) were included. Multiple propensity score-based inverse probability weighting (IPW) was used to reduce confounding by indication. Linear mixed-effect models with IPW were applied to examine changes in the clinical disease activity index (CDAI) at 24 weeks after multiple imputation by chained equations. [Results] A total of 1224 treatment courses from 1095 patients was included (SAR-SC, 274; TCZ-SC, 657; TCZ-IV, 293). The improvement in CDAI at 24 weeks as the primary outcome was significantly greater in the SAR-SC group than in the TCZ-SC group (-2.66, 95% confidence interval: -4.27 to -1.06, $p = 0.001$), with differences observed as early as week 4 (-2.33 [-3.65 to -1.02], $p = 0.001$). The improvement in CDAI was similar between the TCZ-IV and the TCZ-SC group (0.84 [-0.78 to 2.47], $p = 0.31$). The effect of SAR-SC compared with TCZ-SC on change in CDAI was more prominent in patients with inadequate response to JAK inhibitors, patients with anemia, and patients without functional remission. [Conclusion] Among IL-6R inhibitors, SAR-SC showed greater effectiveness compared with TCZ-SC in disease activity from early administration while no significant difference was identified between TCZ-IV and TCZ-SC. SAR-SC may represent an effective treatment option for patients with multiple poor prognostic factors.

## ICW6-1

**Improvement in Disease Activity Assessment Frequency in Rheumatoid Arthritis Patients through the Introduction of the "MiRAi" System: An Observational Study on Enhancing Quality in Routine Clinical Practice**

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Conflict of interest: None

[Background] In the realm of rheumatoid arthritis (RA) management, the accurate assessment of disease activity and subsequent treatment decision-making poses substantial challenges. Quality indicators (QIs) in RA care underscore the significance of grasping the nuances of disease activity. However, the intricate scoring systems required for such assessments have presented obstacles to their practical implementation in routine clinical practice. Currently, there exists a gap in the literature regarding the impact of the introduction of the Rheumatoid Arthritis Management Support System (MiRAi). This system offers semi-automated disease activity assessment based on both patient input and clinical evaluation, seamlessly integrated into electronic health records, and whether it has led to changes in the frequency of assessments. [Objective] This study aims to investigate the influence of MiRAi on the frequency of disease activity assessments. [Methods] We conducted assessments on 884 rheumatoid arthritis (RA) patients attending the outpatient clinic of a tertiary healthcare facility over the period spanning from April 2022 to March 2023. During outpatient consultations, we employed the MiRAi system to evaluate CDAI and mHAQ scores. [Results] Since its implementation in June 2022, MiRAi has been utilized during outpatient consultations. Among the 884 RA patients, 236 cases (26.7%) made use of the MiRAi system. Our outpatient clinic typically accommodates approximately 480 RA patients monthly, resulting in an increased number of CDAI and mHAQ evaluations. To illustrate, the evaluations surged from 29 cases (5.9%) in June to 81 cases (19%) in November. [Conclusions] The introduction of MiRAi has prompted an augmentation in the frequency of disease activity assessments. Our ongoing research will explore whether this heightened frequency corresponds to alterations in treatment decisions.

## ICW6-2

**Circulated cooperation of the hospital and polyclinic for rheumatoid arthritis treatment in Yamagata area-Current Status and Challenges of YARANNA NET over the Past 10 Years-**

Naomi Hanaka[1], Yuya Takakubo[1], Masashi Aso[1], Yoshihiro Wanezaki[1], Hiroharu Oki[2], Yasushi Naganuma[5], Suran Yan[1,3], Ryusuke Honma[1], Juji Ito[1], Akiko Sasaki[4], Hiroshi Orui[6], Michiaki Takagi[1]

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Conflict of interest: None

[Objective] The patients with rheumatoid arthritis (RA) which make regular visit with our hospital has increased 4.5 times over the past 13

years and the number of patients using biologics has increased 7.3 times, compared to 2007 when we started collecting statistics. We have established the group of the circulated cooperation of the hospital and polyclinic for RA treatment in Yamagata (Yamagata Area Rheumatoid Arthritis Neo Noticeable Associated Network; YARANNA NET) since 2013. The aim of this study is to investigate the YARANNA NET for ten years. [Methods] We investigate numbers of the patients and polyclinics which has agreed and joined the circulated cooperation as YARANNA NET and the drug using for them, and to examine the current situation in the 10th years. [Results] We have 294 patients (13%) with RA which has agreed the YARANNA NET. They included 90 patients receiving biologics, 168 non-biologics, 10 for the treatment of osteoarthritis, 17 for rehabilitation and 9 for osteoporosis. Of the 37 facilities cooperating in the YARANNA NET, 32 were actually engaged. Problems in collaboration included irregular visits to the collaborating facility in 15 cases, dose reduction or discontinuation due to self-judgment in 12 cases, refusal to use biologics in 12 cases, refusal of blood sampling and consultation at the collaborating facility, and refusal to continue in 5 cases, 2 cases, and 2 cases, respectively, and problems with insurance claims due to differences in medical specialties in 2 cases. Adverse events occurred in 19 cases. [Conclusions] 13% of all patients agreed the YARANNA NET, an increase over the last 10 years. The patients with RA which prefer regular visit with university hospital may continue to increase, because of the unique right and insurance system of free-access to any hospital for Japanese patients and increasing elderly people with many complications. It seems to be important to spread this circulated cooperation system of YARANNA NET in our area.

## ICW6-3

**Association between continuous achievement of 2022 American College of Rheumatology /EULAR revised remission criteria and functional remission in patients with rheumatoid arthritis- results from the IORRA cohort**

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Conflict of interest: Yes

[Objective] American College of Rheumatology (ACR)/EULAR remission criteria was revised in 2022. Analysis using randomized trials data showed that changing the threshold of patient global assessment (PtGA) for Boolean from 1.0 cm (Boolean1.0) to 2.0 cm (Boolean2.0) resulted in a higher inclusion of patients achieving remission without worsening radiological and functional outcomes. We investigated whether continuous achievement of Boolean2.0 predicts functional benefit using real-world data. [Methods] We analyzed data from the Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort participants between 2022 and 2023 who had simplified disease activity index (SDAI), clinical DAI (CDAI), and Boolean (1.0 and 2.0). Continuous remission (CR) was defined as achieving the remission criteria in two consecutive surveys six months apart. We assessed functional outcomes using the Japanese version of the Health Assessment Questionnaire (J-HAQ) and defined a minimal clinically important difference in J-HAQ change (ΔJ-HAQ) as 0.22. We defined good function without progression (GFWP) as J-HAQ $\leqq$ 0.5 at one year and ΔJ-HAQ during one year $\leqq$ 0.22. We calculated the proportions of patients achieving CR and GFWP, and assessed the association between CR and GFWP. [Results] 1,694 patients were enrolled. At baseline, 1,487 (90%) were female, mean (SD) age was 63 (12) years, 1,484 (86%) were seropositive, and mean SDAI, CDAI, and J HAQ were 4.3 (4.8), 4.0 (4.5), and 0.53 (0.66), respectively. The proportions of CR and GFWP achieved were 21% and 87% for Boolean1.0, 37% and 76% for Boolean2.0, 43% and 78% for SDAI, and 41% and 77% for CDAI. Adjusted ORs (95%CI) of achieving CR for GFWP were 4.3 (3.0, 6.3) for Boolean1.0, 2.5 (1.9, 3.2) for Boolean2.0, 3.3 (2.6, 4.3) for SDAI, and 3.2 (2.5, 4.1) for CDAI. [Conclusions] Boolean2.0 could classify more patients with remission. The achievement of GFWP in Boolean2.0 was lower than that of Boolean1.0 and comparable to index-based criteria.

## ICW6-4

**Investigation of major cardiovascular events (MACE) in recent Japanese patients with rheumatoid arthritis: results from the IORRA cohort**

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Conflict of interest: None

[Objective] The objective of this study is to investigate the occurrence of major cardiovascular events (MACE) among Japanese patients with rheumatoid arthritis (RA) in recent years. [Methods] This study analyzed data from patients with RA who participated in the IORRA cohort between October 2013 and March 2022. We calculated the age-sex standardized mortality rates attributed to MACE and the age-sex standardized incidence rates of MACE, acute myocardial infarction (AMI), and stroke. Additionally, we exploratory analyzed risk factors of MACE using a time-dependent multivariate Cox proportional hazards model. [Results] The analysis included 8,254 patients, with 84.9% being female. The mean age and the mean disease duration of RA at enrollment were 59.4 years and 13.0 years, respectively. During a cumulative observation period of 53,376.2 person-years, we identified 65 deaths related to MACE. Furthermore, we observed 187 cases of MACE, including 55 cases of AMI and 66 cases of stroke. The standardized mortality rate attributed to MACE during the observation period (per 100 person-years) was 0.13 [95% CI: 0.10, 0.16], the standardized incidence rate of MACE was 0.38 [95% CI: 0.33, 0.44], AMI was 0.11 [0.08, 0.14], and stroke was 0.15 [0.12, 0.18]. Hazard ratio associated with the occurrence of MACE was 2.23 [95%CI: 1.45, 3.44] for male, 1.06 [1.04, 1.08] for age (per 10 years), 1.38 [1.10, 1.74] for higher J-HAQ at baseline, 3.04 [1.76, 5.24] for renal dysfunction at baseline, 2.44 [1.46, 4.06] for previous angina pectoris, and 3.40 [1.89, 6.11] for prior heart failure. [Conclusions] The incidence rate of MACE in Japanese patients with RA in recent years is numerically higher than that of 0.31 [95%CI: 0.26, 0.37] observed in the IORRA cohort between 2000 and 2013 (Michaud K. Ann Rheum Dis 2016).

## ICW6-5

**Comparative risks of biological and targeted synthetic DMARDs on incident chronic kidney disease in patients with rheumatoid arthritis: the ANSWER cohort study**

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Conflict of interest: None

[Objective] Although the administration of biological DMARDs (bDMARDs) has been reported to lower the risk of incident chronic kidney disease (CKD) and progressive estimated glomerular filtration rate (eGFR) decline, the impact of individual b/targeted synthetic DMARDs (tsDMARDs) on renal function in patients with rheumatoid arthritis (RA) has not been fully evident. We aimed to determine the comparative effects of b/tsDMARDs on the incidence of CKD in RA patients in a multicenter cohort study. [Methods] RA patients who had baseline eGFR ≧60 mL/min/1.73m$^2$ and started a b/tsDMARD (TNF inhibitors (TNFi), CTLA4-Ig, IL-6 receptor inhibitors (IL-6Ri), and JAK inhibitors (JAKi)) were included. CKD was defined as 2 times of eGFR levels <60 mL/min/1.73m$^2$ separated by at least 90 days and a >25% decrease from baseline eGFR. Multiple propensity score-based inverse probability weighting (IPW) was used to adjust confounders. The incidence of CKD was compared among b/tsDMARDs using IPW mixed-effect Cox proportional hazards models and linear mixed-effect models with IPW were used to examine trajectories of eGFR. [Results] Among 2187 patients with 3068 treatment courses and up to 11 years follow-up, the incidence of CKD was 275. Compared to the CTLA4-Ig group, the incidence of CKD was significantly lower in TNFi (HR 0.63, 95%CI 0.45-0.90, p=0.01), significantly higher in JAKi (HR 1.76, 95%CI 1.05-2.93, p=0.03) and not significantly different between IL-6Ri and CTLA4-Ig use (HR 0. 85, 95%CI 0.58-1.23, p=0.39). The renal impairment rate was significantly greater in JAKi use than in CTLA4-Ig (CTLA4-Ig: -1.44 mL/min/1.73m$^2$/year, JAKi: -2.74 mL/min/1.73m$^2$/year, p<0.01). [Conclusions] TNFi use was suggested to reduce the risk of incident CKD and eGFR decline in RA patients, whereas JAKi had less renal protective effect. Our findings are relevant for the selection of b/tsDMARDs especially in patients at a high risk of developing CKD, such as elderly patients or those with comorbidities.

## ICW6-6

**Efficacy and safety of bDMARDs in interstitial lung disease of rheumatoid arthritis (RA-ILD): from the FIRST registry**

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Conflict of interest: None

[Objective] It is unclear which bDMARDs are most appropriate for the treatment of rheumatoid arthritis (RA) patients with interstitial lung disease (ILD). The purpose of this study was to clarify the efficacy and safety of bDMARDs for RA-ILD patients in the real world. [Methods] Patients with RA-ILD who received the bDMARDs from April 2011 to June 2022 were enrolled. (TNF inhibitor (TNFi) n=46, CTLA4-Ig n=80, Anti IL-6R antibody (IL-6Ri) n= 95, total n=221) They had respiratory symptoms and exacerbations of ILD on imaging before induction of bDMARDs. Selection bias was minimized by propensity-score based inverse probability weighting (PS-IPTW). The primary endpoint was the changes in %FVC one year after the introduction of bDMARDs. [Results] After adjusted PS-IPTW, there was no difference in patient background and one-year retention rate among the three groups (p=0.74). There was no difference in the rate of CDAI remission six months after the introduction of bDMARDs (p=0.40). The changes in the %FVC did not differ (p=0.96), and the %FVC at one year did not worsen in all groups (p=0.98). The %FVC improvement was significantly higher in the IL-6Ri group than the others (TNFi vs CTLA4-Ig vs IL-6Ri = 6.6% vs 7.6% vs 16.5%, p<0.05). There was no difference in the deterioration rate of %FVC among the three groups (TNFi vs. CTLA4-Ig vs IL-6Ri = 6.4% vs. 7.0% vs 8.3%, p=0.91). The rate of adverse events tended to be lower in the CTLA4-Ig group than the others (TNFi vs CTLA4-Ig vs IL-6Ri = 41.3% vs 30.7% vs 41.1%, p=0.32), particularly the incidence of respiratory infections (TNFi vs CTLA4-Ig vs IL-6Ri = 19.6% vs 13.8% vs 19.0%, p=0.59). [Conclusions] In patients with RA who had exacerbation of ILD, all bDMARDs prevented the worsening of respiratory function. In particular, IL-6Ri may improve respiratory function better than the other bDMARDs.

## ICW7-1

**Serum Anti-NR2 Exhibits Higher Specificity than Sensitivity in the Diagnosis of Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)**

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Conflict of interest: None

**Objective**: Anti-NR2, a subset of anti-NMDA receptor antibodies, has been associated with neuropsychiatric systemic lupus erythematosus (NPSLE) syndromes. However, the diagnostic accuracy of anti-NR2 varies in prior studies. Therefore, our objective was to quantitatively synthesize data on the sensitivity and specificity of anti-NR2 for diagnosing NPSLE. **Methods**: We performed an extensive search across PubMed, Embase, and CINAHL using highly-sensitive search strategies. Additionally, we conducted citation checks for the included studies and relevant reviews through the Web of Knowledge Science Citation Index. Two investigators (SFA, GZ) independently managed study inclusion, extracted data using a standardized form, evaluated study quality, and compiled participant-level data to create 2×2 contingency tables. To conduct the meta-analysis, we employed the HSROC model developed by Rutter & Gatsonis (2001). **Results**: A total of 1583 records were screened, resulting in the inclusion of data from 8 studies involving 984 patients (Figure 1). The pooled data represented a wide spectrum of NPSLE manifestations, including acute confusional state, seizure disorders, cerebrovascular disease, aseptic meningitis, headaches, cognitive dysfunction, psychoses, mood disorders, chorea, myasthenia gravis, demyelinating syndromes, myelopathy, plexopathy, and mono, poly, and cranial neuropathies. Sensitivity ranged widely from 5% to 100%, while specificity exhibited a narrower range of 64% to 92% (Figure 2). Meta-analysis yielded the following pooled results: Sensitivity 53% (95% CI: 24-80%), Specificity 77% (69-83%), negative likelihood ratio (LR) 0.61 (0.30-1.25), and positive LR 2.26 (1.07-4.76) (Figure 3). **Conclusions**: Serum anti-NR2 antibodies exhibit non-significant sensitivity and negative LR, but they demonstrate statistically significant specificity and positive LR for diagnosing NPSLE. Therefore, patients with suspected NPSLE may benefit from assessing their anti-NR2 levels.

## ICW7-2

**Associations of Antinuclear antibody with mitochondrial antibody and smooth muscle antibody in autoimmune liver diseases**

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Conflict of interest: None

[Objective] Autoimmune liver diseases (ALD) is a chronic disease characterized by immunological and autoimmunological features, generally including the presence of circulating autoantibodies. The main types of autoantibodies present are antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), and anti-mitochondrial antibodies (AMA). [Methods] We aimed to determine the significance of ANA patterns in patients with ALD. We check associations of ANA with ASMA and AMA. ANA staining patterns were identified by HEp-2 cells with serum of the patients by IFA assay. ASMA and AMA were identified by rats tissue with serum of the patients by IFA. We retrospectively reviewed 902 patients were sent to our laboratory from 2022 till 2023 for ANA, ASMA and AMA. [Results] These patients were from division of Rheumatology and Gastroenterology in the hospital. Among 902 cases, 36 (3.9%) patients were detected ASMA positive. These ASMA positive cases, that ANA with low titer (between 1:40~1:80) and almost were negative. From 36 ASMA positive cases, there were 24 female and 12 male. The mean age of presentation was 52.3 years. Further analysis, according to the ANA ICAP classification, the ANA manifestations were AC1, AC4/5, and AC15~20.

Among 902 cases, 30 (3.4%) patients were detected AMA positive. These 30 AMA positive cases, there were 25 female and 6 male. The mean age of presentation was 61.1 years. On the contrary, we found these cases with high titer cytoplasmic fluorescence ANA pattern (between 1:640~ 1:2560). It has been shown that cytoplasmic staining, including AC21, AC11/12, and AC15~20. In particular, In particular, AC21 showed extremely high correlation with PBC. [Conclusions] When ALD was suspected, ASMA must be combined with ANA for interpretation. It some timely had no special characteristics for ALD, and must relyed on other clinical data. Thus, it is important to check cytoplasmic ANA patterns for ALD evaluation, even when nuclear ANA patterns are negative.

## ICW7-3

**Serum C-type lectin domain family 7 member A as a potential novel biomarker for disease activity in patients with systemic lupus erythematosus**

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Conflict of interest: None

[Objective] Monitoring disease activity in patients with systemic lupus erythematosus (SLE) is challenging due to the scarcity of sensitive biomarkers. The aim of this study was to investigate new biomarkers to monitor the disease activity in SLE. [Methods] Sera were collected from 34 patients with SLE and 10 healthy controls (HC), and 368 inflammation-associated proteins were analyzed. Peripheral blood mononuclear cells were also isolated, and the proportion of 47 peripheral immune cell types was assessed by flow cytometry. Clinical data were collected, and correlation analyses were performed. [Results] Of the 34 patients, 31 were females and the median age was 40 years old. The median SLE Disease Activity Index (SLEDAI) was 6.0 and 24 (71%) patients were on prednisolone (PSL), at a median dose of 7.5 mg/day. From the protein profile, 82 proteins showed significant differences between SLE and HC. Among them, 14 had positive and 4 had negative correlations ($|r|>0.4$) with SLEDAI. Based on these data, we focused on C-type lectin domain family 7 member A (CLEC7A). CLEC7A functions as a pattern recognition receptor for glucans and plays a role in the innate immune response. Serum CLEC7A levels were upregulated in SLE and correlated with SLEDAI ($r=0.48$). CLEC7A was higher even in SLE with low disease activity (SLEDAI$\leqq$4) compared to HC ($p<0.001$), higher in the group without PSL compared to the PSL-treated group ($p<0.05$), and decreased after the treatment in the new-onset or relapsed patients ($p<0.001$). Interestingly, CLEC7A levels were correlated with the frequency of activated CD4 ($r=0.76$), activated CD8 ($r=0.52$), type 17 follicular helper T ($r=0.37$), and type 17 peripheral helper T cells ($r=0.50$). Furthermore, SLE with normal complement and ds-DNA antibodies (C3$\geqq$73, C4$\geqq$11, CH50$\geqq$31.6, ds-DNA<12) also showed a significant increase in CLEC7A levels compared to HC ($p<0.001$). [Conclusions] CLEC7A could be a novel biomarker to monitoring disease activity in patients with SLE.

## ICW7-4

**Serum calprotectin as a potential marker for macrophage activation syndrome in patients with systemic lupus erythematosus**

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Conflict of interest: None

[Objective] Calprotectin is released by activated neutrophils and monocytes, leading to activation of innate immunity via Toll-like receptor 4. Systemic lupus erythematosus (SLE) can rarely develop macrophage activating syndrome (MAS), which resembles the manifestation of adult-onset Still's disease (AOSD). Several reports suggest that serum calprotectin (SC) reflects AOSD activity, but little is known concerning whether this is also true for SLE-MAS. Accordingly, this study aimed to clarify the association between SLE-MAS and SC, and the roles of SC in SLE-MAS. [Methods] This was a single-center cross-sectional study. We randomly selected patients with SLE or AOSD whose serum were stocked at our department and obtained their clinical information. SC was measured by Human S100A8/S100A9 Heterodimer DuoSet ELISA (R & D Systems). MAS was defined by a composite item including ferritin, platelets, AST, triglycerides, and fibrinogen according to the Raveli criteria (Ann Rheum Dis. 2016;75:481-9.). [Results] A total of 54 patients, including 8 patients with SLE-MAS, 39 with SLE-nonMAS and 7 with AOSD, and 8 healthy controls (HC) were enrolled. SC levels were comparable between SLE-MAS (median (interquartile range), 9267.3 (3238.5, 10053.0) ng/mL) and AOSD (9569.9 (3238.5, 10053.0) ng/mL), and they were significantly higher than SLE-nonMAS (3668.2 (1442.6, 7057.2) ng/mL) or HC (1204.2 (558.9, 1627.1) ng/mL). In SLE, SC levels were positively correlated with those of LDH ($rs=0.38$, $p=0.01$), CRP ($rs=0.39$, $p=0.01$), ferritin ($rs=0.41$, $p=0.02$) and C4 ($rs=0.34$, $p=0.05$), while they were not in AOSD. In a receiver operating curve analysis, the sensitivity and specificity of SC indicating MAS in SLE were 62.5% and 94.9%, respectively, with a cut-off level 9184.4 ng/mL (Area Under the Curve=0.77). [Conclusions] SC may be a potential marker for diagnosis of MAS and reflect MAS condition in SLE.

## ICW7-5

**Serum C-reactive protein levels can predict organ damage within 2 years in patients with systemic lupus erythematosus who meet Lupus Low Disease Activity State**

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Conflict of interest: None

[Objective] C-reactive protein (CRP), one of the inflammatory markers, has been previously reported to be relatively low in systemic lupus erythematosus (SLE) patients, except in the presence of specific organ in-

volvement such as serositis. However, the significance of CRP in inactive SLE is not fully understood. Therefore, we analyzed the association between CRP levels and organ damage in SLE patients with low disease activity. [Methods] This multi-center, retrospective observational study used Lupus Registry of Nationwide Institutions (LUNA) cohort database. SLE patients who met Lupus Low Disease Activity State (LLDAS) at registration were divided into two groups: those with serum CRP levels ≧ 0.07 mg/dL (high CRP group) or < 0.07 mg/dL (low CRP group) both at registration and in the first year. The cutoff for CRP levels was determined as the median value in patients who met LLDAS. Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) progression was defined when the score increased ≧1. [Results] Among 106 SLE patients who met LLDAS, 55 were in a high CRP group and 51 were in a low CRP group. In the high CRP group, patients were older (median: 56.8 vs. 41.6, p = 0.002), had higher BMI (median: 22.6 vs. 20.3, p < 0.001), and had higher SDI scores (median: 1 vs. 0, p = 0.03) at registration. Log-rank test showed that the probability of SDI progression within 2 years was significantly higher in the high CRP group (p = 0.007). Furthermore, Cox proportional hazard model also showed that high CRP group was significantly associated with SDI progression when adjusted for predictors regarding SDI (HR: 2.7, 95% CI: 1.1-7.0, p = 0.04). [Conclusions] CRP levels were associated with SDI progression within 2 years in LLDAS patients. Even in patients with inactive SLE, positive CRP levels may suggest the necessity to modify treatment for SLE or atherosclerotic risk factors.

## ICW8-1

**Performance and Concordance of Two Different Methods of Detecting the Commonest Autoantibodies in Systemic Lupus Erythematosus**

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Conflict of interest: None

**Objectives:** Autoantibodies in SLE can be detected by either immunoblot or ELISA. We checked the performance and concordance of these two methods in detecting the eight commonest autoantibodies (antibodies to dsDNA, nucleosomes, histones, SS-A, SS-B, nRNP, Sm & Ribosomal P Protein - RPP). **Methods:** A total of 180 SLE patients' serum samples (all positive for Antinuclear antibodies by indirect immunofluorescence at 1:80 dilution) were tested for the above-mentioned autoantibodies using both immunoblot and ELISA (Euroimmune, Germany). The results from ELISA were categorised as positive or negative as per the kit's cut-off values. For immunoblot, all the intensities from 1+ to 3+ were taken as test positive for the respective antibody. Cohen's kappa was calculated as a measure of agreement between the two tests for each antibody. A p-value of <0.05 was considered significant. **Results:** Positivity rates for the ELISA (for the autoantibodies to dsDNA, nucleosomes, histones, SS-A, SS-B, nRNP, Sm & Ribosomal P protein - RPP) were 65.56%, 50%, 43.89%, 55%, 21.11%, 56.67%, 38.33% and 27.77% respectively whereas for immunoblot, these were 26.11%, 50%, 44.44%, 50%, 18.89%, 65.56%, 48.33% and 37.78% respectively. The differences between the positivity rates were significant for autoantibodies to dsDNA favouring ELISA and RPP favouring immunoblot (p<0.05 for both). The Cohen's kappa for the two methods was 0.14, 0.38, 0.45, 0.54, 0.51, 0.35, 0.49 and 0.48 (p<0.001 for all except for dsDNA - p<0.05) respectively. On immunoblot, omitting 1+ intensities from the positive results also did not improve the agreement between the two methods and lead to significant loss of positivity rate for all autoantibodies. **Conclusions:** Performance of the two methods differs significantly for detecting antibodies to dsDNA (ELISA better) and RPP (Immunoblot better). There is poor (anti-ds DNA antibodies) to modest (anti-SS-A antibodies) agreement between the two methods for detecting autoantibodies in SLE.

## ICW8-2

**Clinical features and peripheral blood immunophenotype of patients with SLE in maintenance phase who were able to discontinue glucocorticoids after intervention with belimumab**

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Conflict of interest: None

[Objective] This study aimed to clarify clinical features and peripheral immunophenotype of patients with SLE who successfully discontinued glucocorticoids (GC) by intervention with belimumab (BLM) in the maintenance phase. [Methods] Patients with SLE (n=267) in the maintenance phase (SELENA-SLEDAI < 10, GC dose ≦ 0.2 mg/kg/day) were assessed. They were divided into the standard of care (SoC) group (103 patients who received hydroxychloroquine or mycophenolate mofetil) and the BLM group (164 patients who received BLM with SoC). In a patient subset (SoC group: n=46; BLM group: n=89), peripheral blood immunophenotypes were analyzed based on the standard human immune cell subset classification protocol by NIH/FOCIS. [Results] After propensity score-based inverse probability of treatment weighting adjustment, no differences in patient characteristics were shown between the SoC and BLM groups. The retention rate of BLM at 52w was 98.2%. SLEDAI scores improved after 52w in both groups. The BLM group also had significantly lower GC doses at 52w (p<0.01) and 31.5% of the BLM group successfully discontinued GC, whereas on 1.8% of the SoC group did (p<0.01). In the BLM group, the proportion of activated T follicular helper cells (p=0.02) and $IgD^{-}CD27^{-}$B (DNB) cells (p<0.01) decreased significantly at 26w, and the proportion of DNB cells at 26w was significantly lower in patients who discontinued GCs (p=0.04). Multiple logistic regression analysis showed that GC discontinuation was associated with low GC doses, low SLEDAI scores at BLM initiation, decreased IgG levels at 52w, and a low percentage of DNB cells at 26w. [Conclusion] Intervention with BLM in patients with SLE reduced DNB cells, thereby controlling the disease activity and enabling GC discontinuation. Among patients who received low GC doses and had low SLEDAI scores, those with decreased IgG levels at 52w successfully discontinued GCs.

## ICW8-3

**Significance of T-bet positive CD11c+ B cells in patients with systemic lupus erythematosus (SLE)**

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Conflict of interest: None

[Objective] A novel subset of $T\text{-}bet^{+}CD11c^{high}$ atypical B cells (ABCs) have been discovered in SLE. This study aimed to explore the clinical significance and development of ABCs in lupus patients. [Methods] 88 newly diagnosed SLE patients were enrolled. ABCs (=$CD19^{+}T\text{-}bet^{+}CD11c^{high}$) and other immune cell subsets in peripheral blood were detected by flowcytometry. Associations between the proportion of ABCs and clinical or immunological characteristics were investigated. The differentiation and function of ABCs were assessed *in vitro* experiments. [Results] The mean age was 42.8 years with the majority being women. The median duration of disease was 0.5 year, and median SLEDAI was 14.9. In lupus patients, the proportion of ABCs was significantly higher compared to age-matched healthy controls (HC) (10.6% vs. 1.3%, p<0.001). This proportion showed a positive correlation with SLEDAI (p<0.001) and was associated with active lupus nephritis. Next, serum cytokines including IL-4, IL-6, IL-9, IL-10, IL-12/23, IL-21, TNF-α, IFN-α, and IFN-γ, were measured by electrochemiluminescence. All cytokines, except for IL-4 and IL-9, showed increased levels in SLE compared to HC. However, only

IFN-γ (p=0.007) and IL-6 (p=0.015) exhibited correlations with the proportion of ABCs. When comparing ABCs to T cell subsets, there were no associations with Th17, Treg or Tfh cells. However, positive correlations were observed with activated Th1 cells (p=0.009) and $CXCR5^{-}ICOS^{+}PD1^{+}$Tph cells (p=0.03). Of note, ABCs decreased as disease activity improved with treatment. *In vitro* study, we found ABCs were maximally induced when $IgD^{+}CD27^{-}$ naïve B cells were stimulated with B cell receptor+CD40 ligand+IL-21+TLR9 ligand, along with IFN-γ (not IFN-α, IL-4, IL-12). Furthermore, IL-6 was predominantly produced when naïve B differentiated into ABCs. [Conclusions] ABCs are expanded in patients with lupus nephritis and are potentially involved in a pathogenetic network with specific T cell subsets and cytokines.

## ICW8-4

**Stratification of treatment-naïve systemic lupus erythematosus into four distinct immune phenotype groups exhibiting variable relapse rates**

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Conflict of interest: Yes

[Objective] Systemic lupus erythematosus (SLE) is highly heterogeneous. We explored immunophenotype diversity in treatment-naïve SLE patients experiencing their initial disease episode. [Methods] We included 123 SLE patients. Using flow cytometric analysis, we profiled immune cells, including T cells, B cells, NK cells, dendritic cells, and monocytes. We then applied cluster analysis, utilizing Ward's method. [Results] In comparison to healthy control, lupus patients exhibited elevated levels of double negative (DN) B cells and plasmablasts in peripheral blood. Additionally, there was an increase in the proportion of activated CD4, CD8, and Th1 cells within the T cell population, with a simultaneous decrease in the CD16+ NK cell subset. Cluster analysis of immunophenotypes classified lupus patients into 4 major groups. One of these groups (cluster 1) closely resembled HC and consisted of a relatively small number of patients. The other three groups were as follows: one with increased DNB cells and modestly elevated plasmablasts (cluster 2), another with a tenfold increase in plasmablasts but no significant change in DNB cells (cluster 3), and a group marked by an increase in activated regulatory T cells (cluster 4). Among these 4 clusters, cluster 1 had the lowest disease activity, with 40% of patients having either one BILAG A or two B manifestations (BILAG A1 or B2). Conversely, cluster 3 showed high disease activity, with 88% of patients having BILAG A1 or B2. Notably, during a 3-year follow-up of patients treated with high-dose glucocorticoid therapy, cluster 1 had no relapses, while over 20% of patients in cluster 3 experienced relapses. The other clusters had relapse rates of approximately 10%. [Conclusions] Peripheral immunophenotyping sorted untreated SLE patients into 4 groups, emphasizing B cell dysregulation. Notably, DNB cell and plasmablast behaved differently, with marked plasmablast proliferation linked to high disease activity and relapse rates.

## ICW8-5

**Clinical significance of follicular helper T (Tfh) cell subsets in systemic lupus erythematosus (SLE)**

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Conflict of interest: None

Objective: We assessed the immune phenotypes of peripheral lymphocytes of patients with untreated SLE to clarify the pathological and clinical relevance of Tfh cell subsets to SLE. Methods: Comprehensive FCM analysis of PBMC from 82 patients with SLE and 62 healthy controls (HD) was performed to investigate the association between immunological characteristics and clinical symptoms. Results: Of 82 patients with untreated SLE, the median disease duration was 7.0 months, median SLEDAI was 10.0, and nephritis was present in 29 cases (35.3%). The proportion of patients with BILAG category A or B features was 84.1%. The proportion of each cell subset was significantly different between patients with SLE and HD, with increased levels of Tfh, Tfh1, Th1, Treg cells, plasmocytes, and double-negative B cells in patients with SLE. Among the T cell subsets, Tfh1 cells were particularly increased in patients with SLE. The proportion of Tfh1 cells was positively correlated with SLEDAI and BILAG (r=0.221, p=0.005 and r=0.218, p=0.05) and was increased in cases with active nephritis (p=0.015). Compared to those in HD, the total Treg cell numbers were increased in patients with SLE, but activated Treg/Tfh1 ratio was decreased in patients with SLE compared with HD. In addition, the number of activated Treg cells decreased as the number of Tfh1 cells increased, confirming a negative correlation only between Tfh1 cells and activated Treg cells. In vitro studies showed that Tfh1 cells were induced by IL-12 stimulation and produced both IL-21 and IFN-γ. Serum IL-12 was increased in SLE patients, and TYK2 inhibitors, which block IL-12-induced signaling, inhibited Tfh1 cell differentiation but did not inhibit Treg cell differentiation. Conclusion: Among Tfh cell subsets, Tfh1 cells play a central role in the pathogenesis of SLE. Inhibition of Tfh1 cell differentiation and maintenance of Treg cells by TYK2 inhibitors may be a new therapeutic option for SLE.

## ICW9-1

**The benefit of preoperative simulated surgery using a 3D model in reverse shoulder arthroplasty in cases of glenoid defect and deformity**

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Conflict of interest: None

Introduction: In reverse shoulder arthroplasty (RSA) for patients with osteoarthritis and rheumatoid arthritis (RA), placement of base-plate, especially in small Japanese patients with severe bone defects or deformity in the glenoid is often troublesome. Simulation software is far from substitution in the process of trial. Intraoperative positioning guides for individual patients are time-consuming and tangled to create. We report application of preoperative simulated surgery using 3D model of scapula prior to RSA. Subjects and Methods: Four patients who underwent RSA using an allograft or wedge-shaped base-plate for severe glenoid bone defects and deformity and were able to follow up for more than 24 months after surgery were included. All cases were female, with an average age of 81 years old. Three patients had RA, and one had rapid destructive shoulder arthritis. 3D model of scapula was created using hard urethane foam by a 3D printer (ZPrinter®) based on preoperative CT data, and a simulated surgery was performed using a demonstration device made of the same material as the actual implant preoperatively. In the actual surgery, bone grafting and implant placement were performed while referring to the 3D model used in the simulated surgery. Results: The average follow-up period was 43.8 months, and none of the patients had any postoperative complications. The average active range of motion from pre- to postoperative improved from 75° to 117.5° in flexion, 6.3° to 20° in external rotation, and no significant improvement in internal rotation. JOA score from pre- to postoperative improved from 47.5 points to 78.6 points. Discussion: In cases such as RA and allied condition, large bone defects or deformities of the glenoid are often encountered. Creating a 3D model of scapula preoperatively and performing a simulated surgery with the model and implants for RSA, can serve as a reference for operations and help in selecting appropriate bone grafts and implants.

## ICW9-2

**An Audit on Monitoring of Non-biological Disease-Modifying Anti-Rheumatic Drugs Among Patients with Inflammatory Rheumatological Diseases, Followed up at Rheumatology Clinic of District General Hospital Nawalapitiya, Sri Lanka**

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Conflict of interest: None

***Objectives*** Conventional disease modifying anti-rheumatic drugs (DMARDs) carry a potential risk of organ damage and close monitoring is needed. 2017 BSR and BHPR guidelines for the prescription and monitoring of non-biologic DMARDs are used for this purpose. This audit was conducted to determine the adherence to current recommendations. ***Method*** A retrospective audit was done over a period of 3 months. Patients on Methotrexate (MTX), Sulfasalazine (SSZ), Leflunomide (LEF) as a single agent/in combination were included in the study. Clinic records of 105 patients were analyzed for immediate past 3 months. ***Results*** The age distribution was 20 to 84 years (median-55) among 89 females and 16 males. 82 rheumatoid arthritis (RA),15 undifferentiated inflammatory arthritis, 3 psoriatic arthritis and 3 other conditions (SLE/polymyositis) and 2 spondyloarthropathy were present. 80 were on MTX, 42 on SSZ and 22 on LEF either as mono/combination therapy. Analysis 41 of patients on MTX stable dose follows: adherence to guidelines for Full blood count (FBC) was 34% (14), liver enzymes (SGOT/PT) 29% (12) and serum creatinine (sCr) 27% (11). Over tested rate for FBC was 59% (24) and SGOT/PT 61% (25). Under tested rate for the above follows respectively 7% (3), 10% (4) and 30% (73%). Out of 21 patients on stable SSZ and/or LEF, adherence to guidelines for FBC was 33% (7), SGOT/PT 57% (12) and sCr 33% (7). 53% (11) of FBC and 38% (8) SGOT/PT were overtested. Undertested rate for above respectively 3% (14), 5% (1) and 67% (14). Only 10 patients on LEF had blood pressure recordings. All 41 patients on dose escalation were undertested. Overall, only 59.5% FBC, 60.5% SGPT/OT and 56.6% sCr of requested were done. ***Conclusion*** DMARDs monitoring is not keeping with 2017 BSR and BHPR guidelines. A large proportion of over testing was done and appropriate testing was not done where indicated. Limited knowledge of doctors and limited resources are major reasons. A protocol for the unit is required to use the resources efficiently.

## ICW9-3

**Mid-term clinical outcomes of non-constrained total elbow arthroplasty in rheumatoid arthritis**

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Conflict of interest: None

[Objective] The objective of this study is to investigate the mid-term clinical outcomes of non-constrained total elbow arthroplasty (TEA) in rheumatoid arthritis (RA). [Methods] Patients included in this retrospective study were operated with Kudo TEA since April 2006 until March 2014. Eighteen elbows of 16 patients (male 1, female 15), were mean age 61 years old (range, 41-76 years old) at the surgery. The mean duration of RA was 18 years (1-38 years) and of postoperative follow-up was 9 years (5-15 years). The Japanese Orthopaedic Association-Japan Elbow Society Elbow Function Score (JOA score), Mayo Elbow Performance Score (MEPS), complications, and the radiographical loosening of prosthesis at the final follow-up were investigated. Statistical analyses were evaluated with *t*-test and Mann-Whitney U test and values of $p<0.05$ were considered statistically significant. [Results] The JOA score significantly improved from 45 points (18-73 points) to 72 (43-94) ($p<0.01$). The MEPS scores were averaged 95 points (45-100 points), and classified to 1 for poor, 1 for fair, 4 for good and 11 for excellent. Complications occurred in 27.8% of five elbows, of which three cases were performed reoperation because of deep infection, dislocation, and ulnar nerve injury respectively. The radiographical loosening of ulnar component was indicated in three elbows. [Conclusions] In this study, TEA for RA was also excellent procedure for pain relief and reconstruction of elbow function, but three elbows were required for revision surgery. In addition, it is necessary to consider both the indication and timing of revision of TEA for three cases which showed radiographical loosening of ulnar components.

## ICW9-4

**Long-term clinical outcome of the metatarsophalangeal joint arthroplasty (Swanson silicone hinge-toe implant) for rheumatoid foot deformities**

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Conflict of interest: Yes

[Objective] The long-term outcome of Swanson hinge toe silicone implant has not been clarified well. The aim of this study was to evaluate the clinical long-term outcome of Swanson hinge toe silicone implant for rheumatoid arthritis (RA) cases. [Methods] Twenty cases with RA (29 feet) were registered. Women was 18 cases, 90%. The mean age on the surgery was 65 ± 8 years old (50 to 77). Swanson implant was inserted for all the hallucis and shortening oblique osteotomy was performed for the lesser toes. All cases with hallucis metatarsophalangeal joint were Larsen III. Hallucis valgus angle (HVA), Intermetatarsal angle between the first and the second metatarsus (M1M2A), Intermetatarsal angle between the first and the fifth metatarsus (M1M5A), Functional outcome was also evaluated with Japanese Orthopedic Association (JOA) score and Japanese Society of Surgery of Foot (JSSF) score. The adverse events and the survivorship were examined. [Results] The mean followed up period was 9 years. HVA significantly improved from 53° (before surgery) to 9.4° (just after the surgery), and 9.6° (at the final follow up). M1M2A significantly improved from 16°to 11°, and 12°. M1M5A significantly improved from 37°to 25°, and 32 °. Both JOA score and JSSF score significantly improved from 50 (before surgery) to 75 points (at the final follow up) in JOA score, and from 49 (before surgery) to 74 points (at the final follow up) in JSSF score. The recurrence of callosity was detected in 2 cases. Of these, Revision surgery of shortening oblique osteotomy was performed. Surgical site infection was detected in 2 cases and Swanson implant was removed and debridement was done. The 9-year survivor ship rate of the implant was 90%. [Conclusions] The significant improvement of anatomical parameters and functional outcome and high survivorship for long term (9 years) would induce that the clinical outcome of this implant was good for severe forefoot RA deformities.

## ICW9-5

**Short-term and long-term outcomes of rheumatoid arthritis patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is associated with an increased risk for coronary artery disease. Percutaneous coronary intervention (PCI) remains one of the primary modalities in acute coronary settings. The post-PCI outcomes in RA patients are still inconclusive. This is the first meta-analysis to evaluate short and long-term outcomes of PCI in patients with RA. [Methods] Embase, Cochrane, PubMed, and Google Scholar were systematically reviewed using the PRISMA protocol for cohorts published in the last ten years comparing outcomes of PCI between patients with and without RA. The risk of bias assessment for each cohort included used the Newcastle-Ottawa Scale (NOS). The primary endpoints analyzed for the short-term outcomes were in-hospital mortality and 30-day major adverse cardiovascular events (MACEs); while long-term outcomes (with a follow-up period of >1 year) were all-cause mortality and myocardial

infarction (MI). [Results] We included 6 cohorts with a total of 6,986,129 patients assessed for the short-term outcomes (275,605 with RA; 6,710,524 without RA) and 5 cohorts with a total of 523,014 patients for the long-term outcomes (50,165 with RA; 472,849 without RA). NOS showed all of the cohorts included were of good quality. Patients with RA had a significantly **higher** risk for 30-day MACEs (risk ratio [RR] 1.17; 95% confidence interval [CI] 1.14-1.21) and long-term all-cause mortality (RR 1.28; 95% CI 1.17-1.40), but not significant for long-term incidence of MI (RR 1.03; 95% CI 0.91-1.17). However, although not significant, patients with RA had a **lower** risk for in-hospital mortality (RR 0.80; 95% CI 0.52-1.22). [Conclusions] There were consistent data showing worse 30-day and long-term outcomes in patients with RA undergoing PCI in comparison to patients without RA. In-hospital outcomes still need to be studied further. Thus, this study recommends the post-PCI subpopulation of RA patients should be monitored more closely in order to improve outcomes.

## ICW9-6

**Sufficient methotrexate-polyglutamate concentration predict future improvement of joint inflammation detected by ultrasonography in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To assess the relationship of erythrocyte methotrexate-polyglutamate (MTX-PG) levels with disease activity including assessment with musculoskeletal ultrasonography (MSUS) findings in patients with rheumatoid arthritis (RA)_ subanalysys on the MAGIK study. [Methods] We prospectively enrolled 79 MTX-naïve patients with RA in 76-week cohort study. Twenty-six patients were completely assessed 40 joints of MSUS at baseline, 12-week, and 36-week after MTX initiation. RA patients who started biologics within 36-week were excluded. Erythrocyte MTX-PG levels were measured by mass spectromy. The associations of MTX-PG concentrations with disease activity including DAS28 and gray scale (GS)/power doppler signal (PD) score of MSUS were analyzed. [Results] We included 14 RA patients in the analysis. The median age was 65 years, 85.7% were female, and a median DAS28 of 4.03. Dose escalation of MTX resulted in increased erythrocyte MTX-PG concentrations, while MTX-PG3 concentrations showed a slow, delayed increase after 12-week. The mean number of GS- and PD-positive joint counts are significantly higher than swollen joint counts by physical examination at all visits. Linear regression analysis revealed higher MTX-PG3 and total MTX-PG concentrations at 24-week were significantly associated with greater improvement in the number of PD-positive joint counts with MSUS at 36-week (r=0.63, p=0.02) and total 40 and 28 joints of MSUS scores at 36-week, especially in the total PD score. (r=0.69, p=0.02 and r=0.70, p=0.01, respectively) On another front, no relationship was observed between MTX-PG concentrations and the changes in DAS28-CRP, swollen/tender joint counts, and serum CRP levels. [Conclusions] Sufficient MTX-PG3 and total MTXPG concentration may predict future improvement in joint inflammation detected sensitively with MSUS in RA patients with MTX monotherapy.

## ICW10-1

**Clinical significance of ceramide antibody in antiphospholipid syndrome**

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Conflict of interest: None

[Objective] To investigate the distribution and clinical significance of Ceramide antibodies (Ceramide-Ab) in antiphospholipid syndrome (APS). [Methods] One hundred and forty-one APS patients, 48 patients with other autoimmune diseases as disease controls and 54 healthy controls were included in this study. The clinical data and laboratory indicators of patients with APS were collected. The titers of Ceramide-Ab were detected by enzyme-linked immunosorbent assay (ELISA). SPSS26.0 was used to analyze the relationship between Ceramide-Ab and clinical and laboratory parameters. [Results] The titers and positive rate of Ceramide-Ab in APS patients were significantly higher than those in healthy controls [titers: 147.1 (139.9~154.4) ng/mL vs. 129.2 (123.9~134.5) ng/mL, P =0.0019; positive rate: 24.82% vs. 5.56%, P =0.0020] and disease controls [titers: 147.1 (139.9~154.4) ng/mL vs. 127.1 (117.4~136.7) ng/mL, P =0.0066; positive rate: 24.82% vs. 12.5%, P =0.0406]. The prevalence of comorbidity such as hypertension (48.6% vs. 19.8%, P =0.001), coronary heart disease (17.1% vs. 5.1%, P =0.035) and venous thrombosis (57.1% vs. 38.7%, P =0.011) in Ceramide-Ab positive group was significantly higher than that in Ceramide-Ab negative group. The area under the ROC curve of Ceramide-Ab was 0.643 (95% CI 0.566~0.720, P = 0.0021), and the sensitivity, specificity and Youden index were 0.475, 0.889 and 0.364, respectively. [Conclusions] Ceramide-Ab was associated with hypertension, coronary heart disease and venous thrombosis, it could serve as a non-criteria antibody in APS.

## ICW10-2

**Mass cytometrical approach to reveal immune cell profiles associated with Sjögren's syndrome**

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Conflict of interest: Yes

[Objective] Sjögren's syndrome (SS) is a systemic autoimmune disease characterized by the secretory gland dysfunction and the presence of autoantibodies. However, its pathogenesis still remains unclear, and immunosuppressive therapies including glucocorticoids or B-cell targeted agents have not shown convincing effect in previous clinical trials. To determine the cell subsets related to SS immunopathogenesis, we conducted mass cytometry (CyTOF) to compare peripheral blood mononuclear cell (PBMC) profiles between healthy individuals and patients with primary SS. [Methods] We employed CyTOF with a 37-marker panel in PBMCs from 27 SS patients, and 23 healthy controls (HC). All SS patients fulfilled the 2016 ACR-EULAR classification criteria for primary SS. CyTOF data was analyzed by dimensional reduction with tSNE (t-Distributed Stochastic Neighbor Embedding) and unsupervised clustering with CITRUS (Cluster identification, characterization, and regression), to identify unique cell populations in primary SS patients. Conventional biaxial manual gating methods were conducted to verify the results. [Results] Significant increase in monocytes (SS vs HC, p<0.01) and the decrease in memory B cells (p<0.01) and CD3brightCD4-CD8-CD45RA- T cell subsets (p=0.02) were detected in SjS patients compared to HC. Increased PDL1 expression was observed in B cells (p<0.01), CD4+ memory T cells (p<0.01) and CD8+ TEMRA (p<0.01). Increased CD38 expression and decreased CXCR3 expression were observed in Tim-3+CD16+NK cells (p<0.01) and CD8+ TEMRA (p<0.01). CD3brightCD4-CD8-CD45RA- T cell clusters, which may represent γδT cell subset, imply the importance of this unique T cell subset in the pathogenesis of SS. [Conclusions] Mass cytometry analysis identified several cell subsets in SS, which may become the possible therapeutic targets in the future. Further research is needed to determine the function and pathogenicity of these cell populations.

## ICW10-3

**Significance of clinical domains (venous or arterial thrombosis) in the 2023 ACR/EULAR antiphospholipid syndrome classification criteria**

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Conflict of interest: None

[Objective] The presence of antiphospholipid antibodies (aPL) is highly correlated with venous and arterial thrombotic events; therefore, thrombosis is recognized as major clinical manifestations of antiphospholipid syndrome (APS). On the other hand, many other risk factors are

known for developing thrombosis. To understand the thrombotic pathophysiology of APS or to design clinical trials for APS, the homogeneity of the subjects' group is critical. In the 2023 ACR/EULAR APS classification criteria (New criteria), patients with arterial/venous thrombosis with macrovascular risk factors are not included as APS patients for clinical trials. The aim of this study is to clarify the characteristics of APS patients fulfilling the 2006 Sydney revised Sapporo criteria (Sapporo criteria) but not the New criteria. [Methods] This study comprised 85 patients with thrombotic APS of Hokkaido University hospital. All patients were evaluated based on the macrovascular domain; domain 1 (venous thromboembolism) and domain 2 (arterial thrombosis), and then categorized based on whether they met the clinical criteria of Sapporo and/or domain 1/2 of the New criteria as follows: Sapporo/New (+/+) and (+/-). The clinical characteristics of the patients were reviewed. [Results] Of 85 thrombotic APS patients, 80 included in Sapporo/New (+/+) and 5 with (+/-). All 5 patients in Sapporo/New (+/-) presented with arterial thrombosis with low scores due to the presence of three or more moderate cardiovascular disease risk factors. Among them, two presented with ischemic heart disease and both had only single positive aPL, representing low risk aPL profile. Three had lacunar infarction; 2 had triple positive aPLs; high risk aPL profile. Of the triple positive aPL patients, one had autoimmune thrombocytopenia. [Conclusions] The definition of APS patients using the clinical domains in New criteria would improve the recognition of this syndrome with higher specificity as an autoimmune disorder.

## ICW10-4

**Platelets are highly activated and might participate in immune abnormality of APS**

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Conflict of interest: None

[Objective] Platelets play a pivotal role in the process of coagulation and other biological process. Studies have shown that platelets are highly activated in APS, and have the ability to enhance the activity of other cells like endothelial cells, monocytes, and neutrophils. [Methods] We included patients who fulfilled the 2006 Sydney classification criteria of APS. Activation of platelet was measured by flow cytometry. Reactive oxygen species (ROS) production and mitochondrial respiration was measured. RNA-sequencing was performed. [Results] Thirty-five APS patients and 16 age and gender-matched healthy controls (HC) were included. Platelet activation was detected by the surface expression of CD62p after gating with CD41a. The mean fluorescent intensity of CD62p was significantly increased in APS patients ($p< 0.05$). After stimulated with adenosine diphosphate (ADP, 0.1U/ml) and thrombin (2U/ml), the activation was similar between patients and HC. We examined the surface expression of CD42b and found no statistic difference. Then we detected the ROS production and found that platelets of APS patients both in original state and activated with thrombin produced significantly more ROS than the HC. Mitotracker was used to label mitochondria in platelets. The quantity of mitochondria was similar. We used seahorse analysis to examine mitochondrial respiration and found that maximum respiration was evidently higher in platelets from APS patients. In RNA sequencing, 748 differently expressed genes with adjusted p-value < 0.01 and $|\log_2 FoldChange| > 1.5$ were screened and tested enrichment in KEGG pathways. It is evident that multiple immune related pathways were enriched including inflammatory signaling pathways (JAK-STAT, IL-17 signaling pathways) and T cell associated pathways (Th1, Th2, and Th17 differentiation). [Conclusions] Platelet activation and mitochondrial respiration is highly increased in APS. Platelets might interact as immune cells to modulate T cell activity.

## ICW10-5

**TLR2 promotes cytotoxicity and inflammatory response of CD8+T cells by activating mitochondrial autophagy in primary Sjogren's syndrome**

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Conflict of interest: None

[Objective] The aim of this study is to: 1) detect the frequency of $CD8^+$T cells in peripheral blood, and screen and validate $CD8^+$T cell genes through transcriptome sequencing analysis; 2) Characterization of potential molecular mechanisms involved in $CD8^+$T cell dysfunction [Methods] Phenotypical analysis of $CD8^+$T cell in PBMCs from 37 pSS patients and 40 healthy donors (HD) was performed by flow cytometry. Isolating $CD8^+$T cells from PBMCs and observing their morphology under transmission electron microscopy. Transcriptional analysis of sorted $CD8^+$T cell from six pSS patients and five HD was performed by RNA-seq. Differential gene expression was validated using RT-PCR and WB. Additionally, primary $CD8^+$T cells cultured in vitro were used to detect their functional effects under activation or inhibition of TLR2. [Results] Here, we observed an increase in the proportion of $CD8^+$T cells in the blood of pSS patients, exhibiting cytotoxic effects ($p<0.01$) and enhanced inflammatory response ($p<0.05$). Besides the organelle damage was also observed in $CD8^+$T cells of pSS patients by TEM. The transcriptome sequencing results identified 9 key genes through the bioinformatics algorithm, among which TLR2 was found to have the most significant expression difference ($p<0.001$) by RT-PCR. During in vitro culture of $CD8^+$T cells, activation of TLR2 expression significantly promoted the cytotoxicity and inflammatory response of $CD8^+$T cells ($p<0.05$). Specially mitochondria observed with partial or complete loss of cristae and increase significantly in autophagosomes was observed under transmission electron microscopy ($p<0.01$). [Conclusions] In summary, our research results demonstrate the mechanistic role of TLR2 in disrupting cellular mitochondrial fitness, which further leads to the pathogenic role of $CD8^+$T cells in pSS. Our research provides new potential therapeutic targets for pSS.

## ICW10-6

**Monocyte/HDL-Cholesterol Ratio as a Potential Indicator of Recurrent Thrombosis inPatients with Antiphospholipid Syndrome**

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Conflict of interest: None

[Objective] This study aims to investigate the association of the monocyte/high-density lipoprotein cholesterol (HDL-C) ratio (MHR), a novel biomarker associated with inflammation and oxidative stress, with recurrent thrombosis in antiphospholipid syndrome (APS) patients. Monocyte activation is a key factor in APS-related thrombosis, and HDL-C has been shown to impede monocyte activation and recruitment. Despite its predictive role in cardiovascular events and atherosclerosis in patients with chronic kidney disease or diabetes mellitus, the significance of MHR in APS remains unclear. [Methods] This is a retrospective longitudinal study comprising 107 APS patients from Hokkaido University Hospital. MHR at the time of APS diagnosis was calculated and compared between patients with and without subsequent recurrent thrombosis. Additionally, within the recurrent thrombosis group, mean MHR levels were compared between 0-6 months and 6-36 months prior to the thrombotic event. [Results] The cohort of patients exhibited a median [IQR] age of 46 years [31-56], at APS diagnosis, with a follow-up of 16 years [10-19]. Recurrent thrombosis occurred in 31 patients, with 22 of arterial and 9 of venous thrombosis. At APS diagnosis, MHR did not significantly differ between groups with and without recurrent thrombosis (MHR 5.0 [3.4-8.0], vs 5.3 [3.5-8.6], $p = 0.57$). However, within the recurrent thrombosis group, the mean MHR was significantly higher 0-6 months than 6-36 months before the thrombotic event (6.1 [4.3-8.3] vs. 5.1 [3.8-8.6], $p = 0.04$). [Conclusions] Our findings suggest that the increase of MHR occurs within 6 months before recurrent thrombotic events in APS patients. MHR may serve as an indicator of thrombotic recurrence in APS.

## ICW11-1

**Change in the SLE mortality rate and prevalence of lupus nephritis overtime: Single center retrospective study in Japan**

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Conflict of interest: Yes

**Objectives:** With approvals of belimumab (2017) and anifrolumab (2021), systemic lupus erythematosus (SLE) treatments have evolved. Yet, the impact of changes in the standard of care on SLE mortality and the prevalence of lupus nephritis remains understudied. This study was conducted to fill this knowledge gap. **Methods:** Data of SLE patients treated at our hospital from April 2006-February 2023 were analyzed, stratified by diagnosis timing and age at onset. We utilized Gray's test to examine differences in mortality rates and the prevalence of lupus nephritis among the groups. **Results:** Of the 484 SLE patients, lupus nephritis and lupus nephritis class III/IV were observed in 26.0% and 17.4% of the patients, respectively. Chronic kidney disease (CKD) stage 4 or 5 was noted in 2.7% of the patients, while 2.5% died during the follow-up period. When patients were segregated according to the calendar year of diagnosis, lower cumulative incidence of lupus nephritis, lupus nephritis class III/IV, and mortality was noted in those diagnosed in the 2010s and 2020s, as compared to those diagnosed in the 2000s and prior. Additionally, the incidence of new lupus nephritis and lupus nephritis class III/IV was lower among patients who initiated hydroxychloroquine (HCQ) at diagnosis. HCQ was demonstrated to be a protective factor against the development of CKD stage 4 or 5 and all-cause mortality (CKD stage 4 or 5: Hazard Ratio [HR] 0.21, 95% Confidence Interval [CI] 0.06-0.80, p=0.022; all-cause death: HR 0.144, 95% CI 0.03-0.66, p=0.013). Furthermore, the prevalence of lupus nephritis and lupus nephritis class III/IV was higher among patients diagnosed with SLE before the age of 40, compared to those diagnosed at or after 40. However, even among this group, the mortality rate was lower. **Conclusions:** Advancements in lupus treatment have considerably improved SLE mortality and the prevalence of lupus nephritis. Moreover, initiating treatment with HCQ notably improves lupus outcomes.

## ICW11-2

**apopDNA promotes lupus nephritis in mice by mediating macrophage pyroptosis through AIM2/Caspase-1/GSDMD pathway**

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Conflict of interest: None

[Objective] Lupus nephritis infiltrates many macrophages, which affects the development of LN. Pyroptosis is a programmed cell death form, which is distinguished by pro-inflammatory effects. But the role of pyroptosis in LN is unclear. Therefore, we aimed to investigate whether apopDNA induces pyroptosis of macrophages and participates in the pathological process of LN. [Methods] Firstly, pyroptosis were investigated after stimulating BMDM by apopDNA. Secondly, knockdown GSDMD and AIM2 protein in BMDM and then assessed pyroptosis. In LN mice, detect LN-related indexes and pyroptosis in kidney tissue. Furthermore, after depletion and reconstitution of macrophages in mice, then induced LN and assessed LN-related indexes. Finally, induced LN in WT or GSDMD KO mice. [Results] After apopDNA stimulating BMDM, caspase-1+PI+ cells, LDH release, GSDMD-N, caspase-1 p20, IL-18 and IL-1β protein, the levels of GSDMD, caspase-1, IL-18 and IL-1β mRNA were increased (pyroptosis-related indexes). Then, after both GSDMD and AIM2 knockdown, the pyroptosis-related indexes were reduced, accordingly the pores on the cell surface were decreased. In addition, by stimulating RAW264.7-ASC cells, it was found that ASC protein was involved in apopDNA-induced pyroptosis pathway. In LN mice, serum anti-dsDNA and urine protein were increased, and renal pathology was aggravated in the apopDNA group. Furthermore, the level of GSDMD-N protein and mRNA in the kidney tissue were increased. Finally, after depletion of macrophages in mice, transferred BMDM or BMDM (siGSDMD) or BMDM (siAIM2) to reconstitute the macrophage, then induced LN. It was found that LN were alleviated in BMDM (siGSDMD) and BMDM (siAIM2) groups. Similar results were obtained in GSDMD KO mouse. [Conclusions] These results suggested that apopDNA induces macrophage pyroptosis by activating AIM2, and ASC protein is required for this pathway. In the apopDNA-induced LN model, regulating GSDMD and AIM2 of macrophage alleviate LN.

## ICW11-4

**Effectiveness and safety of rituximab in patients with lupus nephritis -LOOPS registry-**

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Conflict of interest: None

[Objective] RTX was approved for LN in August 2023 in Japan; however, its real-world effectiveness and safety remained unvalidated. This study aimed to assess the efficacy and safety of RTX for LN in clinical practice. [Methods] High-dose GC+RTX±HCQ (RTX group, n=58) and high-dose GC+CY and MMF±HCQ (SoC group, n=59) in remission induction therapy for LN were included. The effectiveness and safety were compared between groups. The primary endpoint was the achievement rate of Complete Renal Response (CRR) and uPCR<1.0 at week 52. In addition, peripheral blood immunophenotyping was performed on age-/gender-matched HCs and RTX groups before and after RTX treatment. Selection bias was minimized by the propensity score-based inverse probability of treatment weighting (PS-IPTW). [Results] The treatment retention rate was 94.8% (55/58) in the RTX group and 83.1% (49/59) in the SoC group. Infusion reactions were the most frequent adverse event in the RTX group (20.7% (12/58)), and infections were most frequent in the SoC group (47.5% (28/59)). Patient baseline characteristics were adjusted by PS-IPTW. The primary endpoint was 1) CRR achieving rate: RTX group; 58.1%, SoC group; 52.2% (p=0.38), uPCR<1.0 achieving rate: RTX group; 83.2%, SoC; 81.3% (p=0.54). There was no significant difference between the groups. There was also no difference in GC sparing effect (RTX group; -81.1%, SoC group; -89.3%, p=0.65). Immune phenotyping revealed class-switched memory (CM) B cells and plasmocytes (PCs) were increased in SLE compared to HCs. Naïve B cells, CM B cells, and PCs disappeared after 26 weeks of RTX treatment. PCs remained low up to 52 weeks in cases that achieved the primary endpoint. In contrast, CM B cells and PCs increased in cases that did not achieve the primary endpoint. [Conclusions] RTX can be an effective treatment option for LN. Although there were no significant differences in efficacy between the groups, safety concerns such as infections appeared lower in the RTX group than in the SoC.

## ICW11-5

**Efficacy, safety and optimal intervention of belimumab in patients with active lupus nephritis in the real-life clinical setting from LOOPS registry**

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Conflict of interest: None

[Objective] This study aimed to determine effectiveness and safety of belimumab (BEL) in induction therapy for patients with active lupus nephritis (LN) in real world settings. [Methods] Patients with biopsy-proven ISN/RPS class III or IV LN with or without coexisting class V, who underwent standard induction therapy (Standard-of-care (SoC); glucocorticoid (GC) and either mycophenolate mofetil or cyclophosphamide) were included. The effectiveness of BEL combined with SoC (BEL group, n=27) was compared with that of SoC (SoC group, n=31). The primary endpoint was the complete renal response (CRR) at one year. [Results] The baseline patient background between the two groups was not significantly different. The one-year retention rate of BEL was 88.9%. Compared to those in the SoC group, the BEL group had higher achievement rates of CRR (SoC vs. BEL=41.9% vs. 70.4%, p=0.031), primary efficacy renal response (SoC vs. BEL=54.8% vs. 81.5%, p=0.049), LLDAS (SoC vs. BEL=41.9% vs. 85.2%, p=0.001), and DORIS remission (SoC vs. BEL=16.1% vs. 74.1%, p<0.001) at one year. GC dosage at one year and the incidence of adverse events were significantly lower in the BEL group (p<0.001 and p=0.017, respectively). Multivariate analysis showed that in the BEL group, earlier intervention with BEL was a predictive factor for achieving CRR (p=0.002), with a cutoff value of 42 days. In the SoC group, a lower eGFR improvement rate (ΔeGFR) at 4 weeks was a risk factor for CRR failure (p=0.037), with a cutoff value of 3.734%. In patients with BEL administered within 42 days of induction therapy, a high CRR achievement rate was maintained regardless of the ΔeGFR (≧3.734% vs. <3.734%=90.9% vs. 77.8%, p=0.566). [Conclusions] Intervention with BEL in addition to SoC in patients with active LN results in better disease control and makes reduction in GC possible. Although the patients with ΔeGFR <3.734% at 4 weeks have treatment resistance, BEL addition within 42 days may help achieve CRR.

## ICW12-1

**Successful Treatment of Systemic Lupus Erythematosus with Residual Disease Activity by Switching from Belimumab to Anifrolumab**

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Conflict of interest: Yes

Background: Biological agents, including the human monoclonal anti-BLyS antibody Belimumab (BEL) and the human anti-I-type interferon receptor monoclonal antibody Anifrolumab (ANI), have been approved through clinical trials for systemic lupus erythematosus (SLE). Accumulating evidence supports their effectiveness and safety. However, there is limited information on switching between biological agents with different Modes of Action (MOA) for SLE. Methods: This study analyzed SLE cases in Nagasaki Prefecture rheumatology facilities that switched from Belimumab (BEL) to Anifrolumab (ANI) during treatment to evaluate their effectiveness and safety. The primary outcome was the reduction in SLEDAI-2K scores 12 months after the switch, and the secondary outcome was the decrease in the dose of prednisolone (PSL) usage during the same period. The Wilcoxon signed-rank test (one-tailed) was used for statistical analysis. Information regarding adverse events during the treatment period was also collected. Results: Among 22 cases, 10 had a history of BEL use, with 7 switching to ANI for treatment intensification. One case was discontinued after the initial dose due to a skin rash, leaving 6 cases for analysis. All six patients continued ANI for 12 months. SLEDAI-2K decreased from 8.8 ± 4.3 before the switch to 2.0 ± 1.8 after 12 months (p=0.02). The dose of PSL decreased from 10.3 ± 6.6 mg/day before the switch to 5.4 ± 3.0 mg/day after 12 months (p=0.03). Three cases experienced mild adverse events (infectious enteritis, herpes zoster, and mild COVID-19, respectively), all of which resolved. Conclusion: Switching to a drug with a different MOA showed potential benefits for improving residual disease activity. However, since a few of our patients had active nephritis in the present analysis, the effect of switching to ANI at the currently approved dose in patients with residual active LN despite the use of BEL is uncertain and should be investigated further.

## ICW12-2

**Prediction of the low disease activity and remission after 1-year of treatment with Belimumab in Patients with Systemic Lupus Erythematosus**

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Conflict of interest: None

Objective: To identify predictors of achieving low disease activity (LDA) and remission at one year in systemic lupus erythematosus (SLE) patients treated with Belimumab (BEL). Methods: SLE patients with moderate to high disease activity (SLE-DAS > 2.48) at the time of BEL initiation and had been on BEL for at least 1-year were included. Normal blood counts were defined as the absence of low white blood cell or platelet counts and clinical characteristics at the start of BEL were analyzed for patients who had achieved LDA/remission as defined by the SLE-DAS at 12 months of treatment, and predictors were extracted using logistic regression analysis. Results: A total of 74 (69 female) patients were selected with an age range of 43.5 [17-84] (median [range]) years, and an SLE-DAS 5.36 [2.96-24.94]. Among them, 37 achieved LDA, 29 achieved remissions. Patients who achieved LDA had a significantly higher rate of normal blood cell counts (97.2% vs 78.3%, P=0.028) and normal serum complement levels (70.2% vs 32.4%, P=0.001) than those who did not. Patients who achieved remission had lower prednisolone (PSL) use at the baseline (6.0 [0-25] mg/day vs 10 [0-25] mg/day, P=0.029) and had significantly higher frequency of arthritis (47.3% vs 19.0%, P=0.003), normal blood cell counts (96.6% vs 77.8%, P=0.042), and normal serum complement levels (62.0% vs 33.3%, P=0.015). In multivariate analysis, the presence of arthritis was significantly associated with achieving LDA (odds ratio (OR) 2.932, 95% confidence interval (CI) 1.101-8.169, P=0.034) and remission (OR 3.798, 95%CI 1.351-11.25, P=0.013). Conclusions: The presence of arthritis was a factor for achieving LDA and remission. SLE patients with arthritis are more likely to have a stronger involvement in pathologic mechanisms of blood BAFF enhancement.

## ICW12-3

**Efficacy and safety of telitacicept in patients with systemic lupus erythematosus: a retrospective, multicenter real-world study**

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Conflict of interest: None

[Objective] To examine the efficacy and safety of telitacicept in the treatment of patients with systemic lupus erythematosus (SLE) in real clinical practice. [Methods] Seventy-two patients with active SLE who received telitacicept for more than 24 weeks from 2019 to 2022 at multiple centers in China were retrospectively reviewed. Among these cases, twenty-one patients received 52 continuous weeks of telitacicept treatment, and patients with renal and hematologic abnormalities were separately selected to observe the treatment outcome in the two systems. Trajectory analysis was performed to identify the limited response group. Multivariable logistic regression analysis was used to explore the factors contributing to limited response. [Results] After telitacicept treatment, SLE Responder Index 4 (SRI-4) was attained by 22.22%, 54.17%, 72.22% and 80.95%, the Lupus Low Disease Activity State (LLDAS) by 8.33%, 26.39%, 34.72%,

and 47.62%, and remission by 0%, 4.17%, 8.33%, and 23.81% at 4, 12, 24, and 52 weeks, respectively. A significant decline in serum IgA, IgG, and IgM was observed at 4 weeks and showed a downward trend at 12, 24 and 52 weeks. The median 24-h urinary protein declined from 1323.5 mg to 224.0 mg in patients with lupus nephritis treated with telitacicept at 52 weeks. In addition, a large proportion of patients with hematologic abnormalities (10/13) recovered after 52 weeks of telitacicept treatment. No severe adverse events were reported during the observation period. Age seemed to be a negative factor for treatment efficacy. [Conclusions] Telitacicept treatment demonstrated favorable efficacy and safety in active SLE patients and notably improved renal and hematological system involvement.

## ICW12-4

**Potentially different effects of biologics for patients with systemic lupus erythematosus (SLE) on short-term changes of patient-reported outcome**

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Conflict of interest: None

[Objective] The impact of anifrolumab (ANF) and belimumab (BEL) on patient-reported outcomes (PRO) may lead to insights to novel pathogenesis of SLE. To demonstrate the short-term effects of biologics on PRO in SLE patients. [Methods] We collected data from SLE patients where ANF or BEL had been introduced in our hospital. Disease activity was evaluated using SLEDAI-2k and PRO was assessed with the lupus impact tracker (LIT) 3 months after the introduction of biologics. [Results] Patients treated with ANF (N=11) or BEL (N=29) were analyzed. At baseline, patients treated with ANF had longer disease duration (p=0.099), more skin lesions (p=0.001), and higher total LIT scores (p=0.006) and SLEDAI (p=0.050). After 3 months, SLEDAI significantly improved in patients treated with ANF (p=0.002), while it remained consistent in those treated with BEL (p=0.177). However, daily prednisolone dose was significantly reduced in both the ANF (p=0.031) and BEL (p<0.001) groups. In addition, the total LIT score was significantly reduced in ANF group (p=0.043), but not in the BEL group (p=0.142). Among the items included in the LIT, the median LIT score for pain was significantly reduced only in patients treated with ANF (p=0.016), while the score for fatigue was significantly reduced only in patients treated with BEL (p=0.016). Interestingly, in a multivariate analysis, BEL had a higher odds ratio (OR) (1.65) for improving fatigue scores, compared to SLEDAI (1.15), disease duration (0.9) and total LIT score (1.04). Meanwhile, the OR for pain improvement with ANF was 2.75, despite the ORs for other confounders being close to 1.0. [Conclusions] BEL may contribute more to rapid improvement in fatigue than to disease activity, while ANF may alleviate pain in conjunction with improving disease activity. These differential short-term effects by two biologics with different mode-of-action could provide valuable insights into the pathogenesis of SLE.

## ICW12-5

**Safety and Efficacy of Anifrolumab in patients with Systemic Lupus Erythematosus (SLE) with minor flares after achieving LLDAS from LOOPS registry**

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Conflict of interest: None

[Objective] LLDAS is the treat-to-target of SLE, but many patients relapse after achieving it and dose-increase of glucocorticoid (GC) is often required. This study aimed to analyze the safety and efficacy of anifrolumab in patients with SLE with minor flares after achieving LLDAS. [Methods] This study enrolled 73 SLE patients who experienced minor flares after LLDAS achievement, 29 were treated by adding GCs or immunosuppressants (standard of care (SoC) group), 47 with anifrolumab (anifrolumab group). Minor flare was defined as the revised SELENA-Flare Index (rSFI). The LLDAS achievement rate at 26 weeks in the SoC and anifrolumab group were compared after adjusting with inverse probability of treatment weighting using propensity score (PS-IPTW). [Results] The retention rate of anifrolumab was 87.2% (41/47 patients) at week 26. The anifrolumab group had a higher the rate of LLDAS achievement (SoC: anifrolumab=56.4:89.1%, p<0.01) and DORIS remission (SoC: anifrolumab=9.8:40.8%, p<0.01) at week 26. GC doses at week 26 were lower in the anifrolumab group (SoC: anifrolumab=6.3±4.8: 3.1±3.8 mg/day, p<0.01). The incidence of adverse events was fewer in the anifrolumab group (p=0.0009), especially infections (p<0.01). Compared to patients treated for minor flares by GC dose increase (GC dose increase group, n=18), the anifrolumab group had a higher rate of LLDAS re-achievement (GC dose increase: anifrolumab=39.8:89.1%, p<0.01) and DORIS remission (GC dose increase: anifrolumab=12.4:40.8%, p<0.01). GC dose at week 26 was lower in the anifrolumab group (GC dose increase: anifrolumab= 7.5±4.8:3.1±3.8 mg/day, p<0.01). In anifrolumab group, three patients discontinued GC 52 weeks after anifrolumab. The incidence of adverse events (p<0.01) and infection (p=0.04) were significant lower in the anifrolumab group. [Conclusions] In patients with minor flares after achieving LLDAS, anifrolumab improves disease activity without adding GC or immunosuppressive drugs.

## ICW13-1

**Dynamin-Related Protein 1 Binding Partners MiD49 and MiD51 promote atherosclerosis by increasing the mitochondrial fission, adhesion and proliferation of vascular endothelial cells**

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Conflict of interest: None

[Objective] Novel components of the mitochondrial fission machinery, mitochondrial dynamics proteins of MiD49 and MiD51, have been recently described, which have been shown their potential therapeutic targets for treating cardiovascular disease including anthracycline cardiomyopathy and pulmonary arterial hypertension. Here, we examine the role of MiD49 and MiD51 in atherosclerosis. [Methods] Immunohistochemistry and immunofluorescence of aorta sections and immunoblot of vascular endothelial cells (ECs) were used to assess the expression of MiD49 and MiD51. siRNAs targeting MiDs or a microRNA mimic were delivered via tail vein injection to $ApoE^{-/-}$ C57/BL male mice. Mitochondrial fission was studied by fluorescence microscopy. The effects of manipulating MiDs on cell adhesion and proliferation were assessed in human umbilical vein endothelial cells (HUVECs). Immunoblot was used to assess the expression of related-proteins after downregulating MiDs. The expression of miR was assessed with quantitative reverse transcription-polymerase chain reaction in HUVECs. A miR involved in the regulation of MiD expression was identified using Dual-Luciferase Reporter. [Results] MiD49/51 expression is increased in the aortic valve ECs of atherosclerotic mice and IL-8-induced ECs which accelerates Drp1-mediated mitochondrial fission. Silencing MiD49/51 decreases atherosclerotic plaque size and decreases adhesion and proliferation of IL-8-induced HUVECs. MiD51 upregulation results from decreased miR-107 expression and increased HIF-1α expression. Treatment with mimics miR-107 decreases atherosclerotic plaque size by reducing HIF-1α and MiD51 generation. [Conclusions] Both MiD49 and 51 are involved in the atherosclerotic plaque formation through Drp1-mediated mitochondrial fission, and the involvement of MiD51 in this process is the result from decreased miR-107 expression and increased HIF-1α expression. The miR-107-HIF-1α-MiD51 pathway offers new therapeutic targets for atherosclerosis.

## ICW13-2

**Inflammatory glycoprotein 130 antagonist reduces atherosclerotic plaque formation by reducing mitochondrial division**

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Conflict of interest: None

[Objective] Inflammatory glycoprotein 130 (GP130) is the receptor subunit of IL-6 family. Inflammation and immune dysfunction with activated GP130 are significant mechanisms for the progression of atherosclerosis (AS). Mitochondrial fission a new target for alleviating inflammatory diseases. Studies have found that AS cells often exhibit excessive mitochondrial fragmentation. In addition, we targeted mitochondrial dynamics proteins of 49 kDa (MID49) and MID51, two novel proteins involved in the mitochondrial division machinery. This study aimed to investigate the mechanism of GP130 antagonist SC-144 in the treatment of AS by reducing mitochondrial division. [Methods] Immunohistochemistry and immunofluorescence of aorta sections were used to assess the expression of GP130. The GP130 antagonist SC-144 were delivered intraperitoneal injection to ApoE-/-C57/BL male mice. Human umbilical vein endothelial cell line HUVEC and rat smooth muscle cell line A7R5 were used for in vitro exploration. The mitochondrial morphology was detected by MitoTracker. Immunoblot was used to assess the expression of components of the mitochondrial fission machinery after downregulating GP130. The effects of inhibition of GP130 on cell functions were evaluated in HUVECs and A7R5. [Results] In vivo, GP130 was highly expressed in the aorta of AS mice. SC-144 alleviated aortic lesions in mice with AS. The expression of MID49/MID51 decreased after downregulating GP130. In vitro, MID49/MID51 expression levels and DRP1 phosphorylation levels were regulated by inhibition of GP130 signaling pathway, which inhibited IL-8-induced excessive mitochondrial division of HUVEC and A7R5. GP130 antagonist inhibited IL-8-induced the proliferation, adhesion and migration of HUVEC and A7R5, and promoted their apoptosis. [Conclusions] The GP130 antagonist SC-144 slowed the progression of AS by preventing excessive mitochondrial division in blood vessel wall cells, which provides a new idea for the treatment of AS.

## ICW13-3

**Different osteoclasts differentiation during the inflammatory process**

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Conflict of interest: None

[Objective] Osteoclasts (OCs) differentiation have been shown to differentiate from bone marrow cells (BMOCs) and dendritic cells (DCOCs). DCOCs are reported to have the ability not only to resorb bone but also to present antigens. Recently, arthritis-associated osteoclastogenic macrophages expressing CX3CR1$^{high}$ and FoxM1$^{high}$ have been reported as the local bone-resorbing osteoclast progenitors in a mouse model of arthritis. The aim of this study is to clarify the role of DCOCs in the inflammatory process and the relationship with CX3CR1 and FoxM1. [Methods] Murine bone marrow cells and bone marrow-derived dendritic cells were cultured with RANKL and M-CSF under the stimulation with; (1) media, (2) TNF-α, (3) IL-6, (4) TNF-α and IL-6. Tartrate-resistant acid phosphatase (TRAP) staining, quantitative PCR (qPCR) for mRNA expression, and immunofluorescence staining were performed. [Results] Differentiation into BMOCs and DCOCs was confirmed by TRAP staining and Nfatc1 mRNA expression. The expression of CX3CR1 mRNA was significantly increased in DCOCs compared to BMOCs, while no significant difference was observed for FoxM1 mRNA, but a trend of increased expression in DCOCs compared to BMOCs was observed. Intranuclear translocation of FoxM1 was observed in both BMOCs and DCOCs by immunofluorescence staining. Inflammatory stimulation with TNF-α and/or IL-6 during osteoclastogenic stimulation revealed the effect of IL-6 promoting the differentiation into DCOCs and TNF-α promoting the differentiation into BMOCs. [Conclusions] DCOCs expressed CX3CR1 and FoxM1 while CX3CR1 was significantly higher compared to BMOCs indicating their difference in function including the ability of migration. On the other hand, the paradoxical effect of TNF-α and IL-6 on the differentiation of OCs indicates the different role of OCs in the inflammatory process of arthritis.

## ICW13-4

**5,6-dimethylxanthenone-4-acetic acid (DMXAA), a Partial STING Agonist, Competes for Human STING Activation**

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Conflict of interest: None

[Objective] 5,6-dimethylxanthenone-4-acetic acid (DMXAA) is a mouse-selective stimulator of interferon gene (STING) agonist exerting STING-dependent anti-tumor activity. Although DMXAA can't activate human STING, DMXAA reached phase III in lung cancer clinical trials. How DMXAA is effective against human lung cancer is completely unknown. [Methods] We investigated whether DMXAA has agonistic or antagonistic effects on the STING pathway using human peripheral blood mononuclear cells. Next, we screened DMXAA derivatives which have STING antagonistic activity. Then we tried them to cells which have *STING* gain-of-function mutations causing STING-associated vasculopathy with onset in infancy (SAVI). We also tried the compounds to SAVI model mice. [Results] DMXAA was a partial STING agonist interfering with agonistic STING activation, which may explain its partial anti-tumor effect observed in humans, as STING was reported to be pro-tumorigenic for lung cancer cells with low antigenicity. We developed a DMXAA derivative--3-hydroxy-5-(4-hydroxybenzyl)-4-methyl-9*H*-xhanthen-9one (HHMX)--that can potently antagonize STING-mediated immune responses both in humans and mice. Notably, HHMX suppressed aberrant responses induced by *STING* gain-of-function mutations causing SAVI in *in vitro* experiments. Furthermore, HHMX treatment suppressed aberrant STING pathway activity in peripheral blood mononuclear cells from SAVI patients. Lastly, HHMX showed a potent therapeutic effect in SAVI mouse model by mitigating disease progression. [Conclusions] HHMX offers therapeutic potential for STING-associated autoinflammatory diseases.

## ICW13-5

**Phenotypic plasticity in suppressive function of dendritic cells mediated by Treg cells**

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Conflict of interest: None

[Objective] Dendritic cells (DCs) are characterized to be professional T cell stimulator in adaptive immunity. They are classified into several categories by surface markers, secreting cytokines, or key transcription genes. However, the functional plasticity of DC through the interaction with other immune cells is not well understood. Here we studied the functional plasticity of CD11c+ DC from mice splenocyte. [Methods] (1) To render DC to regulatory phenotype, DCs were pulsed with antigen peptides (one or mixture of two kinds) and were cocultured with Foxp3+ Treg cells specific to either kind of the presented antigen on DCs. To evaluate the suppressive stability of DC phenotype, DCs were separated from the initial culture by congenic markers and tested their ability to stimulate T naive cells in the second culture. (2) DCs isolated from Treg cocultures were passively loaded with peptide antigen and tested DC's phenotype for T cell stimulatory function. [Results]: (1) DC remained suppressive phenotype for the T cell response to Treg targeted peptide, and remained stimulatory phenotype for the T cell response to Treg non-targeted peptide in

the initial coculture. (2) The antigen specific suppressive phenotype formed by initial Treg coculture was abrogated by re-presenting antigen peptide. [Conclusions] Suppressive phenotype of DC rendered by Treg interaction was stable but not irreversible. The phenotype was stable in that the suppressive function remained even after Treg cells were removed from the initial culture. The suppression was only for the Treg targeted antigen, while the same DC still had an ability to stimulate other T cell response to Treg non-targeted antigens. The bidirectional change of DC function may indicate the plasticity of Treg mediated DC suppressive phenotype.

## ICW13-6

**Quantification of the escape from X chromosome inactivation with the million cell-scale human blood single-cell RNA-seq datasets reveals heterogeneity of escape across immune cells**

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Conflict of interest: None

[Objective] One of the two X chromosomes of females is silenced through X chromosome inactivation (XCI) to compensate for the difference in the dosage between sexes. Several X-linked genes escape from XCI, which could contribute to the differential gene expression between the sexes. However, the differences in the escape across cell types and tissues are still poorly characterized because no methods could directly evaluate the escape under a physiological condition at the cell-cluster resolution with versatile technology. [Methods] We investigated the escape across immune cell types utilizing the million-cell scale scRNA-seq datasets. We performed differential expression gene (DEG) analysis between sexes across immune cell types. In addition, we newly developed a method, **s**ingle-**c**ell **L**evel **ina**ctivated **X** chromosome mapping (**scLinaX**), which directly quantifies gene expression from the inactivated X chromosome (Xi). We also developed an extension of **scLinaX** for a **multi**-modal dataset (**scLinaX-multi**) to evaluate the escape at the chromatin accessibility level. [Results] The scLinaX and DEG analyses with blood scRNA-seq datasets consistently identified the relatively strong escape in lymphocytes compared to myeloid cells. The scLinaX-multi analysis suggested a stronger escape in lymphocytes than myeloid cells at the chromatin accessibility level. The scLinaX analysis with the human multiple organ scRNA-seq datasets also identified the relatively strong escape from XCI in lymphatic tissues and lymphocytes. Finally, effect size comparisons of genome-wide association studies (GWAS) between sexes identified the larger effect sizes of the *PRKX* gene locus-lymphocyte counts association in females than males, suggesting the potential impact of escape on the GWAS association. [Conclusions] scLinaX identified the heterogeneity of escape across cell types and tissues and would contribute to expanding the current understanding of the escape and sex differences in gene regulation.

## ICW14-1

**Prognostication of patients with interstitial lung disease associated with systemic sclerosis using quantitative computed tomography**

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) is a leading cause of death in patients with systemic sclerosis (SSc). Abnormal lung volume (ALV) of clearly >20% based on high-resolution CT has been suggested to be a predictor of mortality, and therefore staged as an extensive disease (Goh criteria). However, it lacks a sensitive and precise quantification. Further, a longitudinal sectional view is also lacking. We elucidate prognostic factors of SSc-ILD using quantitative CT (qCT) and by observing changes in ALV over time. [Methods] Among 123 patients with SSc who attended Hokkaido University Hospital from 2010 to 2021 and met ACR/EULAR 2013 classification criteria, those with available chest CT within 10 years from the disease onset were included and evaluated retrospectively. ALV was calculated by fully automated analysis using the software (*Synapse Vincent®, Fujifilm, Tokyo*). The primary endpoint was the introduction of home oxygen therapy (HOT) or death related to SSc. [Results] A total of 113 patients were included and followed up for 7.1 (3.4-11.2) years. Of them, 17 (15.0%) and 12 (10.6%) resulted in HOT and death, respectively. First, patients were stratified according to baseline (<12 months from the onset of SSc) ALV. Hazard ratios for the events were 5.44 (95%CI 0.70-42.2) in the group with an ALV of 20-30% and 5.57 (95%CI 1.38-22.5) in that with an ALV of ≧30%, compared to that with an ALV of <20%. Next, patients were re-stratified according to ALV at 12-24 months after the onset of SSc. Hazard ratios for the events were 1.81 (95%CI 0.12-28.2) in the group with an ALV of 20-30% and 9.34 (95%CI 1.86-46.9) in that with an ALV of ≧30%, compared to that with an ALV of <20%. [Conclusion] The current results would confirm the Goh criteria and provide a new prognostication in SSc-ILD. An ALV of ≧30% after one year from SSc onset as well as an ALV of ≧20% at baseline may be predictors of mortality, highlighting the role of longitudinal changes in chest CT findings.

## ICW14-2

**Study design of the FIBRONEER-ILD trial of BI 1015550 in patients with progressive pulmonary fibrosis and a comparison with the INBUILD trial of nintedanib**

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Conflict of interest: Yes

**Objective** The Phase 3 INBUILD study demonstrated the efficacy of nintedanib in treating chronic fibrosing interstitial lung diseases with a progressive phenotype as it slowed FVC decline over 52 weeks. BI 1015550 is a preferential phosphodiesterase 4B inhibitor that, at a dose of 18 mg BI 1015550 twice daily (BID), prevented the decline of FVC in patients with idiopathic pulmonary fibrosis (IPF) over 12 weeks in a Phase 2 study. Here, we describe the study design of the Phase 3 FIBRONEER-ILD trial in patients with progressive pulmonary fibrosis (PPF) and compare it to that of INBUILD. **Methods** Patients with pulmonary fibrosis other than IPF that meet prespecified criteria for progression are randomised (1:1:1) to BI 1015550 (9 mg or 18 mg) BID or placebo over at least 52 weeks. Randomisation is stratified by baseline use of nintedanib (yes/no). Similar to INBUILD, patients in FIBRONEER-ILD are stratified by high-resolution computed tomography pattern (usual interstitial pneumonia-like vs other fibrotic patterns). Certain immunosuppressive agents (other than corticosteroids) are permitted in the case of underlying systemic disease, whereas cyclophosphamide, tocilizumab, mycophenolate, rituximab and high-dose steroids are not permitted. In contrast to INBUILD, tacrolimus and azathioprine are allowed in this study. In FIBRONEER-ILD, the primary endpoint is absolute change from baseline in FVC (mL) at Week 52, whereas in INBUILD it was annual rate of decline

in FVC (mL/year). This was guided by the results of the Phase 2 study of BI 1015550 in IPF, where a non-linear FVC course until Week 12 was observed in the active treatment arm. **Results** Approximately 1041 patients with PPF will be enrolled (99 Japanese patients) in FIBRONEER-ILD from 45 countries. The estimated completion date is November 2024. **Conclusions** FIBRONEER-ILD will provide data on the efficacy and safety of BI 1015550 in patients with PPF. The population in FIBRONEER-ILD is expected to be similar to that of INBUILD.

## ICW14-3

**Predictive factors for pulmonary hypertension in patients with rheumatic and musculoskeletal disease**

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Conflict of interest: None

[Objective] Pulmonary hypertension (PH) associated with rheumatic and musculoskeletal diseases carries a particularly poor prognosis, and its early detection with appropriate intervention is essential. This study aims to identify factors predicting pulmonary hypertension in patients with rheumatic and musculoskeletal diseases. [Methods] We underwent right heart catheterization (RHC) in patients whose tricuspid regurgitation pressure gradient (TRPG) was ≧ 30 mmHg with the signs of right heart strain on transthoracic echocardiography. PH was diagnosed according to the mean pulmonary arterial pressure (mPAP) ≧ 20 mmHg with RHC. Patients were divided into two groups according to the presence of PH, and the clinical characteristics were compared between patients with and without PH. [Results] A total of 39 patients (14 with overlap syndrome, 7 with MCTD, 9 with SSc, 2 with SLE, 1 with Sjogren syndrome, and 6 with others) were included in the analysis. Twenty two (56.4%) patients were diagnosed as PH. Patients with PH had significantly higher TRPG ($p<0.05$), lower levels of saturation of percutaneous oxygen (SpO2) at 6-minute (min) in 6-min walk test (6MWT) ($p<0.05$), and higher positive rate for anti-SSA antibody (anti-SSA) ($p=0.08$). Receiver operating characteristic curve identified 33 mmHg as a cut-off value of TRPG and 92% of SpO2 at 6-min in 6MWT that discriminated patients with PH from those without. Compared to evaluation using TRPG alone (specificity 0.27, sensitivity 1.00), using either 6MWT or SSA in addition to TRPG threshold yielded higher specificity (specificity 0.67, sensitivity 0.93). [Conclusions] More than 33 mmHg of TRPG, less than 92% of SpO2 at 6 min in 6MWT, and SSA-Ab positivity can predict the presence of PH in patients with rheumatic and musculoskeletal diseases.

## ICW14-4

**Risk factors for mortality in connective tissue disease-associated thrombotic microangiopathy**

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Conflict of interest: None

[Objective] Thrombotic microangiopathy (TMA) is a pathological condition characterized by microangiopathic hemolytic anemia, destructive thrombocytopenia, and associated organ damage. TMA includes several diseases, such as thrombotic thrombocytopenic purpura (TTP), and has a poor prognosis in connective tissue diseases (CTD). However, the risk factors for mortality in CTD-associated TMA (CTD-TMA) are unknown. The aim of this study was to identify the risk factors for mortality in CTD-TMA. [Methods] This single-center retrospective observational study comprised 31 patients with CTD-TMA who visited Hokkaido University Hospital from 2006 to 2023. TMA was defined as having all of the following: thrombocytopenia, microangiopathic hemolytic anemia (presence of schistocytes or absence of direct Coombs test), and organ dysfunction. Clinical and laboratory data were collected at the onset of TMA. Univariate and multivariate Cox regression analyses were performed to identify the risk factors for mortality. [Results] Of the 31 patients, 25 (81%) were female, and the mean age was 49 years. Six patients (19.4%) were diagnosed with TTP. Nineteen (61%) and 9 (29%) had underlying systemic lupus erythematosus and systemic sclerosis, respectively. One-year survival rate was 61.3%. In univariate Cox regression analysis, age at onset of TMA, direct bilirubin, aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) were identified as risk factors for mortality. Multivariate Cox regression analysis showed that age at onset of TMA (hazard ratio=1.06, $p=0.01$) and LDH at baseline (hazard ratio=1.12, $p=0.03$) were identified as independent risk factors for mortality. Based on the ROC curve, LDH≧ 500 U/L was considered the best cutoff for predicting mortality. [Conclusions] Age at onset of TMA and LDH at baseline were independent risk factors for mortality in CTD-TMA. Rapid intensive treatment would be required in patients with these risk factors.

## ICW14-5

**Anti-Interferon gamma inducible protein 16: Identification of a novel autoantibody of idiopathic interstitial pneumonias and its clinical characteristics from multi center cohort study**

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Conflict of interest: None

[Background] Autoantibodies are often found in patients with idiopathic interstitial pneumonias (IIPs), even though any specific connective tissue disease is not diagnosed. The clinical significance of autoantibodies in such cases remains unclear. We routinely screened sera from patients of IIPs for autoantibodies, and discovered a novel autoantibody which was not previously reported to be associated with IIPs. Herein, we identified its corresponding autoantigen and investigated the clinical implications of the antibody. [Methods] Sera of 300 patients diagnosed as IIPs from our multicenter-cohort were screened for autoantibodies and their clinical records were reviewed. For screening, 35S-methionine labeled protein-immunoprecipitation (IP) was used. The candidate autoantigens were explored using HuPEX Comprehensive protein array, and then the target antigen was confirmed by IP assay utilizing products of in vitro transcription/translation (IVTT) system. Finally, we compared the clinical characteristics of IIPs with and without the novel autoantibody. [Results] Among the 300 IIP patients, six sera (2%) immunoprecipitated common tetrameric proteins with molecular weights of approximately 100 kDa. Protein array identified interferon gamma inducible protein 16 (IFI16) as the candidate autoantigen, which was confirmed by immunoprecipitation of recombinant IFI16 by each six serum. Anti-IFI16-positive patients were 63.8±8.5 years old. The high-resolution computed tomography patterns of six patients were UIP in two, NSIP/OP in two, PPFE in one, and unclassifiable in one. The 5-year survival from diagnosis was 42% and 70% with and without anti-IFI16, respectively ($P=0.16$) and the acute exacerbation-free rate at 5 years was 100% and 85% ($P=0.39$). [Conclusions] Anti-IFI16 is a novel autoantibody associated with IIPs. Further investigation of its clinical significance will help us to establish the detailed stratification and management of IIPs.

## ICW15-1

**Genetic tests including asymptomatic family members are useful to speculate the pathogenicity of variants: A patient with familial Mediterranean fever harboring two MEFV variants and a novel NLRP12 variant**

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Conflict of interest: None

[Introduction] When we diagnose inherited autoinflammatory diseases, we sometimes encounter genetic variants whose clinical significance is uncertain. Furthermore, it is uncommon to conduct genetic tests for whole family members, especially when they have no symptoms. We experienced a patient with familial Mediterranean fever (FMF) harboring three variants in two genes, including one novel variant. The clinical significance of the two variants was unclear. Genetic tests of his asymptomatic family members were useful in speculating the clinical significance of his variants. [Case] The patient is a 17-year-old male suffering from recurrent fever accompanied by arthritis, peritonitis, and skin erythema. His symptoms were self-limited, and laboratory tests showed transient elevation of acute phase proteins. Colchicine administration ameliorated his symptoms. His parents and sibling were asymptomatic. He was clinically diagnosed with FMF. A genetic test revealed that he had three missense variants in two genes (MEFV M694I, L110P, and NLRP12 S702G). MEFV M694I was reported to be pathogenic, but the clinical significance of MEFV L110P was uncertain. There was no previous report about NLRP12 S702G. Because the clinical significance of these variants was obscure, we performed genetic tests on his family. His mother shared MEFV M694I and NLRP12 S702G, his father had MEFV L110P, and his sibling had only NLRP12 S702G. Therefore, we assumed that his symptoms were caused by compound heterozygote variants in MEFV, and each variant was insufficient to cause the symptoms solely. [Conclusions] Our case suggests that genetic tests of asymptomatic family members help speculate the clinical significance of the variants detected in patients with autoinflammatory diseases. Also, by speculating the clinical significance of variants, we could explain the inheritance pattern of autoinflammatory diseases to the patients.

## ICW15-2

**Hyperuricemia is associated with higher levels of fasting plasma glucose and insulin resistance in non-diabetic subjects**

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Conflict of interest: None

**Objective** Glucose metabolism disorders are well-established major contributors to morbidity and mortality. Elevated serum uric acid (SUA), which is an essential precursor of gout attacks, is closely linked to insulin resistance syndrome and its cardiometabolic consequences. Elevated SUA is also proven to be linked to various other comorbidities and mortality. In this study we explore the relationship between elevated SUA and fasting plasma glucose (FPG), insulin levels, and insulin resistance in an older Finnish adult cohort. **Methods** We used data from GOAL (**GO**od **A**geing in **L**ahti region) study – a prospective, population-based study of Finnish individuals aged 52–76 years. Data of SUA levels, fasting blood glucose levels and other laboratory parameters, comorbidities, lifestyle habits and socioeconomic factors were collected. Subjects with SUA values of >410 µmol/L (≈6.9 mg/dL; 75$^{th}$ percentile) were regarded hyperuricemic. We investigated the relationship between hyperuricemia and FPG, insulin levels and insulin resistance (HOMA-IR ≥2.65). **Results** We found statistically significant sex-, age- and BMI-adjusted small to moderate relationships (Cohen′s standard for β values above 0.10 and 0.30 respectively) between hyperuricemia and FPG, insulin levels and insulin resistance in the whole study population as well as in the female and male subgroups. The higher the SUA level, the higher is the HOMA-IR [(adjusted β=0.21 (95% CI: 0.17 to 0.25)] and it rises drastically if SUA is above 400 µmol/L (≈6.7 mg/dL). The probability of a subject having insulin resistance is linearly related to SUA level. **Conclusions** Hyperuricemia is associated with elevated FPG and insulin resistance, emphasizing the importance of addressing both conditions. Further research may explore hyperuricemia treatment's role in preventing glucose metabolism disorders and their cardiometabolic consequences.

## ICW15-3

**Tyrosine phosphatase SHP2 regulates macrophage polarization and participates in the mechanism of gouty arthritis**

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Conflict of interest: Yes

[Objective] To explore whether SHP2 is participated in the process of gouty arthritis, and its specific mechanism is to regulate macrophage polarization. [Methods] Synovial specimens from normal/gout patients are stained by HE, Immunofluorescence staining was used to observe the expression of SHP2. We construct THP-1 cells as an in vitro model, use SHP2 specific inhibitor Shp099, siRNA, overexpression plasmids and other interventions, qPCR and WB methods to detect macrophage polarization status and mitochondrial function. The control mice and Shp099 intervention mice were used to establish acute gouty arthritis models. Use flow cytometry to analyze the polarization of macrophages and the number of neutrophils. Use PCR Array to detect signal molecules in mitochondria and explore the possible mechanism of SHP2 transport from cytoplasm to mitochondria. [Results] The expression of SHP2 in the acute gouty arthritis increased. After inhibiting SHP2 activity, the expression of inflammatory factors IL-1β and IL-6 in THP-1 cells induced by MSU decreased, the expression of anti-inflammatory factors increased, polarized toward M2 macrophages, decreased mitochondrial ROS, restored membrane potential JC-1, decreased mPTP opening, and maintained steady-state differences in mitochondria were statistically significant ($p<0.05$). Inhibiting the activity of SHP2 can alleviate the acute gouty arthritis induced by MSU in mice and induce the polarization of macrophages to M2 macrophages. After MSU intervention, the mitochondria were separated and the expression of SHP2 in the mitochondria increased. Immunofluorescence showed that the transport of SHP2 from the cytoplasm to the mitochondria increased after the intervention of MSU and may be related to TSPO. [Conclusions] In acute gouty arthritis, SHP2 is participated in the process of gouty arthritis, and its specific mechanism is to transport into mitochondria and regulates mitochondrial homeostasis, mediating macrophage polarization.

## ICW15-4

**Pregnancy outcomes and perinatal disease activity in Behçet's disease patients at two Yokohama City University related centers**

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Conflict of interest: None

[Objective] Behçet's disease (BD) is a recurrent inflammatory disease of unknown pathogenesis that frequently occurs in gestational age, but there are few reports investigating delivery outcomes and perinatal disease activity changes in BD patients. [Methods] We conducted a retrospective study using medical records of BD patients who had attended and delivered at the Department of Obstetrics and Gynecology of Yokohama City University Hospital or Perinatal Center of Yokohama City University Medical Center between January 2000 and October 2020. A total of 4,226 healthy pregnancies who delivered at Yokohama City University Medical Center during the same period were used as controls. Statistical analysis was performed by matching analysis using propensity scores calculated using generalized estimating equations. [Results] There were 32 pregnancies in 26 BD patients (BD types as follows; 4 complete type, 26 incomplete type, 2 suspected, 4 ocular lesions, 9 gastrointestinal lesions, 3 vascular lesions, 2 neural lesions). There were 27 live births (3 preterm (OR 3.24 (95%CI, 0.77-19.35), 6 Small For Date (OR 3.76 (95%CI, 1.32-12.3))), 3 spontaneous abortions, and 2 artificial abortions. Complications of pregnancy were gestational hypertension in 3 cases, gestational diabetes in 5 cases, and intrauterine fetal growth retardation in 1 case. 10 (31.3%) cases had exacerbations of BD. BDCAF (mean (SD)) transition were 1.21 (0.98) before pregnancy, 1.16 (1.05) early, 1.41 (1.19) mid, 1.07 (1.09) late, and 1.36 (1.20) postpartum. Exacerbation was observed especially in the second trimester, cutaneous mucosal and gastrointestinal lesions. 7 cases required intensified treatment or hospitalization. [Conclusions]

Preterm delivery was observed more frequently in pregnancies with BD than healthy cases. There were exacerbations of disease activity in some cases that requiring close multidisciplinary management in BD pregnancies.

## ICW15-5

**Atypical pruritic rash as a prognostic factor in adult Still's disease - a single center retrospective study**

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Conflict of interest: None

[Objective] Though evanescent non-pruritic rash is considered a typical rash in adult Still's disease (ASD), recent reports of atypical rash has been rising. Interestingly, some of them possess distinctive histologic pattern and tend to show higher disease activity. The aim of this study is to evaluate the prevalence of atypical rash, their clinical and histological features compared to those with typical rash in ASD patients. [Methods] We retrospectively reviewed 30 ASD patients who were treated between January 2009 and October 2023 at our department. Patients were divided into groups according to the presence of rash and pruritis. We assessed the histology of pruritic and non-pruritic rash, then evaluated blood samples (Ferritin, CRP) and compared the clinical course (Macrophage activation syndrome, disease relapse) of patients from each group. [Results] Among 30 patients, 50% (15/30) had pruritic rash, 37% (11/30) had typical evanescent rash, and 13% (4/30) had no rash. Histology samples were available in 10/15 patients from the pruritic rash group and 3/10 from the non-pruritic group. Histologically, 60% (6/10) of patients from the pruritic group displayed dyskeratosis, a feature not found in the non-pruritic rash group. The ferritin level was 7068 [4767, 19345] in the pruritic rash group, higher than 6325 [986, 16757] in the non-pruritic group. Mean while the CRP level was similar in both groups, 13 [10.05, 15.05] in the pruritic group and 12 [7.45, 27.00] in the non-pruritic group. MAS complication and disease relapse in the pruritic group was 27% (4/15) and 33% (5/15) respectively, higher than 9% (1/11) and 18% (2/11) in the non-pruritic rash group. [Conclusions] Atypical pruritic rash is not uncommon among ASD patients. Patients with pruritic cutaneous manifestation tend to have more severe clinical course and skin biopsy can display distinctive histology pattern. Recognition of this clinical variant can be helpful in early diagnosis and awareness for poor prognosis.

## ICW15-6

**Shared immunological signature of Adult-onset Still's disease and other autoinflammatory diseases unveiled by transcriptome analysis**

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Conflict of interest: None

[Objective] Adult-onset Still's disease (AOSD) manifests as a systemic inflammatory disorder characterized by spiking fever, rash and arthritis. The comprehensive genome database "ImmuNexUT" indicates that AOSD, ANCA-Associated Vasculitis (AAV) and Beçhet's disease (BD) might have overlapping immunological attributes tied to innate immunity. Our goal was to shed light on these shared traits. [Methods] The transcriptome data from immune cells of 16 AOSD, 19 AAV, 23 BD patients, and 28 healthy controls from the ImmuNexUT study were analyzed. Differential gene expression (DEG) analysis was performed to pinpoint genes linked with immunological characteristics shared among the three diseases. Subsequently, weighted gene co-expression network analysis (WGCNA) was conducted to identify gene clusters contributing to the pathogenesis. [Results] Among patients, significant DEGs were observed in $CD3^-CD19^+HLA\text{-}DR^+CD56^-CD16^+$monocytes, $CD19^+IgD^-CD27^+CD38^+$plasmablasts and $CD3^-CD19^-HLA\text{-}DR^+CD56^-CD14^-CD16^-CD11c^+$myeloid dendritic cells (DCs) relative to healthy individuals. Highlighting $CD16^+$monocytes and myeloid DCs with the highest number of DEGs, WGCNA revealed disease-related gene clusters. Some could be suppressed by oral-corticosteroids, while others appeared corticosteroid-unresponsive, suggesting that these steroid-independent disease-linked genes characterize the disease state of these 3 autoinflammatory diseases and may offer potential therapeutic avenues. [Conclusions] Our findings illuminate the shared immune features among AOSD, AAV and BD, holding promise for novel treatment approaches or drug repositioning in the future.

## ICW16-1

**Clinical features of medication-related osteonecrosis of the jaw associated with denosumab in patients with rheumatic disease**

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Conflict of interest: None

[Objective] This study aimed to determine the risk of medication-related osteonecrosis of the jaw (MRONJ) after denosumab use in patients with rheumatic disease. [Methods] We retrospectively compared the clinical features of patients with and without MRONJ associated with denosumab in rheumatic diseases between April 2013 and September 2023. We examined the following clinical features with and without MRONJ: age, gender, history of rheumatoid arthritis, history of glucocorticoids and bisphosphonate use, history of diabetes, cumulative dose and days of denosumab, smoking history, history of dental extraction, serum albumin levels. Serum albumin levels were evaluated within one year prior to the onset of MRONJ. [Results] A total of 277 patients (age; 77.5±13.3 years, female; 243 cases (87.7%)) with rheumatic diseases have given denosumab, and all of them were used for osteoporosis (60 mg subcutaneously every 6 months). The observation period after administration of denosumab is 1704.2±69.2 days, among them, five patients (1.81%) developed MRONJ; 2 patients had rheumatoid arthritis, 2 patients had polymyalgia rheumatica, and 1 patient had systemic lupus erythematosus. The patients with MRONJ had diabetes more frequently than in those without (60% vs. 15.4% ($p=0.0074$)), and serum albumin levels were significantly lower in those with MRONJ than those without (3.16±0.17 vs. 3.84±0.03 ($p=0.0001$)). No significant differences were observed in the other clinical features including cumulative denosumab dose or days. [Conclusions] We determined the risk of MRONJ associated with denosumab in rheumatic diseases. Presence of diabetes and hypoalbuminemia might be a risk factors. This study found no significant differences for cumulative denosumab dose or days. We consider that management of diabetes and improvement of nutritional status are necessary to prevent the development of denosumab MRONJ in patients with rheumatic diseases.

## ICW16-2

**Antiretinal antibodies in hydroxychloroquine eye toxicity**

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Conflict of interest: None

[Objective] Autoimmune retinopathy (AIR) is a disease in which circulating antibodies against retina-specific antigens can lead to blindness. Hydroxychloroquine (HCQ) can cause retinal toxicity for which routine

screening is recommended in systemic lupus erythematosus (SLE) patients. AIR has been reported in SLE but the frequency of antiretinal antibodies in SLE patients is not well described. This abstract aims to determine whether patients diagnosed with HCQ retinal toxicity are more likely to have antiretinal antibodies compared to controls. [Methods] Patients in this study were selected from a longitudinal cohort of SLE patients. We performed antiretinal antibody testing on plasma samples from 269 SLE subjects. We reviewed charts for the presence of HCQ retinal toxicity and risk factors for HCQ toxicity. Our primary outcome was frequency of antiretinal antibodies in SLE patients with HCQ retinal toxicity compared to SLE patients with no retinal toxicity. [Results] Patients with HCQ retinal toxicity had a higher likelihood of testing positive for arrestin antibodies (60.7% of patients vs. 30.7% of patients, p=0.001) and PKM2 antibodies (46.4% of patients vs. 28.2% of patients, p=0.047). Patients with HCQ eye toxicity also had a trend towards a higher number of anti-retinal antibodies (mean 2.96 ± 2.40 vs. 2.05 ± 1.74). In multivariate analysis, the presence of arrestin antibodies was associated with OR 3.2 for developing HCQ eye toxicity. The mean lifetime dose of HCQ was 1.596g, with an average SLE disease duration of 12.39 years. [Conclusions] Antiretinal antibodies, especially arrestin and PKM2, were more common in patients with HCQ retinal toxicity compared to patients without HCQ retinal toxicity. When controlling for other risk factors associated with HCQ eye toxicity, arrestin antibodies were associated with increased odds for the development of eye toxicity, suggesting a potential role for antiretinal antibodies as a biomarker of HCQ eye toxicity risk.

## ICW16-3

**Effect of remission, clinical remission with active serology, and glucocorticoid dosage on the pregnancy outcome of pregnant patients with systemic lupus erythematosus**

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Conflict of interest: Yes

**Background:** Remission is a key treatment target in systemic lupus erythematosus (SLE) management to reduce flares and adverse pregnancy outcomes (APOs) ratio. However, the association between clinical remission with active serology, and the risk of APOs is not thoroughly understood. Additionally, determining the optimal glucocorticoid dosage during pregnancy to mitigate APO risks remains under-researched. Therefore, we conducted this study. **Methods:** Pregnant patients with SLE, who were followed up at two Japanese tertiary referral centers, and had their remission status (Zen/Doria remission) assessed at conception, were included in this study. We categorized the patients into two groups based on remission status at conception and analyzed the APO ratio. We also examined the influence of serological activity in pregnant patients with clinical remission and analyzed the optimal glucocorticoid dosage to minimize the APO ratio. **Results:** Of the 96 pregnancies included, 59 achieved remission at conception. Remission was linked to a reduced APO ratio. (overall APO: OR 0.27, 95% CI 0.11-0.65, p<0.01, maternal APO: OR 0.34, 95%CI 0.13-0.85, p=0.021, neonatal APO: OR 0.39, 95%CI 0.17-0.90, p=0.028). Conversely, no statistical difference was observed in the APO ratio based on serological activity in pregnant patients with clinical remission. (overall APO: OR 0.62, 95%CI 0.21-1.79, p=0.37, maternal APO: OR 1.25, 95%CI 0.32-4.85, p=0.75, neonatal APO: OR 0.83, 95%CI 0.29-2.39, p=0.73). A glucocorticoid dose of prednisolone equivalent ≧7.5 mg/day at conception correlated with increased APO. (overall APO: OR 3.01, 95%CI 1.23-7.39, p=0.016, neonatal APO: OR 2.98, 95% CI: 1.23-7.22, p=0.016). **Conclusions:** Achieving clinical remission, even with active serology, is crucial for decreasing APO risks in SLE patients planning conception. In addition, if clinically feasible, reducing the glucocorticoid dosage to <7.5 mg/day before conception could be another treatment target.

## ICW16-4

**Risk of sulfa allergy with skin rash or mucocutaneous symptoms that would require discontinuation of sulfa drugs**

Misako Higashida-Konishi[1], Keisuke Izumi[1,2], Hiroki Tabata[1], Satoshi Hama[1], Tatsuhiro Ohshige[1,2], Hisaji Oshima[1], Yutaka Okano[1], Katsuya Suzuki[1]

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Conflict of interest: None

[Objective] Sulfa drugs (sulfamethoxazole-trimethoprim (SMX/TMP) and salazosulfapyridine (SASP)) were frequently used in patients with autoimmune diseases. There was a high incidence of allergy to sulfa drugs. Our objective was to determine the risk of sulfa allergy that would require discontinuation of sulfa drugs. [Methods] We retrospectively studied patients at our hospital who took sulfa drugs from 2006 to 2023. Patients with sulfa allergy were defined as those who developed skin rash and mucocutaneous symptoms after taking sulfa drugs. At first, the risk of sulfa allergy was analyzed. Secondly, the risk of SMX/TMP allergy was analyzed. Thirdly, the risk of SASP allergy was analyzed. Clinical and laboratory data of patients with each allergy were compared with those of patients without each allergy at their first visit to our hospital. [Results] There were 1363 patients were enrolled. There were 548 patients with SMX/ TMP, 897 patients with SASP, and 82 patients with both drugs. At first, in 1363 patients who took sulfa drugs, there were 68 patients with sulfa allergy and 1295 patients without sulfa allergy. Patients with sulfa allergy had no significant differences in autoimmune disease, autoantibodies, or glucocorticoids compared to patients without sulfa allergy. Secondly, in 548 patients who took SMX/TMP, there were 20 patients with sulfa allergy and 528 patients without SMX/TMP allergy. Patients with SMX/TMP allergy had significantly higher rates of AOSD compared to patients without SMX/TMP allergy (15.4% vs 3.4%, p=0.02). Thirdly, in 897 patients who took SASP, there were 49 patients with sulfa allergy and 848 patients without SMX/TMP allergy. Patients with SASP allergy had no significant differences in autoimmune diseases or autoantibodies compared to patients without SASP allergy. [Conclusions] Patients with AOSD are at risk for SMX/TMP allergy and should be careful when patients took SMX/TMP. The risk of sulfa drug allergy or SASP allergy was not clear.

## ICW16-5

**The retrospective analysis for the association of anti-SSA/Ro antibodies with adverse pregnancy outcomes in patients with systemic lupus erythematosus**

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Conflict of interest: None

[Objective] We aimed to clarify the influence of anti-SSA/Ro antibody and other factors on adverse pregnancy outcomes in SLE patients. [Methods] We retrospectively extracted first pregnancies after the onset of SLE from LUNA registry (2016-2022, n=1775). Patients who are not clear about anti-SSA/Ro or pregnancy outcomes, and cases of abortion were excluded. First, we analyzed effects of anti-SSA/Ro on pregnancy outcomes by comparing the anti-SSA/Ro positive and negative group. Second, we assessed clinical features in the fetal loss group and live birth group. Factors associated with fetal losses were analyzed by logistic regression. Third, we performed the analyses after adjusted for antiphospholipid antibodies (aPL). [Results] Overall, 247 pregnancies were included: 194 live births (122 full-term births, 57 pre-term births, 15 not clear) and 53 fetal losses (miscarriages and stillbirths). Compared with the anti-SSA/Ro positive group (n=145) and negative group (n=102), frequencies of live birth (77% vs 80%, p=0.64) and preterm birth (31% vs 33%, p=0.87) were not different. In comparison with the fetal loss group and the live birth group, the fetal loss group had significantly higher positivity for (57% vs 35%, p=0.0066) and history of steroid pulse (62% vs 34%, p=0.0010). There were no significant differences in anti-SSA/Ro, ages at pregnancy, disease duration until the pregnancy, smoking history, lupus nephritis, SLEDAI scores at diagnosis, the maximum dose of prednisolone and the use of cyclophosphamide. These results were confirmed by logistic regression: anti-SSA/Ro (OR [95%CI], 1.21 [0.65-2.26]), aPL (2.45 [1.32-4.55]), steroid pulse (3.16 [1.60-6.22]). Furthermore, when data were adjusted for aPL, there were no significant associations of anti-SSA/Ro with fetal losses. [Conclusion] There were no significant associations between anti-SSA/Ro antibody and fetal losses in SLE, while aPL and history of steroid pulse were predictive factors for fetal losses.

## ICW16-6

**Effects of low-dose acetylsalicylic acid in pregnancy among patients with Systemic Lupus Erythematosus**

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Conflict of interest: None

[Objective] This study aimed to investigate the impact of low-dose acetylsalicylic acid (LDASA) on pregnancy outcomes in Systemic Lupus Erythematosus (SLE) patients. [Methods] We retrospectively analyzed data from 75 pregnancies in SLE patients, dividing them into two groups: those receiving LDASA and those not. We compared: 1) patient demographics, and 2) their association with adverse pregnancy outcomes (APOs). Within the LDASA-administered group, we examined the relationship between 3) the timing and dosage of LDASA and pregnancy outcomes. [Results] Out of 75 pregnancies, LDASA was prescribed in 31 pregnancies (41.3%), and APOs occurred in 32 pregnancies (42.6%). 1) We found no differences in age, medication, renal involvement, and disease activity between LDASA and non-LDASA groups. The LDASA group had higher positivity for antiphospholipid antibodies (aPL), including non-criteria aPL as low titer, or not persistent aPL, than non-LDASA groups. (criteria aPL; 46.6% vs 2.2%, p<0.0001, non-criteria aPL; 36.6% vs 10.0%, p=0.0068). 2) Incidence of APOs was similar between the two groups, even after excluding criteria aPL-positive patients. 3) Among LDASA-receiving patients, including aPL-positive individuals, 19 (61.2%) received LDASA before 6 weeks of gestation, and 12 (38.7%) were after 6 weeks. LDASA 81 mg was prescribed in 14 (45.1%) and 100 mg in 17 (54.8%). Birth weight was significantly higher in those receiving LDASA before 6 weeks (2578.4g±641.7g vs 1903.3±908.5g, p=0.02). Additionally, early-onset preeclampsia incidence was lower in those given LDASA before 6 weeks (0/19 vs 3/12, p=0.04). When comparing the 81 mg LDASA with 100 mg LDASA, the 100 mg group had higher birth weights (2617±693.5g vs 2116.2±631.4g, p=0.002). [Conclusions] Positive aPL was the primary factor for LDASA prescription. While no other factors identified LDASA benefits, early LDASA administration and using 100 mg over 81 mg appeared to improve pregnancy outcomes in LDASA-requiring SLE patients.

## ICW17-1

**Clinical association between bone destruction progression and interstitial lung disease in rheumatoid arthritis patients undergoing JAK inhibitor or CTLA4-Ig treatment**

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Conflict of interest: None

[Objective] This study aimed to investigate the clinical association between the progression of bone destruction and interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA) undergoing treatment with JAK inhibitors (JAKi) or CTLA4-Ig. [Methods] We conducted a retrospective analysis of 22 RA patients who initiated JAK inhibitor or CTLA4-Ig therapy at our department between July 2016 and January 2022. All patients had undergone plain radiographs of both hands and feet and plain chest CT scans before and after treatment. We compared the progression of modified total Sharp score (mTSS) (ΔmTSS) and the progression of the Ichikado CT score (ΔCT score), before and after treatment initiation. Additionally, we examined the correlation between these two variables. [Results] Of the 22 patients included in the study, 16 were female, with a median age of 66 years. The median age at the start of treatment was 72 years, and the median disease duration was 7 years. Among the patients, 20 were RF-positive, 17 were ACPA-positive, and 16 had CDAI-positive status. The median CDAI was 18.5, the CT score was 145.8, and the mTSS was 14.5. The study population comprised 12 patients in the JAKi group and 10 patients in the CTLA4-Ig group. Correlation analysis revealed no significant association between ΔmTSS and ΔCT score in all patients (correlation coefficient r = -0.1067). However, a significant correlation was observed between the baseline CT score (representing the inflammatory component) and baseline mTSS erosion (r = 0.5949, p = 0.0035). [Conclusions] We did not show a direct correlation between the progression of bone destruction and the progression of ILD in RA patients treated with JAK inhibitors or CTLA4-Ig. Nonetheless, a notable association was found between the baseline CT score and baseline mTSS erosion, suggesting the importance of addressing inflammation in the assessment and management of RA-associated lung and joint pathologies.

## ICW17-2

**Comparing the impact on renal function in rheumatoid arthritis patients using JAK inhibitors versus those utilizing TNF inhibitors**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) has been linked to various kidney disorders due to chronic inflammation and exposure to nephrotic agents. The prevalence of chronic kidney disease among RA patients is higher than that of the general population. Previous reports suggested that RA patients with bDMARDs have a reduced risk of chronic kidney disease. Nevertheless, no prior studies have compared the impact on renal function between RA patients receiving JAK inhibitors and those with TNF inhibitors in a real-world setting. [Methods] We enrolled 120 RA patients treated with JAK inhibitors (tofacitinib (n=51) or baricitinib (n=69)), as well as 98 those treated with TNF inhibitors (adalimumab (n=48) or etanercept (n=50)), all of whom had continued their b/ts

DMARDs for a minimum of six months. We calculated the reduction in eGFR over one year and compare this between the two treatment groups. We also investigated factors associated with a decrease in the eGFR using multivariable logistic regression analyses. [Results] The reduction in the eGFR was 3.65 in RA patients treated with JAK inhibitors and 2.87 in those treated with TNF inhibitors (p=0.71). Multivariable logistic regression analyses revealed that older age and a lower baseline eGFR were the independent risk factors, while a longer drug duration was an independent favorable factor. [Conclusions] We observed no significant differences in the reduction of eGFR between RA patients with JAK inhibitors and TNF inhibitors. It is important to be exercise caution regarding declining renal function in older patients or those with a low baseline eGFR. However, maintaining a stable state with b/ts DMARDs can be protective for renal function.

## ICW17-3

**Switch to biological DMARDs vs. other JAK inhibitors in patients with rheumatoid arthritis and with inadequately response to JAK inhibitors: from FIRST registry**

Yusuke Miyazaki[1], Shingo Nakayamada[1], Koshiro Sonomoto[2], Hiroaki Tanaka[1], Kentao Hanami[1], Shunsuke Fukuyo[1], Satoshi Kubo[3], Ippei Miyagawa[1], Ayako Yamaguchi[4], Yasuyuki Todoroki[3], Yoshino Inoue[1], Yurie Satoh Kanda[1], Masanobu Ueno[1], Yoshiya Tanaka[1]

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Conflict of interest: None

**Objectives**: This study aimed to identify the characteristics of rheumatoid arthritis (RA) patients with inadequate response to JAK inhibitors (JAKinibs-IR) and to determine which bDMARDs or tsDMRADs are appropriate for these patients. **Methods**: The study included patients with RA who initiated JAKinibs treatment (n=434) in the FIRST registry. The efficacy and safety of switched bDMARDs or tsDMARDs were analyzed 26 weeks after switching treatment in JAKinibs-IR patients. **Results**: Patients with JAKinibs-IR RA accounted for 31.8% among those treated with JAKinibs. Multiple logistic regression analysis of characteristics contributing to JAKinibs-IR identified the following factors: a larger number of prior bDMARDs use, more patients who could not receive JAKinibs at optimal doses, and higher HAQ-DI. When RA patients with JAKinibs-IR who switched to another JAKinibs (n=31) were compared with those who switched to bDMARDs (n=45), there were no differences in patient characteristics between the groups. In patients who switched to another JAKinibs, the CDAI was lower at week 26 (p=0.02), and the CDAI-remission rate was higher (p<0.01) than those switched to bDMARDs. No differences were observed in the retention rate and the rate of adverse events between two groups. Based on the growth mixture modeling, the trajectories of the CDAI in RA patients with JAKinibs-IR were divided into three groups. Among them, the group in which disease activity promptly improved after drug switching and remained improved until week 26 (treatment response group) included numerous patients who switched to another JAKinibs (p<0.01). The multiple logistic regression analysis of the patient characteristics in the treatment response group identified switching to another JAKinibs as the only factor contributing to the treatment response. **Conclusions**: This study indicates that switching to another JAKinibs was appropriate for RA patients with JAKinibs-IR.

## ICW17-4

**Factors associated with drug retention of biologics and Janus kinase inhibitors in patients with difficult-to-treat rheumatoid arthritis: the ANSWER cohort study**

Ryu Watanabe[1], Kosuke Ebina[2], Takaho Gon[1], Tadashi Okano[3], Koichi Murata[4], Kosaku Murakami[5], Yuichi Maeda[6], Sadao Jinno[7], Iku Shirasugi[7], Yonsu Son[8], Hideki Amuro[8], Masaki Katayama[9], Ryota Hara[10], Kenichiro Hata[11], Ayaka Yoshikawa[11], Wataru Yamamoto[12], Masao Katsushima[1], Kazuo Fukumoto[1], Shinsuke Yamada[1], Motomu Hashimoto[1]

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Conflict of interest: Yes

[Objective] Difficult-to-treat rheumatoid arthritis (D2T RA) is defined as RA in which disease activity is uncontrolled despite the use of ≧2 biologics or Janus kinase inhibitors (JAKi) with different mechanisms of action (MOA). In this study, we aimed to assess the drug retention of biologics and JAKi in patients with D2T RA, and to clarify the factors associated with their retention in a real-world cohort. [Methods] This multicenter retrospective study included 6666 treatment courses (TCs), of which 826 TCs were D2T RA (TNFi=310, aIL-6R=194, CTLA4-Ig=147, and JAKi=175). D2T RA was defined clinical disease activity index (CDAI) >10, DAS28-ESR>3.2, or prednisolone≧7.5 mg despite the use of ≧2 biologics or JAKi with different MOA. Multiple imputations by chained equations were performed for disease duration and baseline disease activity. The reasons for discontinuation were divided into four categories (ineffectiveness, toxic adverse events, non-toxic reasons, and remission). Multivariate Cox proportional hazards modeling by potential confounders was used to analyze the HRs of treatment discontinuation. [Results] aIL-6R (HR=0.53, 95% CI: 0.37 to 0.75) and JAKi (HR=0.64, 95% CI: 0.46 to 0.90) showed a lower discontinuation rate due to ineffectiveness than TNFi. Improvement of disease activities evaluated by CDAI was comparable across four groups (P>0.05). Multivariate analysis demonstrated that discontinuation due to ineffectiveness was associated with prior use of aIL-6R (HR: 1.49, 95%CI: 1.01 to 2.19, P=0.04), but inversely associated with current use of aIL-6R (HR: 0.53, 95%CI: 0.37 to 0.75, P<0.001) and JAKi (HR: 0.64, 95%CI: 0.46 to 0.90, P=0.01). Concomitant use of oral glucocorticoids at baseline was associated with higher discontinuation rate due to toxic adverse events (HR: 1.65, 95%CI: 1.11 to 2.47, P=0.01). [Conclusions] In patients with D2T RA, aIL-6R and JAKi showed a lower discontinuation rate due to ineffectiveness than TNFi.

## ICW18-1

**Clinical heterogeneity and prognostic factors of anti-synthetase syndrome: a multi-centered retrospective cohort study**

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Conflict of interest: None

[Objective] Anti-synthetase syndrome (ASyS) patients have heterogeneous clinical manifestations with different initial presentations, complications, and outcomes. This study aimed to assess the clinical characteristics and complications in patients with ASyS, and to identify factors that were associated with the survival of ASyS patients. [Methods] This was a retrospective multicenter longitudinal study. Patients fulfilling either the Connor's criteria or Solomon's criteria for ASyS were recruited. Electronic health records were reviewed until October 2022. Multivariate Cox-regression analysis was used to determine the independent prognostic factors. Auto-antibodies were checked by commercial immunoassays. [Results] A total of 205 patients (anti-Jo-1 49.3%, anti-PL-7 19.0%, anti-EJ 11.2%, anti-PL-12 10.2% and anti-OJ 3.4%) were included. The median follow-up time was 4 years. The time from symptoms onset to diag-

nosis was significantly longer for non-anti-Jo1 patients (median 5 vs 3 months). Common initial presentations included myositis (56.1%), arthritis (54.6%), and interstitial lung disease (ILD) (54.1%). Patients with anti-Jo-1 had significantly higher muscle enzyme levels and more arthritis. All patients with anti-EJ would develop ILD on follow-up and malignancy was noted in 28.6% of the anti-OJ positive patients. 15.6% of the patients died and pulmonary diseases (ILD or pneumonia) were the major causes. Age at diagnosis, malignancy and rapidly progressive-ILD were independently associated with mortality, while joint manifestation was a protective factor. [Conclusions] In view of the heterogeneity of clinical presentation of ASyS, high index of suspicion and early checking of specific autoantibodies might help prompt diagnosis of ASyS and detection of related complications. Lung involvement is almost invariable and constitutes an important cause of death. Malignancy risk should not be overlooked in non-Jo-1 patients.

## ICW18-2

**Risk factors for rapidly progressive interstitial lung disease in dermatomyositis**

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Conflict of interest: None

[Objective] Rapidly progressive interstitial lung disease (RPILD) is a major cause of death in patients with dermatomyositis (DM). Although we have previously shown that myofascia-dominant involvement in whole-body (WB)-MRI is one of the risk factors for RPILD, MRI cannot be performed in severe patients. The objective of this study was to investigate the risk factors for RPILD in patients with DM. [Methods] This single-center retrospective observational study comprised 98 patients with DM who visited our hospital from 2010 to 2022. RPILD was defined as worsening of dyspnea, hypoxemia and radiographic ILD/fibrosis within 3 months after the onset of respiratory symptoms. WB-MRI was performed in 41 patients and muscular and myofascial signals were scored on 42 muscular groups. The myofascia/muscle ratio was calculated and used to define the relevance of myofascia-dominant involvement. To investigate the alternative risk factors instead of myofascia/muscle ratio, correlations between the ratio and the results of laboratory examinations were assessed using Spearman's rank order correlation coefficient (r). Multivariate logistic regression analysis was performed to identify the risk factors for RPILD. [Results] Among the 98 patients, 26 were diagnosed with RPILD. Anti-melanoma differentiation-associated gene 5 (MDA5) and anti-aminoacyl tRNA synthetase antibodies were detected in 30 and 20 patients respectively. Aldolase creatinine ratio (Ald/CK) correlated with the myofascia/muscle ratio (r=0.55, p=0.003) and anti-MDA5 antibody titer (r=0.55, p<0.001). Multivariate logistic regression analysis showed Ald/CK (p=0.02), KL-6 (p=0.04) and CRP (p=0.002) were identified as independent risk factors for RPILD. Based on the ROC curve, Ald/CK≧0.04, KL-6≧400 U/mL, and CRP≧1.7 mg/dl were considered the best cutoffs for predicting RPILD. [Conclusions] High Ald/CK ratio indicated myofascia-dominant involvement in WB-MRI. Ald/CK, KL-6 and CRP were independent risk factors for RPILD.

## ICW18-3

**Predictive factors for non-responsiveness to triple therapy in anti-MDA5 antibody-positive dermatomyositis-associated interstitial lung disease**

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Conflict of interest: None

[Objective] The aim of this study is to investigate the early predictive factors for the response to triple therapy with cyclophosphamide, tacrolimus, and prednisolone in patients with interstitial lung disease (ILD) complicated with anti-MDA5 antibody-positive dermatomyositis. [Methods] We retrospectively reviewed consecutive patients with ILD with anti-MDA5 antibody-positive DM who visited our institution from 2012 to 2023. We defined non-response as requirement of additional therapy including steroid-pulse, immunosuppressants and/or plasma exchange. We compared the clinical characteristics at diagnosis and thereafter ever week. [Results] We included 22 patients, with a median age of 51.5 years. Eleven patients were responder (50%), while 11 patients were non-responder (50% with five patients deceased). The median time to treatment intensification was one week for the non-survivors, and four weeks for the survivors in the non-responder group. The baseline characteristics of non-responder were older and had significantly higher CRP levels compared to the responders. Throughout the course, no significant difference was found in the anti-MDA5 titers and KL-6 levels between the two groups. However, in the non-responder group, LDH and ferritin levels were significantly elevated one and three weeks after treatment initiation, respectively. The predictive cutoff value of baseline CRP levels, LDH at one week, and ferritin at three weeks for non-responsiveness were 1.07 mg/dL, 237 U/L, 869 ng/mL respectively. Although there were no significant differences between non-survivors and survivors in age, KL-6, MDA5, LDH and ferritin levels, CRP level was significantly higher in non-survivors one week after treatment (0.72 vs 0.02 mg/dL, p=0.04). [Conclusions] Our study suggests that persistent elevation of CRP, LDH and ferritin levels after treatment predict non-responsiveness to triple therapy in ILD complicated with anti-MDA5 antibody-positive DM.

## ICW18-4

**Clinical characteristics of relapses in patients with idiopathic inflammatory myopathy-associated interstitial lung disease**

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) is a common extra-muscular manifestation in idiopathic inflammatory myopathies (IIM), and relapse of ILD results in deterioration of pulmonary function. Since the study of recurrence in IIM-associated ILD (IIM-ILD) is limited, we examined the clinical features of relapses of IIM-ILD. [Methods] IIM-ILD patients in a single center were retrospectively examined. IIM were defined based on Bohan and Peter criteria or 2017 ACR/EULAR classification criteria. We referred "relapse" as recurrence of IIM-ILD, which was defined as exacerbation of interstitial pulmonary findings with increasing glucocorticoid dose. Progressive fibrosing ILD (PF-ILD) was characterized by ≧ 10% reduction in FVC after treatment, or ≧ 5% reduction in FVC with ≧ 15% reduction in %DLCO, or ≧ 5% reduction in FVC with progressive fibrosis on CT. [Results] Among the 86 IIM-ILD patients, 21 (24.4%) experienced relapse, and median relapse free period was 36 [18.5-119.5] months. Between the relapse and non-relapse groups, the frequency of PF-ILD was higher in the relapse group (38.1% vs 7.7%, p=0.0022). In addition, patients treated without IVCY in remission induction were more likely to have relapse of ILD compared with patients treated with IVCY (35.2% vs 7.14%, p=0.0043). Also, the frequency of relapse was higher in patients treated with GC alone than patients with GC and any immunosuppressive agents in maintenance therapy (47.4% vs 20.7%, p=0.027). Although there was no significant difference, anti-ARS antibody prevalence tended to be higher in the relapse group (76.2% vs 53.9%, p=0.058). Compared with the non-relapse group, there were no significant differences in the type of IIM, RP-ILD, FVC, and %DLCO. [Conclusions] Our study indicated that recurrence of IIM-ILD was associated with treatment regimen both in induction and maintenance therapy. Further analysis of immunological status in IIM-ILD patients might stratify patients to predict the recurrence.

## ICW18-5

**Prognostic Biomarkers and Radiological Features of Idiopathic Inflammatory Myopathy Associated Interstitial Lung Disease**

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Conflict of interest: None

[Objective] This study aimed to identify the radiological features and specific biomarkers for predicting the short-term prognosis of Idiopathic inflammatory myopathy (IIM)-associated interstitial lung disease (ILD). [Methods] We enrolled 123 patients with IIM-associated ILD, in either rapidly progressive ILD (RPILD) (n = 59) or non-RPILD (n = 64), who had visited Nagasaki University Hospital between 2007 and 2022. The high-resolution CT (HRCT) patterns of ILD, which included DAD, NSIP, NSIP with OP, OP and UIP pattern, were classified by the experienced pulmonologist. Serum levels of 43 cytokines/chemokines were measured by a multi-suspension cytokine array. These serum variables were ranked by their importance by a multivariate classification algorithm termed random forest analysis (RFA). [Results] Within the RPILD group, the HRCT patterns were categorized as follows: NSIP (44.1%), NSIP with OP (23.7%), OP (20.3%), DAD (8.5%), and other (3.4%) patterns. We found the most important cytokine/chemokine for predicting one-year mortality in the RPILD patients was Platelet-derived Growth Factor-AA (PDGF-AA) using RFA. The levels of PDGF-AA were significantly lower in the RPILD patients with non-survivors than in those with survivors. Among the patients with anti-MDA5 antibody, the HRCT patterns were classified as NSIP (43.3%), NSIP with OP (33.3%), OP (16.7%), and DAD (6.7%) patterns. The RFA revealed C-C motif chemokine 22 (CCL22) was the most significant cytokine/chemokine for predicting one-year mortality in the patients with anti-MDA5 antibody. The CCL22 levels were significantly lower in the patients with non-survivors than in those with survivors. CCL22 was also the most significant cytokine to predict death within one year in the patients with anti-MDA5 positive RPILD. [Conclusions] This study identified a unique set of serum biomarkers that could predict the short-term prognosis of IIM-associated ILD and characteristic radiological features for each phenotype.

## ICW18-6

**Relapse rate after glucocorticoid-free remission in idiopathic inflammatory myopathies with validation of the International Myositis Assessment & Clinical Studies Group (IMACS) criteria for remission and relapse using the Swedish Rheumatology Quality Register (SRQ)**

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Conflict of interest: Yes

Objectives: Our aim was to explore whether maintenance of remission in patients with idiopathic inflammatory myopathy (IIM) depends on glucocorticoids (GCs) after achieving remission. We also examined the compatibility of IMACS criteria for remission and relapse in IIM. Methods: Data were from the Swedish Rheumatology Quality Register (SRQ). For compatibilities of the definition of IMACS-remission, we investigated whether changes in IMACS core sets were within 15% between 6 months before and after the physician's statements of remission/inactive. Relapse defined as either fulfilling IMACS criteria for relapse (within 20-30% changes in a month), or modified IMACS criteria (those from remission to a visit), or administration of GC/immunosuppression (IS) were compared. Relapse rate after GC-free remission and factors affecting relapses were explored. Results: From 566 patients, 169 patients were identified with GC-free remission. Variables that fulfilled IMACS-remission over 6 months before and after remission were CK (22%, 23%, respectively), MMT8 (89%, 95%), extramuscular data (76%, 83%), Pt-GA (56%, 70%), Ph-GA (64%, 81%), and HAQ (42%, 51%). After GC-free remission, relapses were observed in 70 of the 169 patients, up to 9.4 years, with a cumulative relapse rate of 77% over 14 years for the Kaplan-Meier curve. Relapses were as follows: IMACS-relapse, n=34 (49%); modified IMACS relapse, n=40 (57%); GC/IS administration, n=51 (73%). Characteristics in patients with IMACS/modified IMACS-relapse were worsened MMT8, extramuscular data, HAQ, Pt-GA, and Ph-GA. In contrast, Pt-GA worsened in patients with GC/IS defined relapse. Anti-Jo1 autoantibodies were shown as a risk factor for relapses by logistic regression analyses (odds ratio: 9.0, [95%CI: 1.4, 57.1]). Conclusion: Cumulative relapse rate was recorded in 77% up to 9.4 years. The criteria for remission and relapse in IMACS may need to be modified to fully capture disease flares.

## ICW19-1

**Immune phenotypes associated with clinical phenotypes of rheumatoid arthritis**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) can be classified into clinical phenotypes based on seropositivity, the presence of interstitial lung disease (ILD), and elderly onset or not. However, the specific pathophysiology of these clinical phenotypes remains unclear. This study aimed to elucidate the immune phenotypes associated with distinct clinical phenotypes in RA. [Methods] Treatment-naïve, active patients with RA (n=93) and healthy controls (HC, n=26) were included. A total of 34 immune cell subsets including T peripheral helper (Tph) and T follicular helper (Tfh) cells in peripheral blood were analyzed with flow cytometry. Composite measures such as simplified disease activity index were calculated to assess disease activity. [Results] Our comprehensive immunophenotyping identified that CCR5+Tph, CCR5+Tph1, CCR5+Tph2, TIGIT+Tfh, TIGIT+Tfh1, TIGIT+Tfh2, and TIGIT+Tfh17 were significantly increased in RA compared with HC. Among them, CCR5+Tph2 was positively correlated with disease activity indices. In the analysis based on clinical phenotypes, seropositive cases exhibited active acquired immune responses, reflected by a distinctive increase in naive Tfh and TIGIT+Tfh1 compared to seronegative cases. Conversely, seronegative cases showed an increase in Th17 compared to seropositive cases. Among cases with ILD, there was a characteristic increase in CCR5+Tfh, CCR5+Tfh1, CCR5+Tfh2, and CCR5+Tfh17, which possess the ability to migrate to sites of lung inflammation, when compared to non-ILD cases. Elderly-onset cases showed a characteristic increase in Th2 compared to non-elderly-onset cases. [Conclusions] Immune phenotypes associated with clinical phenotypes of RA were identified. The pathophysiology of RA may differ across clinical phenotypes.

## ICW19-2

**Profiles of serum cytokines and peripheral blood immunophenotyping of late-onset rheumatoid arthritis are distinct from those of young-onset rheumatoid arthritis**

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Conflict of interest: None

**Objective**: Patients with late-onset rheumatoid arthritis (LORA) have unique clinical characteristics compared to those of young-onset RA (YORA), but the difference in their pathogenesis is not understood. In this study, we aimed to elucidate cytokine profiles and immunological conditions of LORA. **Methods**: Consecutive newly diagnosed untreated patients with RA who consented to our research between 2015 and 2022 and healthy controls were enrolled. We reviewed clinical data and measured serum 64 cytokines or chemokines and 56 immune cell subsets in the peripheral blood. We compared them between patients with LORA and YORA, defined by the cut-off of 65 years old of RA diagnosis. **Results**: We enrolled 46 patients with LORA, 60 patients with YORA, and 14 healthy controls. Among 16 cytokines or chemokines that significantly overexpressed in patients with LORA ($p<0.05$), interleukin (IL)-1 receptor antagonist, IL-6, IL-8, IL-15, vascular endothelial growth factor-A, tumor necrosis factor receptor (TNFR)-1, and TNFR-2 were significantly positively correlated with disease activity score for 28 joints-erythrocyte sedimentation rate (DAS28-ESR) in patients with LORA ($p=0.01$, $p<0.001$, $p=0.005$, $p=0.007$, $p=0.002$, respectively). These cytokines were not associated with age. Immunophenotyping revealed the number of naïve CD4 cells, naïve CD8 cells, IgD+ memory B cells, and transitional B cells were significantly lower in patients with LORA than those with YORA ($p=0.005$, $p<0.001$, $p=0.006$, and $p=0.003$, respectively). Number of B cells lineages including CD19+ B cells, naïve B cells, memory B cells, and transitional B cells were significantly inversely correlated with DAS28-ESR ($p=0.03$, $p=0.01$, $p=0.03$, and $p=0.02$, respectively). **Conclusion**:

LORA has distinct unique cytokine and immune cells profiles from YORA. Overexpression of inflammatory cytokines and immunosenescence, especially decrease in B cells lineages may be associated with its unique characteristics.

## ICW19-3

**Evaluation and prediction of difficult-to-treat rheumatoid arthritis by immunophenotyping**

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Conflict of interest: None

**Objective:** Molecular targeted therapies have improved clinical outcomes of rheumatoid arthritis (RA), but not a few patients are refractory to the treatments and referred to as having difficult-to-treat (D2T) RA. In this study, we aimed to stratify RA patients and predict clinical outcome by immunophenotyping. **Methods:** D2T were defined as failure of more than two different mechanisms of action biologic or targeted DMARDs. Multi-color flow cytometric analysis of PBMC isolated from the enrolled patients to evaluate subpopulation of $CD4^+$ T, $CD8^+$ T, B, dendritic cells (DCs), monocytes, and natural killer cells was conducted. After evaluating immunophenotyping, prospective observational cohort of the enrolled patients with adding or switching DMARDs was conducted to evaluate therapeutic response. **Results:** Total 28 patients including 7 treatment-naïve, 17 DMARDs-resistant, and 4 D2T RA were enrolled. Immune cell profiling of PBMC from the three group was significantly different in proportions of effector memory (EM) $CD8^+$ T cells, naïve B cells, and myeloid DCs, although age, sex, serological status and disease activity were equivalent. Analysis of the prospective observational cohort showed that 7 were defined as D2T RA and 21 were responsive to adding or switching DMARDs without D2T state. Compared with immune cells from non-D2T RA patients, proportion of terminally differentiated EM $CD8^+$ T cells were decreased (11.7% and 21.8% in $CD3^+CD4^-CD8^+$, $p = 0.047$) and proportion of EM $CD8^+$ T cells and myeloid DCs were increased (27.4% and 16.3% in $CD3^+CD4^-CD8^+$, $p = 0.048$; 51.2% and 38.6% in $CD3^-CD19^-HLA\text{-}DR^+CD56^-CD14^-CD16^-$, $p = 0.048$) in immune cells from D2T RA patients. **Conclusion:** This is the first study to evaluate the immune cell profiling of D2T RA patients and reveal that evaluation of EM $CD8^+$ T cells and myeloid DCs predicted treatment responses. Immunophenotypic stratification might contribute to the management of RA for better clinical outcomes.

## ICW19-4

**Circulatory Age-Associated B Cell and its Clinical Significance in Patients with Rheumatoid Arthritis**

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Conflict of interest: None

**Objectives**: This study aimed to investigate the transcriptomic profiles and clinical significance of age-associated B cells (ABCs), a pathological cell subset not fully understood in rheumatoid arthritis (RA). **Methods**: We performed single-cell RNA sequencing analysis in the peripheral blood mononuclear cells (PBMCs) of patients with RA and healthy controls (HCs), for identifying and characterizing ABCs. We used flow cytometry to assess the frequency of ABCs, defined as $CD19^+$ $CD11c^+$ cells, in PBMCs from 17 HCs and 56 patients with early RA, before and/or 3 to 6 months after treatment with anti-rheumatic drugs; these results were compared with the clinical characteristics of RA patients. **Results**: Sub-clustering through B cell extraction enabled the identification of nine B cell populations, including ABCs. Pseudotime analysis revealed that, compared with B cells in HCs, B cells in patients with RA were distributed at a later stage in the trajectory from naïve B cells to ABCs. The expression of ABCs was highly correlated with innate immune-related pathways, including antigen presentation, phagosome, and Fcγ receptor-mediated phagocytosis. Network analysis indicated that SYK was a key regulator of such pathways. Flow cytometry analysis validated that SYK was upregulated in ABCs; in addition, the proportion of ABCs was expanded in RA patients, particularly in drug naïve RA patients, compared to that in HCs. ABCs were substantially reduced following treatment with anti-rheumatic drugs, as observed through serial monitoring using flow cytometry. The frequency of ABCs was positively correlated with the levels of RA activity markers, such as $DAS_{28}$, ESR, CRP, and serum IL-6 levels. Notably, the cut-off of 1.5% or more ABCs could discriminate the presence of RA with 94.1% specificity. **Conclusion**: This study elucidated the innate immune features of ABCs regulated by SYK in RA patients. ABCs were highly relevant to active RA, and they hold potential as a biomarker in RA patients.

## ICW19-5

**Immunophenotypic stratification of rheumatoid arthritis underscores the potential of precision medicine**

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Conflict of interest: Yes

[Objective] To advance precision medicine in rheumatoid arthritis (RA), we stratified RA patients by immunophenotyping [Methods] 533 treatment-naïve RA patients and 96 healthy controls (HC) underwent immune cell profiling via flow cytometry. Inverse probability weighting with propensity score adjusted patient clinical backgrounds for treatment response. Validation was conducted with an additional cohort of 183 RA patients. [Results] Cluster analysis stratified 533 patients into 5 clusters. 2 of these showed distinctive RA phenotypes differing HC, marked by significant increases in CD4 effector memory T cells re-expressing CD45RA (TEMRA). TCR repertoire analysis indicated CD4 TEMRA as an oligoclonal expanded and autoreactive population. Notably, the clinical effectiveness of each targeted therapy (b/tsDMARDs) varied significantly among the different clusters. In each cluster, we designated the group using promising b/tsDMARDs as "preferred," while the "non-preferred" included those using other b/tsDMARDs. The preferred group outperformed the non-preferred group, with significantly higher 24-week remission rates (38.6% vs. 24.7%, $p<0.01$) and low disease activity achievement (79.7% vs. 60.8%, $p<0.01$). Trajectory analysis showed the non-preferred group's 24-week disease activity was influenced by CDAI at baseline, unlike the preferred group, where both high and low pre-treatment disease activity cases exhibited a significant CDAI reduction after 24 weeks. To validate, immunophenotyping was conducted in a new cohort of 183 bio-naïve patients, then redistributed into the existing clusters using the k-nearest neighbor method. When 183 cases were grouped based on their DMARD usage into preferred/non-preferred groups, the preferred group had over twice the 24-week remission rate ($p=0.02$), further confirming the observed trend. [Conclusions] Immunophenotypic stratification underscores the significance of CD4 TEMRA in the pathogenesis of RA and the potential of precision medicine.

## ICW20-1

**Incidence of Rheumatoid Arthritis in HIV-Infected Patients**

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Conflict of interest: None

[Objective] To assess the incidence of rheumatoid arthritis (RA) in patients with HIV, who are on Antiretroviral Therapy (ART) in these immunosuppressed patients. [Methods] Patients included in this study were HIV-infected patients from the ART centers. All the eligible patients who were ready to give written consent were included in the research. For the Rheumatoid Arthritis investigation, serum samples were collected and tested for rheumatoid factor (RF) by Mispa i2, which was based on the turbidity principle. Baseline demographic variables, history including duration of antiretroviral therapy (ART), joints involved, and CD4 cell count were evaluated. All the data were analyzed by SPSS and a P value less than 0.05 was considered significant. [Results] This cross-sectional study included 150 patients with HIV infections. Of the 150 individuals in the study who were reviewed for a diagnosis of RA based on the data collected. The incidence rate of RA was found to be 23.3% (35 of 150) of HIV patients. In multivariable analysis, these levels were found higher in the 20-40 years age group, in females, in married, in illiterate, and unknown about their transmission of HIV. The incidence rate of Rheumatoid arthritis was found to be 23.3%. Similarly, the association of sex and other variables' significant value was found in education, mode of transmission, and age category as 0.05, 0.001, and 0.002 respectively. [Conclusions] The incidence rate of RA was higher in patients with HIV. The result of our research suggests the need for regular screening of Rheumatoid factor (Rf) to reduce mortality and pain full life of HIV-infected individuals due to rheumatoid arthritis.

## ICW20-2

**Rheumatic manifestations among HIV-positive attending the ART Centers**

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Conflict of interest: Yes

*[Objective]* Rheumatic manifestations are a common issue in HIV patients. Disease spectrum mainly depends on factors like CD4 count, and Antiretroviral therapy (ART). This study included HIV patients from ART centers and was designed to determine the prevalence and clinical pattern of rheumatic manifestations. *[Methods]* 300 HIV-positive patients were consecutively recruited into the study, evaluated for rheumatic manifestations, and their clinical and laboratory findings by Rheumatoid factor (RF) by Mispa i2 which is based on the turbidity principle. Age, sex, family history, education level, mode of transmission, and CD4 count were recorded. The Ethical Review Committee approved the study, and written consent was obtained from the research participants. All the results and data obtained from the study were entered in SPSS and analysis was done for the association and chi-square was done. *[Results]* The prevalence of rheumatic manifestations was 24% (72 of 300) and was detected by the rheumatoid factor by turbidity technique. The lower limbs were the most commonly affected with the knees (22.6%) and ankles (19.2%) contributing the highest. In multivariable analysis, these levels were found higher in the 20-40 years age group, in females, in married, and in illiterate. Similarly, the significant association value was found in education, and age categories as 0.004, and 0.001 respectively. *[Conclusions]* Our research suggests the need for regular screening of Rheumatoid factor (Rf) to determine arthritis in HIV-infected patients.

## ICW20-3

**Impact of the COVID-19 pandemic on management of inflammatory arthritis amongst adult outpatients - a tertiary care centre experience**

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Conflict of interest: None

Objectives The Sri Lankan state healthcare system serves a predominantly low-to-medium income population with diverse socio-economic backgrounds. It faced the greatest challenge in recent history during the Covid-19 pandemic during which on-site out-patient consultations ceased and medications were home-delivered. In this background, the study assessed how patients with inflammatory arthritis coped during the pandemic with a focus on its impact on disease monitoring and management. Methods This descriptive, cross-sectional study was conducted at the out-patient rheumatology clinics of the Kandy National Hospital, Sri Lanka. The study recruited 530 patients with inflammatory arthritis meeting inclusion criteria and data were collected over five months using an interviewer-administered multi-structured questionnaire. The questionnaire was aimed to assess medication adherence, healthcare access and disease monitoring. Associations between selected demographic factors and outcomes were verified with Pearson's chi square test. Results Participants were aged between 15 and 87 years (median 62). The majority (515, 97%) were diagnosed with rheumatoid arthritis. 325 (61.3%) patients had a monthly income less than 155 USD. The majority (443, 84%) had received at least three doses of the COVID-19 vaccine. 40 patients (7.6%) developed worrying symptoms due to poor disease control. Evaluation of the impact of the pandemic reveled that medication adherence was not affected across age (p-0.58), educational background (p-0.5) and monthly income (p-0.64). However, disease monitoring was adversely affected by the monthly income ($p<0.001$). Conclusion Home-delivery of medications in the study setting was shown to result in optimal medication adherence by patients with inflammatory arthritis. However, limitation of on-site routine blood testing during the pandemic was shown to adversely impact the optimal disease monitoring and this observation was noted significantly in low-income groups.

## ICW20-4

**Clinical characteristics of human T-cell leukemia virus type 1 (HTLV-1)-positive rheumatoid arthritis patients showing increased HTLV-1 proviral loads during antirheumatic therapies**

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Conflict of interest: None

[Objective] The aim of this study to investigate the clinical characteristics of human T-cell leukemia virus type 1 (HTLV-1) positive RA patients showing increased HTLV-1 proviral load (PVL) during antirheumatic therapy. [Methods] Among 61 participants registered in the Miyazaki HTLV-1-positive RA Registry, 56 patients whose HTLV-1 PVLs were measured at least twice during the observation period from 2019 to 2022 were enrolled in this study. Increased HTLV-1 PVL was defined as more than 1.0 copies/100PBMCs. These patients were divided into increased group and non-increased group. Clinical characteristics including RA disease activity and treatment details were compared between the two groups. Furthermore, the population of HTLV-1 infected cells analyzed by flow cytometry (HAS-Flow) was compared between the two groups. [Results] Among 56 patients, 17 and 39 patients were divided into the increased group and the non-increased group, respectively. In 2019, there were no differences in age and disease duration between the two groups. However, both DAS28 and SDAI values were higher in the non-increased group than in the increased group (2.65 v. s 1.92, p= 0.01. 5.77 v. s 1.52, p= 0.03, respectively). The population of users of glucocorticoid, methotrexate, tacrolimus, and biological agent/JAK inhibitor tended to be higher in the increased group than in the non-increased group (41.2% vs 38.5%, 52.9% vs 43.6%, 35.3% vs 28.2%, 41.2% vs 28.2%, respectively). The HAS-Flow analysis revealed the population of HTLV-1-infected cells (CD4+ CADM1+) and ATL-like cells (CD4+ CD7- CADM1+) was higher in the increased group (21.3% vs 14.7%, p=0.01, 6.1% vs 2.9%, $p<0.001$). There were no patients who developed ATL during the observation period of this study. [Conclusion] HTLV-1-positive RA patients who showed increased HTLV-1 PVL during anti rheumatic therapy may be at risk for developing ATL. Further research is needed to elucidate what types of antirheumatic treatments affects ATL development.

## ICW21-1

**The maintenance dose of glucocorticoid in the management of systemic lupus erythematosus**

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Conflict of interest: None

[Objective] The current "treat-to-target (T2T)" strategy concept has been applied to systemic lupus erythematosus (SLE), stating "lupus maintenance treatment should aim for the lowest glucocorticoid (GC) dosage, and if possible, GC should be withdrawn completely". We have already reported the importance of the trade-off between immunosuppressive agents (ISA) and GC in the prevention of SLE flare. Here we evaluated the most recent SLE treatment status with focusing on the maintenance dose of GC and the use of ISA. [Methods] We enrolled Japanese SLE patients who currently visited our medical center (121 patients). All the patients met the American College of Rheumatology (ACR) 1997 or 2012 revised criteria for SLE classification, and were followed-up > 6 months after diagnosis. We examined retrospectively patient backgrounds, the dose of GC, and the use of ISA from the medical records. [Results] Currently 94% of patients achieved GC dosage of 5 mg/day (prednisolone equivalent) or less and the median GC dosage was 2 mg/day. In addition, 48 (40%) patients were successfully managed without GC, either discontinued or not being initiated, but with hydroxychloroquine (HCQ) and/or ISA. The users of HCQ, ISA, and biologics were 63%, 68%, and 7%. respectively. Among ISA, mycophenolate mofetil (38%) and tacrolimus (35%) were commonly used, including their combination use (16%). [Conclusions] The GC dosage in SLE maintenance therapy is successfully decreasing and GC-free management is becoming a realistic goal with the aggressive use of HCQ, ISA, and biologics.

## ICW21-2

**The impact of shared decision-making on quality of life in SLE patients: Longitudinal evaluation in The TRUMP2-SLE project**

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Conflict of interest: None

[Objective] Shared decision-making (SDM) is essential in contemporary medical practice, and its significance extends to managing systemic lupus erythematosus (SLE). Although improving quality of life (QoL) is a crucial issue due to the need for long-term treatment, there are few reports on the relationship between SDM and QoL. In this study, we analyzed data from a multicenter Japanese SLE cohort to investigate the potential contribution of SDM to enhanced QoL. [Methods] We conducted a longitudinal study using data from the TRUMP²-SLE project, collected annually from June 2020 to August 2021, using medical records and questionnaires. The SDM-Q-9 and LupusPRO were used to measure SDM and QOL, respectively. Patients were divided into high and low SDM groups based on median baseline value, and changes in LupusPRO over the subsequent year were compared using a general linear model. Covariates were age, gender, disease duration, SLEDAI, SDI, prednisolone dose, immunosuppressants, hydroxychloroquine, income, marriage, education, physician factors (age and gender), and baseline LupusPRO domains. Patients with missing outcome values were excluded, and missing values were complemented with multiple imputation. [Results] Data from 438 patients were included in the analysis (87.4% female, age 46.8±14.1 years). There were no significant differences in age or gender between the two groups. The high SDM group had a higher rate of concomitant immunosuppressive medications (74.9% vs. 65.2%, p = 0.033). Multiple regression analysis identified as an independent factor enhancing the overall non-health related QoL and the domain of coping and satisfaction with care (5.91 pts [95%CI 3.04-8.78], 6.04 pts [0.79-11.29], and 14.06 pts [6.93-21.19], respectively). [Conclusions] SDM may contribute to improved psychological or social quality of life.

## ICW21-3

**Antiplatelet Effects of Hydroxychloroquine in Patients with Systemic Lupus Erythematosus evaluated by Total Thrombus-formation Analysis System (T-TAS)**

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Conflict of interest: Yes

[Objective] Hydroxychloroquine (HCQ) has been shown to reduce thrombotic events in patients with systemic lupus erythematosus (SLE), but the mechanisms underlying its anti-thrombotic effect remain unclear. The Total Thrombus-formation Analysis System (T-TAS) allows analysis of platelet thrombus formation under flow condition by applying whole blood into collagen-coated capillaries and recording pressure waveforms until flow obstruction due to thrombus formation. This study aims to investigate the antiplatelet effects of HCQ in SLE patients using T-TAS. [Methods] This is a single-center cross-sectional study. This study included 45 SLE patients who met the following criteria: platelet count >130,000 /μL, hematocrit between 25% and 50%. We measured PL-$AUC_{10}$ (area under the pressure curve for 10 minutes) using T-TAS and analyzed its association with HCQ use. Additionally, HCQ was added to whole blood from seven healthy individuals at concentrations of 0, 1, and 10 μg/mL, and PL-$AUC_{10}$ was measured. [Results] The median age was 45 years (IQR 39-55), with 37 females, and a median disease duration of 9 years (4-21). No significant difference in PL-$AUC_{10}$ was found between HCQ non-users (n=12) and HCQ users (n=33) (378 vs 359, p=0.34). However, analysis using real body weight (RBW) showed that HCQ/RBW ≧5 mg/kg group (n=14) had significantly lower PL-$AUC_{10}$ than <5 mg/kg group (n=19) (283 vs 391, p = 0.007). A negative correlation was observed between HCQ/RBW and PL-$AUC_{10}$ (rs=-0.35, p = 0.046). Analysis using ideal body weight showed similar results. Furthermore, as HCQ concentration increased in whole blood from healthy individuals, PL-$AUC_{10}$ decreased. [Conclusions] We demonstrated, for the first time, the concentration-dependent antiplatelet effects of HCQ under conditions simulating the physiological environment by using T-TAS. These findings would provide supporting evidence for the thromboprotective effects of HCQ in SLE patients.

## ICW21-4

**Clinical features and quality of life in Japanese male patients with SLE: a cross-sectional study using LUNA registry**

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Conflict of interest: None

Objective: There are gender differences in SLE incidence, the majority of SLE patients are female (only 10% of SLE patients are male). The knowledge of clinical features and quality of life (QOL) in male SLE patients was still limited in Japan. This study aimed to investigate specific clinical features and patient-reported outcome (PRO) in male SLE patients compared to females. Methods: This study was a retrospective, cross-sectional cohort study. We investigated clinical features and PROs using a nationwide registry of SLE patients (LUpus registry of NAtionwide institutions: LUNA) in Japan. The data of clinical features, treatment, complications and PROs using Lupus PRO questionnaire were collected and compared between male SLE and female SLE patients. For statistical analysis, the Mann-Whitney U test or Fisher's exact test (categorical data) were used. The significance level was set at $p < 0.05$. Results: Among 1776 patients in the LUNA registry, 1273 patients who had adequate data of health-related quality of life questionnaire (Lupus PRO) were included. The number of male SLE patients were 156 (12.7%) and female SLE patients were 1117. Male SLE patients had higher smoking habits, alcohol intake and status of marriage. General clinical features were similar between male and female SLE patients, however, male SLE showed significantly lower SLEDAI ($p < 0.01$) and higher SDI ($p < 0.02$) values than female SLE. Male SLE patients also had higher cardiovascular events (10.9% vs 5.4%, respectively, $p < 0.01$). Lupus PRO data showed that male SLE patients had significantly lower procreation scores and higher pain-vitality and body image domain scores. Stress coping and support systems were relatively lower than previous studies. Conclusions: Japanese male SLE patients had higher SDI and cardiovascular events. The difference in Lupus PRO scoring sheds light on the gender difference of SLE patients and will help attending physicians to understand the status of male SLE patients.

## ICW22-1

**Immunophenotyping profiles of peripheral B cells in anti-Jo-1 antibody positive idiopathic inflammatory myopathies**

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Conflict of interest: None

[Objective] B cell are likely to play an important role in pathogenesis in anti-Jo-1 antibody positive idiopathic inflammatory myopathies (IIM), however there were few reports about detailed immunophenotyping of B cell in anti-Jo-1 antibody positive IIM. The aim of this study was to understand immunological phenotyping profiles of peripheral B cells from the patients with anti-Jo-1 antibody positive IIM by spectral flowcytometry. [Methods] The enriched B cells from peripheral blood mononuclear cells from 12 patients with anti-Jo-1 antibodies-positive IIM and healthy donors were analyzed on spectral flowcytometry with a 24-marker panel. The dimensionality reduction and clustering analysis were applied to pre-gated CD19+ B cells. [Results] The most common subpopulation was CD27-IgD+ naïve B cells in both the patients with IIM and healthy donors. The expression of CD73, a key enzyme that converts ATP to adenosine, is significantly lower on B cells in patients with IIM compared to healthy donors, which was found in CD27-IgD+ naïve B cells and CD27-IgD-Bcells. Next, Compared the abundances of the metaclusters obtained by clustering analysis, CD73-naïve B cell cluster was increased in the patients with IIM compared to healthy donors. This cluster contained B cells expressing CD45RB, which supposed antigen-experienced B cells. Examined CD73 and CD45RB expression on naïve B cells, CD73-CD45RB+naïve B cells were significantly increased in the patients with IIM. [Conclusions] In anti-Jo-1 antibody positive IIM, activated naïve B cells were increased. Low CD73 expression on peripheral B cells might lead to hyperactivation of B cells through ATP/adenosine pathway in pathogenesis of anti-Jo-1 antibody positive IIM.

## ICW22-2

**Type I interferon may play an essential role in murine melanoma differentiation associated gene 5 induced lung fibrosis model**

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Conflict of interest: None

[Objective] Anti-melanoma differentiation associated gene 5 (MDA5) antibody-positive dermatomyositis is frequently complicated with rapidly progressive interstitial lung disease (RP-ILD), resulting in the high mortality rate in the acute phase. We have established a murine model mimicking anti-MDA5 antibody-positive RP-ILD induced by immunization of MDA5 protein. To clarify the expression level of the factors which were previously reported to related to anti-MDA5 antibody positive RP-ILD, we performed transcriptome analysis of the lung samples from the murine model. [Methods] Recombinant murine MDA5 protein concomitant with complete Freund's adjuvant was injected intradermally to 6-8 weeks-old female wild type (WT) mice and interferon-alpha receptor 1 (IFNAR1) null mice once a week for 4 times. Polyinosinic-polycytidylic acid sodium salt was intranasally administrated to the mice at the same time as the 4th immunization. RNA-sequencing analysis was performed with RNAs collected from the lung samples of WT mice 1 day (day 1) and 14 days (day 14) after the 4th immunization. Differential expressed genes (DEGs), which were considered as the genes of false discovery rate <0.05 compared with control mice, were analyzed by Metascape. [Results] On the RNA-sequencing analysis, 510 and 264 upregulated DEGs were detected from the lungs at day 1 and day 14, respectively. Gene ontology enrichment analysis showed a strong association with inflammatory response (GO: 0006954) in the lungs at day 1, and with myofibril (GO: 0030016) and cellular response to interferon-beta (GO: 0035458) in the lungs at day 14. MDA5-immunized IFNAR-null mice rarely developed ILD features. [Conclusions] Prolonged inflammation including type I interferon signal-

ing plays key roles of the MDA5-induced ILD model, as same as the suspected factors in anti-MDA5 antibody-positive RP-ILD in human. Further analysis of this model may contribute to the exploration of the pathogenesis of anti-MDA5 antibody-positive RP-ILD.

## ICW22-3

**Pathogenicity of functionally activated PD-1+CD8+ cells and a protective role of muscular PD-L1 through IFN-gamma in myositis**

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Conflict of interest: None

[Objective] Programmed-cell-death 1 (PD-1) is associated with T-cell activation and exhaustion. Specifically, PD-1$^+$ T cells present an exhausted phenotype in conditions of chronic antigen exposure, such as tumor microenvironments and chronic viral infection. However, the immune status regarding exhaustion of PD-1$^+$CD8$^+$ T cells in chronic autoimmune diseases including idiopathic inflammatory myopathies (IIMs) remains unclear. We aimed to clarify the role of PD-1$^+$CD8$^+$ T cells and PD-1 ligand (PD-L1) in IIMs. [Methods] PD-1/PD-L1 expressions in the muscles and peripheral blood immunophenotyping of IIM patients were examined. C-protein-induced myositis (CIM), a model of polymyositis, was induced in wild-type (WT), *Cd274*$^{-/-}$, and *Ifng*$^{-/-}$ mice. Cytotoxicity by CD8$^+$ T cells against IFNγ-treated C2C12 myotubes was assessed with an established muscle injury model. [Results] PD-1$^+$ cells infiltrated the PD-L1$^+$ muscles in the patients. According to the immunophenotyping, the PD-1$^+$CD8$^+$ cell proportions were comparable between the active and inactive patients. Of note, PD-1$^+$CD8$^+$ cells in the active patients highly expressed cytolytic molecules, indicating their activation, while PD-1$^-$CD8$^+$ cells expressed low levels of these molecules in the active and inactive patients. A part of PD-1$^+$CD8$^+$ cells highly expressed the HMG-box transcription factor TOX and presented the exhausted phenotype in the active patients. *Cd274*$^{-/-}$ mice developed severer CIM with abundant PD-1$^+$CD8$^+$ cell infiltration than WT mice, indicating the pathogenicity of PD-1$^+$CD8$^+$ cells and the protective role of PD-L1. The deficiency of IFNγ, a general PD-L1-inducer, impaired muscular PD-L1 expression and exacerbated CIM, indicating the IFNγ-dependent PD-L1 regulation. IFNγ-induced PD-L1 on myotubes was protective in the muscle injury model. [Conclusions] PD-1$^+$CD8$^+$ T cells rather than PD-1$^-$CD8$^+$ T cells were a pathogenic subset in IIMs. Muscular PD-L1 was regulated by IFNγ and exerted protective properties in IIMs.

## ICW22-4

**The CX3CL1/CX3CR1 axis is associated with monocyte migration in anti-mealonoma differentiation-associated gene 5 antibody-positive dermatomyositis (MDA5-DM)**

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Conflict of interest: None

[Objectives] CX3CL1 and CX3CR1 are a chemokine and its corresponding receptor that play a significant role in infiltration of monocytes and other immune cells [RH1]. The CX3CL1/CX3CR1 axis is thought to be associated with the pathogenesis of polymyositis/dermatomyositis (PM/DM). However, its detailed differences among myositis subgroups have not been fully elucidated. We aimed to characterize the expression of CX3CL1/CX3CR1 in anti-melanoma differentiation-associated gene 5 antibody-positive DM [RH2] (MDA5-DM) patients, with a focus on monocyte/macrophage activation, and compare it to non-MDA5-PM/DM patients and healthy controls (HC). [Methods] Serum CX3CL1 levels were measured by ELISA (non-MDA5, n=46; MDA5-DM, n=42; HC, n=12). Flow cytometry of peripheral blood mononuclear cells for circulating monocytes was performed (anti-aminoacyl-tRNA synthetase syndrome (ASS), n=12; MDA5-DM, n=17; HC, n=8). Multiplex immunohistochemistry was used to analyze the expression of CD14, 16, 68, CX3CR1, and MxA in the skin (ASS, n=7; MDA5-DM, n=11; HC, n=6) and the lung (MDA5-DM, n=1; HC, n=1). In situ RNA hybridization was performed for CX3CL1 gene. [Results] Compared to controls, MDA5-DM patients showed a significant increase in circulating CD16+monocytes, CD16+CX-3CR1+ macrophages, and MxA+epidermal cells in the skin. Serum CX-3CL1 levels were significantly higher in MDA5-DM than in non-MDA5-PM/DM. Moreover, CX3CL1 levels remained significantly elevated during the first two months in refractory MDA5-DM patients despite a combination of immunosuppressive therapies. CX3CL1 mRNA expression in the epidermis tended to be higher in MDA5-DM than in ASS and HC. Alveolar epithelial cells in the lung tissue of MDA5-DM patients expressed CX3CL1 mRNA. [Conclusion] The primary source of IFN-inducible proteins appeared to be the epidermis and infiltrating macrophages. The epidermis and alveolar epithelial cells likely play an important role in recruiting macrophages through CX3CL1/CX3CR1 axis.

## ICW22-5

**Muscle Filtrating Monocytes as a Potential Pathogenesis in Myositis Revealed by Deconvolution Analysis**

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Conflict of interest: None

**[Objective]** To investigate the immunophenotype of muscle biopsies from patients with dermatomyositis (DM) and polymyositis (PM) using deconvolution analysis. **[Methods]** Bulk RNA-sequence was performed on muscle biopsies from patients with DM and PM (n=25). Cell proportions were estimated through a deconvolution approach, and Spearman correlation analyses were employed to investigate the relationships between cell proportions and clinical features. Gene set variation analysis (GSVA) was used to evaluate pathways and functions, and patients were stratified based on GSVA scores using hierarchical clustering. **[Results]** DM patients (n=16) demonstrated higher proportions of CD16 negative monocytes (CD16n Mono) (p=0.043), whereas PM patients had higher proportions of Th2 (p=0.049). Positive correlations were found between creatinine kinase (CK) and CD16n Mono (r=0.44, p=0.027), and CD16 positive monocytes (CD16p Mono) (r=0.60, p=0.002). The GSVA analysis showed elevated IFN α response and complement signatures in DM (p=0.010, 0.007, respectively), while increased oxidative phosphorylation (OXPHOS) and myogenesis in PM. Hierarchical clustering identified two distinct clusters: cluster 1, characterized by high OXPHOS pathways and high proportions of naïve CD4$^+$ T cells and Th1; and cluster 2, marked by high IFN pathways and high proportions of CD16n Mono and CD16p Mono, which showed notably higher CK (264.50 [45.67, 708.25] to 2000.00 [689.50, 4579.50], p=0.006) and aldolase levels (9.30 [5.90, 12.13] to 26.70 [17.85, 38.65], p=0.002). **[Conclusions]** This research underscores the pathologically significant role of monocytes in muscle damage, particularly in DM patients. Furthermore, it unveils associations between muscle injury and IFN and inflammatory pathways within muscle specimens.

## ICW23-1

**Comparison of anti-angiogenic effect of JAK inhibitor on co-culture of RA patient-derived synovial fibroblasts and human umbilical vein endothelial cells under IL-6 stimulation**

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Conflict of interest: None

[Objective] Angiogenesis is an important target in the treatment of rheumatoid arthritis (RA). Currently, five Janus kinase (JAK) inhibitors are approved for the RA treatment, and each inhibits JAKs with different selectivity, but the effects of these selectivity differences remain unclear. The purpose of this study was to compare the anti-angiogenic effects of five JAK inhibitors, Tofacitinib (TOF), Baricitinib (BAR), Peficitinib (PEF), Upadacitinib (UPA), and Filgotinib (FIL), on IL-6 stimulation of RA patient derived synovial fibroblasts (RA-FLS) and human umbilical vein endothelial cells (HUVEC) cocultures. [Methods] RA-FLS ($6x10^4$cells/well) were seeded on collagen gel and HUVEC ($3x10^4$ cells/well) were added directly. JAK inhibitors; TOF 0.3μM, BAR 0.3μM, PEF 1μM, UPA 0.3μM, and FIL 2μM were added to the medium after treatment with IL-6 (100 ng/ml) and sIL-6R (100 ng/ml). The dose of each JAK inhibitor was determined based on the estimated blood concentration. Tube formation assay was used to evaluate the vessel forming ability (total vessel length). Vascular endothelial growth factor (VEGF) concentration was evaluated by ELISA using the medium at the first exchange. Furthermore, in the migration assay, RA-FLS ($2x10^5$ cells/well) was stimulated with IL-6 and sIL-6R, and HUVEC ($1x10^5$ cells/well) was added into the upper chamber of transwell insert. After 24 hours, the number of HUVEC migrated downward from the insert was evaluated using CD31 fluorescent immunostaining. [Results] Tube formation and migration assays demonstrated each JAK inhibitor significantly suppressed vessel formation and HUVEC migration compared to the control medium. In addition, tube formation assay demonstrated the inhibitory effect of PEF was significantly higher than TOF. No significant difference was observed between JAK inhibitors in migration assay. [Conclusions] All JAK inhibitors significantly suppressed IL-6-stimulated angiogenesis, VEGF production, and migration in RA-FLS and HUVEC co-cultures.

## ICW23-3

**Novel upadacitinib-monotherapy provides the early clinical remission, PRO improvement, synovial amelioration of ultrasound findings and the inhibition of the bone destruction with resolving the current issue of polypharmacy**

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Conflict of interest: Yes

[Objective] To elucidate the early-phase MSKUS amelioration with clinical outcomes, PRO, the inhibition of the bone destruction and the contribution to polypharmacy under the treatment of UPA-MONO. [Methods] Thirty-seven patients with RA refractory to previous treatment of csDMARD, bDMARD and JAKi were included. All patients (n=37) switched to UPA-monotherapy except for glucocorticoids and NSAIDs. DAS28-CRP, CDAI, mHAQ and Patient's global VAS were evaluated as clinical parameter, and MSKUS examination scanned at 40 joints were assessed at baseline (BL), week 2,4,8 and 52. The decrease ratio of patient's number of medications was also calculated through week 8. The structure change from BL van der Heijde Modified Total Sharp Score (ΔmTSS) at week 52 was performed. [Results] BL characteristics of RA patients (n=37): Age: 66.0±2.0 y.o. (M: 7, F: 30), RA disease duration: 10.2±1.9yrs, ACPA positive: 81.1%, DAS28-CRP: 4.0±0.2, CDAI: 20.7±1.4, mHAQ: 0.6±0.13, PtVAS: 56.8±4.2 mm, Total GS scores (TGSs): 13.1±1.8, Total PD scores (TPDs): 11.3±2.3, bDMARD/JAKi-naïve: 45.9%, refractory to bDMARD/JAKi: 54.1%. DAS28-CRP remission rate (%) was 2.7, 61.1,86.1, 94.2 and 100.0 at BL, week2, 4, 8 and 52, respectively. CDAI: 20.7±1.4, 7.0±0.8*, 3.5±0.4*, 2.6±0.4 and 1.7±0.4, mHAQ: 0.6±0.13, 0.23±0.08*, 0.18±0.08, 0.16±0.08 and 0.01±0.01, PtVAS (mm): 56.8±4.2, 32.9±3.4*, 19.5±2.5*, 17.4±2.6 and 13.3±3.2. TGSs: 13.1±1.8, 6.6±1.0*, 3.4±0.5*, 1.8±0.4* and 1.1±0.3*, TPDs: 11.3±2.3, 3.3±0.6*, 1.2±0.3*, 0.7±0.2* and 0.5±0.3*. The decrease ratio (%) of patient's number of medications was -27.8±4.0*, -37.6±4.0*, -42.4±4.3*, and -45.9±3.6* at BL, week2, 4, and 8, respectively (p value vs BL: *p< 0.01). ΔmTSS≦0 at week 52 from BL was 70.8%. [Conclusions] UPA-MONO demonstrated the early efficacy on clinical outcomes and PRO improvement including ultrasound findings with statistical significance and successfully make it possible to decrease the number of medications to slow the radiographic progression.

## ICW23-4

**JAK Inhibitors Sustain Effectiveness in Rheumatoid Arthritis Patients at Second Line, Comparable to Initial Treatment Levels- Insights from the ANSWER Cohort Study -**

Kohei Tsujimoto[1], Kosuke Ebina[2], Yasutaka Okita[1], Yuki Etani[3], Wataru Yamamoto[4], Akira Onishi[5], Hideo Onizawa[5], Iku Shirasugi[6], Naoki Nakano[7], Takuya Kotani[8], Yuri Hiramatsu[8], Motomu Hashimoto[9], Tadashi Okano[10], Yuji Nozaki[11], Chisato Ashida[11], Yonsu Son[12], Akihiro Tanaka[12], Ryota Hara[13], Atsushi Kumanogoh[1]

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Conflict of interest: None

[Objective] Achieving remission in rheumatoid arthritis (RA) patients with initial b/tsDMARDs poses challenges, necessitating careful selection of second-line treatments. This study aimed to assess the effectiveness of b/tsDMARDs, comparing those in the first-line (naïve group) to those in the second-line after switching from the initial b/tsDMARDs (switched group). [Methods] Data were collected from patients initiating b/tsDMARDs in the first or second line, sourced from the ANSWER cohort, an observational cohort study pooled from 9 Japanese multicenter registries. Differences in drug retention rates after treatment initiation were assessed using log-rank tests. Potential confounders were evaluated using Cox regression analysis with and without multiple imputation models. Changes in Clinical Disease Activity Index (CDAI) over time were compared in each group. [Results] A total of 4037 naïve and 1854 switched cases were studied. The overall retention rate decreased from the first to the second line for TNFi, CTLA-4, and IL-6 inhibitors (Log-rank $p< 0.0001$, 0.0188, 0.0023 respectively) but not for tsDMARDs ($p= 0.436$). These findings persisted when analyzing discontinuations due to insufficient efficacy or adverse effects. Adjusted analysis revealed no significant difference in hazard ratio (HR) between the naïve and switched groups in tsDMARDs, even after employing multiple imputation with a withdrawal HR of 1.01 ([0.753 to 1.35] $p= 0.956$). There was no significant difference in CDAI changes between the naïve and switched groups specifically in tsDMARDs at 12 months (naïve -10.8 [-12.8- -8.65] vs switched -8.2 [-10.0- -6.4], $p= 0.06$) and 24 months (naïve -11.9 [-14.7- -9.1] vs switched -9.3 [-11.7- -6.85], $p= 0.16$). [Conclusions] No differences in continuation rates or effectiveness were observed between the naïve and switched groups in tsDMARDs, unlike in the case of bDMARDs. This study suggests the potential benefit of JAK inhibitors as a second-line treatment option.

## ICW23-5

**Effect of Janus Kinase Inhibitors on TNF and IL-6-Induced Osteoclasts and RANKL-Induced Osteoclasts in Rheumatoid Arthritis**

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Conflict of interest: Yes

[Objective] We have previously reported that a combination of TNF-α and IL-6 induces mouse osteoclast (OC)-like cells with bone resorption activity both *in vivo and in vitro* and that TNF-α and IL-6 induces OCs from human peripheral blood monocytes (PBMs) via RANKL-independent pathways. Notably, the number of OCs induced by TNF-α and IL-6 from peripheral blood mononuclear cells in rheumatoid arthritis (RA) patients positively correlated with the modified total Sharp score, whereas RANKL-induced OCs did not. In this study, we aimed to evaluate the effects of addition of the JAK inhibitors (JAKi) on TNF-α and IL-6-induced OCs as well as RANKL-induced OCs in PBMs from RA patients and healthy donors (HDs), and to assess the effects of long-term administration of JAKi on the capacity of induction of OCs with TNF-α and IL-6 or RANKL in RA patients. [Methods] PBMs from 6 RA patients and HDs were stimulated with TNF-α and IL-6 or RANKL, in the presence or absence of JAKi. mRNA levels of *IL-1β, IL-8,* and *MMP-3* were measured. We examined the number of OCs induced by either TNF-α and IL-6 or RANKL from RA PBMs, both before and 6-months after treatment with filgotinib. [Results] Tofacitinib, baricitinib, upadacitinib, and filgotinib suppressed the differentiation of TNF-α and IL-6-induced OCs from PBMs of RA patients in a dose-dependent manner. Conversely, these JAKi did not affect on RANKL-induced OCs. The mRNA levels of *IL-1β*, *IL-8,* and *MMP-3* decreased with filgotinib in TNF-α and IL-6-induced OCs, but not in RANKL-induced OCs. After 6 months treatment with filgotinib, the number of TNF-α and IL-6-induced OCs differentiated from PBMs decreased compared with those of before the treatment. In contrast, the number of RANKL-induced OCs remained consistent by the 6-months administration of filgotinib in the same patients. [Conclusions] Our results suggest that the inhibitory effect of JAKi on bone destruction in RA may be attributed to their suppression of TNF-α and IL-6-induced OCs.

## ICW24-1

**The regulation of lncRNA NR_030732 expression affects the phenotype of rheumatoid arthritis fibroblast-like synoviocytes**

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Conflict of interest: None

Objective Increasing evidence has demonstrated the association between long non-coding RNAs (lncRNAs) and autoimmune disease. However, their exact role in rheumatoid arthritis (RA) remains unclear. This study aimed to investigate the expression profile of lncRNAs in fibroblast-like synoviocytes (FLS) from patients with RA and explore the significance. Methods We performed a comparative analysis of next-generation sequencing (NGS) data from RA FLS and FLS obtained from patients with osteoarthritis (OA). Differential expression analysis was conducted on unstimulated and interleukin-1 (IL-1)-stimulated RA FLS. LncRNA expression was validated using quantitative real-time polymerase chain reaction. In vitro experiments assessed the effects of lncRNA on RA FLS. Results NGS analysis revealed 4 lncRNAs with increased expression, and 6 lncRNAs with decreased expression in common both in RA FLS compared to OA FLS and in IL-1-stimulated RA FLS compared to unstimulated RA FLS. Subsequent validation was performed on the 3 lncRNAs with the highest fold change in each group and increased expression of NR_030732 in RA FLS was validated. NR_030732 upregulated after stimulation with IL-1, IL-6, or TNF-α, and upregulation of NR_030732 increased pro-inflammatory cytokines, including IL-1, IL-6, IL-17, and TNF-α in RA FLS. In comparison, the knockdown of NR_030732 resulted in decreased expression of those cytokines. Additionally, the reduction of NR_030732 attenuated the wound-healing property of RA FLS. Conclusions Our study found a prominent expression of NR_030732 in RA FLS. Pro-inflammatory cytokines regulated NR_030732 expression, and simultaneously, modulation of NR_030732 expression altered the expression of pro-inflammatory cytokines. Furthermore, downregulation of NR_030732 was associated with delayed wound healing. The results indicated that NR_030732 may serve as a candidate lncRNA involved in the pathogenesis of RA.

## ICW24-2

**Analysis of macrophage subtype alteration in the synovium of rheumatoid arthritis**

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Conflict of interest: None

[Objective] Autophagy describes a cellular process of phagocytosis providing cell metabolic needs and is regarded as an anti-inflammatory role. Rheumatoid arthritis (RA) is a chronic inflammatory disease with four subtypes of macrophages dominant hyperplastic synovial membrane, which are M0 (CD11b+CD86-CD206-), M1 (CD11b+CD86+CD206-), M2 (CD11b+CD86-CD206+), and M1/2 macrophages (CD11b+CD86+CD206+). This study evaluated the macrophage subtype and its alteration depending on inflammatory conditions with autophagy molecules. [Methods] i) Flow cytometry: The synovial membrane tissues from active RA (n=6) patients were enzymatically digested into single cells and later incubated with fluorochrome-tagged antibodies. Surface marker anti-CD11b (PE) typifying macrophages, anti-CD86 (APC) for the M1phenotype, anti-CD206 (FITC) characterizing the M2 phenotype, and anti-WIPI2/LC3/p62 (biotin) for autophagy-related proteins. ii) Cell culture: Adherent macrophages derived from synovium were cultured in a medium with or without IFN-γ and LPS, or IL-4, for 48 hours, then detached for a flow cytometry test. [Results] i) Flow cytometry: The average Median Fluorescence Intensity (MFI) of autophagy-related intracellular protein-WIPI2/LC3/p62-in M1/2 was most robust compared to those of M0, M1, and M2. ii) Cell culture: In-vitro analyses showed that the number of M0 cells was the lowest in the anti-inflammatory culture environment. However, the quantity of M1/2 double-positive cells decreased as the inflammatory factors increased but increased in an anti-inflammatory environment. [Conclusions] The data indicates macrophage subtype alteration may occur in the local host responses depending on inflammatory conditions and autophagy expression. This is crucial for a better understanding of the pathophysiology of inflammatory synovitis. However, whether the enhanced autophagic function is associated with subtype switching or anti-inflammatory cellular processes remains to be investigated.

## ICW24-3

**TEAD1, TEAD3 and IFN-gamma-inducible TEAD4 orchestrate the aggressive behavior of rheumatoid arthritis synovial fibroblasts**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) synovial fibroblast (SF) and its recently identified subsets by single cell RNA-seq are an attractive drug target for difficult-to-treat RA. To identify master regulators encoding transcription factors that govern the aggressive behaviors of RASFs and the plasticity among the subsets, we herein performed quantitative nuclear

proteomics with data-independent acquisition (DIA) mass spectrometry. [Methods] RASFs were treated with TNF-α, IL-1β, IFN-γ, and TGF-β (4mix) for 24 hours. Nuclear extracts were prepared and subjected to DIA mass spectrometry. Expression of TEADs were examined by qPCR and Western blot. siRNA knockdown and pan-TEAD inhibitor K975 were employed to assess roles of TEADs in the cytokine/chemokine expression, the proliferation, and the migration of RASFs by using RNA-seq, qPCR, EdU incorporation, and scratch assay. K975 alone or the combination with TNF inhibitor was administered to collagen-induced arthritis (CIA) DBA/1 mice to examine roles of TEADs in vivo. [Results] The treatment of RASFs with 4mix, important drivers of the heterogeneity of RASF subsets, up- and down-regulated hundreds of nuclear proteins including TEAD1, TEAD3, and TEAD4. 4mix down-regulated TEAD1, while IFN-γ up-regulated TEAD4. IFN-γ-inducible TEAD4 was abundantly expressed in RA synovium as compared to OA synovium. siRNA knockdown of each TEAD and K975 revealed that TEAD1, TEAD3 and TEAD4 had redundant roles in the regulation of their target genes such as CCN1/2 and ANKRD1. RNA-seq with K975 demonstrated that TEADs were involved in cell proliferation. K975 suppressed cell proliferation and migration of RASFs. Furthermore, K975 alone and the combination with TNF inhibitor ameliorated CIA. γ [Conclusions] TEAD4 was inducible by IFN-γ, an important driver of the pathological subset of RASFs, and together with TEAD1 and TEAD3 involved in the aggressive behavior of RASFs. TEAD inhibitor would be promising as RASF-targeting drugs.

## ICW24-4

**JAK-STAT signaling regulates autophagy and presentation of citrullinated vimentin in synovial fibroblasts**

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Conflict of interest: None

[Objective] Autoimmunity against citrullinated proteins is a hallmark of rheumatoid arthritis (RA), but its precise mechanism remains to be determined. Our recent work suggests synovial fibroblasts (SFs)' autoimmune potential through citrullination of vimentin and its interaction with MHC class II that are promoted by autophagy and IFN-γ. Recent studies have indicated a role of JAK-STAT signaling in the active phenotype of SFs. In this study, we hypothesized the involvement of JAK-STAT signaling in SFs' autoimmune potential. [Methods] SFs were derived from synovial tissues of RA patients. The JAK inhibitor Upadacitinib (Upa, 10 μM, 6-72h) was used to inhibit JAK-STAT signaling. To induce autophagy, SFs were starved using serum-free medium for 2h. The induction of autophagy was evaluated with the protein level of LC3-II and the mRNA levels of *BECN1*, *ATG5,* and *ATG7*. Citrullinated vimentin (cVIM) was evaluated by immunofluorescence. Presentation of cVIM was evaluated by proximity between cVIM and HLA-DR *in situ* and the expression of CD69 on co-cultured CD4+Tcells. P values were calculated by ratio paired t-test. [Results] Upa decreased the expression of LC3-II ($p=0.024$), *BECN1* ($p=0.03$), *ATG5* ($p=0.003$), and *ATG7* ($p=0.0009$) in starved SFs ($n=6$). cVIM was induced in starved SFs but inhibited by Upa ($p=0.0001$, $n=4$). The interaction between cVIM and HLA-DR was increased in SFs starved and treated with IFN-γ but cancelled by further treatment with Upa ($p<0.0001$, $n=3$). The expression of CD69 on $CD4^+$Tcells was enhanced by co-culture with starved and IFN-γ-treated SFs but not by that with starved, IFN-γ-treated, and Upa-treated SFs ($p<0.0001$, $n=3$). [Conclusions] The current data indicate that JAK-STAT signaling enhance autophagy and presentation of cVIM in SFs. Although JAK inhibitors target MHC class II expression through IFN-γ signaling, it may also target citrullination through autophagy, both of which would be needed for local autoimmunity in the joints.

## ICW24-5

**Essential roles of RasGRP4 in synovial resident cells in serum transfer-induced arthritis**

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Conflict of interest: None

[Objective] Ras guanine nucleotide-releasing protein 4 (RasGRP4) is a calcium-regulated guanine nucleotide exchange factor and mainly expressed in myeloid cells and activated synovial fibroblasts. Previous our and other studies demonstrated that RasGRP4 knockout (KO) mice were totally protective from serum transfer-induced arthritis (STIA) and that the intraarticular injection of siRNA against RasGRP4 ameliorated collagen-induced arthritis in rats. We undertook this study to evaluate more in detail the functional roles of RasGRP4 in rheumatoid arthritis (RA) using RasGRP4 KO mice. [Methods] K/BxN sera were intraperitoneally injected into mice at day 0 and 2 to induce STIA, and arthritic score was evaluated every day up to day 14. Hind paw thickness was measured with a caliper. Histological scores including inflammation and bone destruction were assessed. Whole bone marrow (BM) cells and BM-derived neutrophils were adaptively transferred intravenously into STIA mice. RasGRP4 wild-type (WT) and KO mice were paired by parabiosis and subjected to STIA. [Results] RasGRP4 KO mice were completely resistant to STIA in both arthritic and histological scores as compared to RasGRP4 WT mice. Adoptive transfer of whole BM cells and BM-derived neutrophils from RasGRP4 WT mice into KO mice did not restore STIA. Furthermore, parabiosis between RasGRP4 WT and KO mice demonstrated no STIA in RasGRP4 KO parabiont, although blood circulation was ~50% shared between two parabionts, confirmed by quantitative genomic DNA PCR of whole blood cells. [Conclusions] Collectively, these data indicated that RasGRP4 in synovial resident cells such as synovial resident macrophages or fibroblasts, not shared by blood circulation, was indispensable for STIA. The molecular mechanisms responsible for the essential functions of RasGRP4 in synovial resident cells would be an effective drug target of RA.

## ICW24-6

**Single-cell Spatial Transcriptome Analysis Identifies Disease-Specific Fibroblasts in Rheumatoid Vasculitis**

Atsuko Tsujii[1], Yoshihiko Hoshida[2], Yanakawee Siripongvutikorn[1], Akira Nishigaichi[1], Kurumi Yamamoto[1], Maiko Yoshimura[1], Akihiko Nakabayashi[1], Hyota Takamatsu[1,3], Shiro Ohshima[1,3]

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Conflict of interest: None

[Objective] Various autoimmune diseases cause skin vasculitis, but its pathogenesis is unknown and quite difficult to treat. Rheumatoid vasculitis (RV) is a serious complication in rheumatoid arthritis (RA) and there is no consensus about treatment due to the unknown pathophysiology. We aimed to understand the pathogenesis using patients' specimens. Spatial transcriptome analysis is an advanced technique that adds spatial information to gene expression analyses. CosMx Spatial Molecular Imaging (SMI) is a platform for single-cell spatial transcriptome analysis of formalin-fixed paraffin-embedded tissue samples (NanoString Technologies). We tried to reveal the disease-related cell populations via single-cell spatial transcriptome analysis of the patients' specimens. [Methods] Single-cell spatial transcriptome analysis was performed on tissues from vasculitis associated with five autoimmune diseases, including RV, and a case with toxic rashes as controls. Cell types were annotated using a reference of public datasets. We performed the projection of cells on a spatial map. For validation, immunohistochemistry was performed using the same specimen. We used Seurat and InSituType (R package) for single-cell analysis. [Results] A total of 35,503 cells and 4,530,981 transcripts were analyzed. Clustering of cells based on gene expression levels using external skin reference data revealed a new population of cells unique to RV. The spatial information created by CosMx and immunostaining of the same specimen suggested that the population is especially around blood vessels. Another clustering analysis with external data and immunostaining also suggested that the cell population is fibroblasts, whose characteristic is similar to synovial lining fibroblasts of RA patients. [Conclusions]

Single-cell spatial transcriptome analysis revealed a cell population specific to RV and they may be similar to synovial lining fibroblasts. They may play important roles in the pathophysiology of RV.

## ICW25-1

**Are we treating-to-target in spondyloarthritis (SpA)? A one-year analysis from the Asia Pacific League of Associations for Rheumatology (APLAR) SpA Registry**

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Conflict of interest: None

Objective To evaluate the extent of T2T achievement after 1-year intensive treatment in patients in the APLAR SpA registry Methods Patients fulfilled the CASPAR 2006 criteria for PsA, and 2009 ASAS criteria for AxSpA were recruited. The current analysis included the first 143 patients reaching the 1-yr timepoint across 7 Asia-Pacific regions (Hong Kong, Singapore, Korea, India, Pakistan, Qatar and Thailand). Results 79 patients with PsA (age: 52±13 years, 43 (55%) male, disease duration: 8.0±8.3 years) and 64 patients with AxSpA (age: 41±16 years, 48 (75%) male, disease duration: 4.8±7.2 years) were included. After 1-yr treatment, there were significant improvement in Disease Activity in Psoriatic Arthritis (DAPSA) (22.1±14.4 vs 11.5±10.0, $p$<0.001) while Ankylosing Spondylitis Disease Activity Score (ASDAS) remained stable (2.0±0.9 vs 1.9±0.9). For medication use, there was an increase in the number of patients receiving biologic/target synthetic disease-modifying drug (b/tsDMARDS, 29% at baseline to 61% at 1-year for PsA, and 52% at baseline to 64% at 1-year for AxSpA). Regarding T2T, 62% and 45% of PsA patient achieved DAPSA-low disease activity (DAPSA-LDA) and minimal disease activity (MDA) respectively, while 53% of patients with Axial SpA achieved ASDAS-LDA. The use of b/tsDMARDs was significantly higher in patient who achieved MDA when compared to those who did not. The MDA/ASDAS-LDA achievement rate were comparable to that of the tight control arm of TICOPA cohort (41%) or TICOSPA study (60%). Treatment was escalated in 86% of visits when treatment target was not met. The reason for non-escalation of drug included: patients' choice (42%), mild symptoms only and physician decides to keep current regime (27%), adverse events (19%), no viable alternatives (8%) and others (4%). Conclusion Implementing the T2T strategy in patient with SpA was feasible in selected centres from the APLAR region, with similar target achievement rate compared to T2T studies conducted in Europe.

## ICW25-2

**Treat-to-target in spondyloarthritis (SpA): Are there sex-related differential responses?**

Carson Chun Yin Yip[1], Isaac T Cheng[1], Ho So[1], Ying Ying Leung[5], Kichul Shin[3], Muhammad Ahmed Saeed[4], Praveena Chiowchanwisawakit[6], Mohammed Hammoudeh[10], Muhammad Haroon[12], Subramanian Nallasivan[2], Stanley Angkodjojo[11], Chung James Ho Yin[7], Mitsumasa Kishimoto[8], James Wei[9], Lai Shan Tam[1]

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Conflict of interest: None

[Objective] Studies have reported that female patients with spondyloarthritis (SpA) have different disease courses and treatment responses compared to male patients. Whether patients' sex is associated with a different outcome after receiving one year of tight control treat-to-target (T2T) strategy remains uncertain. This study aimed to evaluate the differences in the clinical response between the two sexes from the APLAR SpA Registry. [Methods] Patients who fulfilled the CASPAR 2006 classification criteria for PsA and 2009 ASAS classification for axSpA were recruited. They received protocolised treatment aiming at 1) MDA or DAPSA-LDA for PsA patients, and 2) ASDAS-LDA for axSpA patients for 1 year. Patients were assessed every 3 months and treatment was escalated if the target was not reached. [Results] 91 male (age: 45.6±16.1, 43 PsA, 48 axSpA) and 52 female (age: 49.2±13.4, 36 PsA, 16 axSpA) subjects were included. There was no significant difference between the 2 sexes at baseline, except a higher ESR and more severe enthesitis in female patients. During the study period, the use of bDMARDs significantly increased across both sexes. Considering the whole cohort, there were significant improvements in disease activity in PsA after 1-year, and remained low in axSpA. Despite similar bDMARDs use at 1-year (67% in female vs 61% in male), female PsA patients had a lower MDA achievement rate (36% in female vs 51% in male). Female patients also had a higher physician global assessment score (2.6±1.8 in female vs 2.0±1.6 in male, p=0.03), greater functional impairment (HAQ: 0.54±0.57 in female vs 0.32±0.46 in male, p=0.01) and more severe enthesitis (SPARCC: 0.8±1.7 in female vs 0.2±1.1 in male, p=0.005) at 1-year. [Conclusions] There may be differential treat-to-target responses between male and female SpA patients. Such causes should be further explored to potentially implement a sex-specific treat-to-target strategy for spondyloarthritis.

## ICW25-3

**Vascular effects of achieving low disease activity in axial spondyloarthritis-a 2-year prospective cohort study**

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Conflict of interest: Yes

[Objective] Patients with r-axSpA is associated with an increased risk for vascular mortality, axSpA may predispose to accelerated atherosclerosis through several mechanisms, including chronically elevated inflammatory cytokines, a higher prevalence of traditional CVD risk factors, and the impact of pharmacotherapies. To elucidate the long-term vascular effects of achieving ASDAS-LDA in patients with AxSpA. [Methods] One hundred consecutive patients with axSpA who fulfilled the ASAS classification criteria (2) and active disease (ASDAS larger than 2.1) will be recruited from the out-patient clinic of the Prince of Wales Hospital (PWH). The primary outcome was the effect of achieving LDA (LDA group) at 12 months on the progression of subclinical atherosclerosis (AP+) over 24 months as evaluated by the increased number of carotid plaque, the region change of carotid plaque or increase of carotid total plaque area (TPA) compared to those who cannot achieve LDA (non-LDA group). [Results] One-hundred r-axSpA patients (age: 39±10 years, 74 (79.6%)) who were recruited in this analysis. There was marked improvement in disease activity after 1 year of treatment (ASDAS-CRP was 3.0±0.6 at baseline vs. 1.8±0.8 at year 1, $p$<0.001). Eighty-three patients had first-year follow-up. Sixty-two (74.7%) patients achieved LDA. Seventy-eight patients had first-year carotid ultrasound follow-ups. Fifteen patients (19.2%) had AP+. Patients in the AP+ group were older, had higher Framingham risk scores (FRS) and had higher exposure to anti-hypertension drugs at baseline. The use of medication throughout the study period was similar across the two groups. For first-year data, the ASDAS-CRP LDA group (n=57) had no significant difference compared to non-ASDAS-CRP LDA group (n=21) (p=0.536). [Conclusions] Achieving ASDAS-CRP LDA was supposed to have a long-term benefit considering the prevention of CVD, while more data were needed to support this view.

## ICW25-4

**Tofacitinib in Spondyloarthritis - Safe and well tolerated drug -Analysis of 102 patients**

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Conflict of interest: None

[Objective] Tofacitinib has been increasingly used in the management of Spondyloarthritis and has shown to be effective and is slowly replacing the role of **TNF** inhibitors. The ease of oral medications and the introduction of the generic form are making it easily the first choice in the management of Spondyloarthritis. while the real world efficacy is still not known [Methods] All Spondyloarthritis patients who were prescribed tofacitinib up to December 2022 with minimum of 6 months follow-up were included for the analysis. Psoriatic arthritis, lost to follow-up and less than 6 months were excluded. The data was retrieved and patients demographics, before and after lab investigations and drug details were noted [Results]: There were a total of 102 patients who were included for the analysis, in this there were 73 males and 29 females. The mean age of the study population was 37.9 (12.3) years and the mean disease duration was 4.1 (4.5) years. The mean duration of tofa intake was 12.7 (5.4) months. 28 of them have already received one anti tnfs with no repsonse. In the 102 at the time of analysis 67 (65.6%) were still on tofa and remaining 35 (34.4) had stopped tofa. The reason for stopping was better17 (48.7%), Poor compliance 9 (25.7), adverse events 6 (17%), not responding 3 (8.5). In comparing before and after tofacitinib there was significant reduction in ESR, CRP and weight however there is no significant change in the liver enzymes indicating they are relatively safe Table I. In Analyzing the adverse events major adverse events like CAD, Infections, CVA were not noted in SPA group, however minor adverse events were relatively common with Minor infections (20.5%), Fatigue (17.6%), headache (13.7%), cough (11.7%), itching, APD (7.84%), UTI (4.90%),, Transaminitis (2.94%), Alopecia (1.96%), Herpes zoster (0.98%). [Conclusions] Tofacitinib in Spondyloarthritis is effective with significant reduction in inflammatory markers and is well tolerated with no major adverse cardiovascular events.

## ICW25-5

**Are we treating-to-target in spondyloarthritis (SpA)? A cross sectional analysis from the Asia Pacific League of Associations for Rheumatology (APLAR) SpA Registry**

Tsz Ho Cheng[1], Carson Chun Yin Yip[1], Ying-ying Leung[2], Praveena Chiowchanwisawakit[3], Stanley Angkodjojo[4], Muhammad Ahmed Saeed[5], Kichul Shin[6], Han Joo Baek[7], Mohit Goyal[8], Muhammad Haroon[9], Eman Hassan Satti El-sayed[10], Subramanian Nallasivan[11], Fariz Yahya[12], Soosan Soroosh[13], Asal Adnan[14], Ho Yin Chung[15], Mitsumasa Kishimoto[17], Cheng Chung Wei[16], Natalia Co Ciang[18], Ho So[1], Lai Shan Tam[1]

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Conflict of interest: None

Objectives To provide a snapshot of the baseline characteristics of participants in APLAR SpA registry including disease activity and medication use. Methods Patients fulfilled the CASPAR 2006 for psoriatic arthritis (PsA), and 2009 ASAS criteria for axial spondylitis (AxSpA) were recruited. The current analysis included the first 395 patients recruited across 12 Asia-Pacific regions (Hong Kong, Singapore, Taiwan, Japan, Korea, Malaysia, Iran, Thailand, India, Iraq, Qatar, Pakistan). Results 164 patients with PsA and 231 patients with AxSpA (age: 42±15 years, 71% male, disease duration: 4.7±6.8 years) were included. They had moderate disease activity (DAPSA in PsA: 17.3±15.2; ASDAS in AxSpA: 2.41±1.15). Majority of PsA patient (76%) received convention synthetic Disease-modifying antirheumatic Drug (csDMARDs) and 39% received biologic/targeted synthetic DMARDs (tsDMARDs). For AxSpA, 79% and 40% received NSAIDs and b/tsDMARDs respectively. Considering disease control, 42%, 33% and 46% of patients achieved Disease activity in Psoriatic Arthritis (DAPSA) low disease activity (LDA), minimal disease activity (MDA) and Ankylosing Spondylitis Disease Activity Score (ASDAS) LDA respectively. Higher proportion of patients receiving b/tsDMARDs achieved LDA, and significantly more female PsA patient achieved DAPSA-LDA. Using multivariate logistic regression, use of b/tsDMARDs (OR: 2.28, 95% CI: 1.08-4.84, $p$=0.031) and female (OR: 2.45, 95% CI: 1.19-5.04, $p$=0.015) were significantly correlated with achievement of DAPSA-LDA; while use of b/tsDMARDs (OR: 2.85, 95% CI: 1.60-5.08, $p$<0.001) and older age (OR: 1.03, 95% CI: 1.01-1.05, $p$=0.005) were significantly related to achievement of ASDAS-LDA. Conclusions SpA patients using b/tsDMARDs were more likely to achieve LDA. We expect that more patients will be able to achieve treatment target when the T2T strategy is widely adopted in this APLAR SpA cohort in the following years. The influence of sex on T2T outcomes shall be further explored.

## ICW26-1

**Risk factor of radiographic progression in seronegative rheumatoid arthritis patients: From the Three-Arrow cohort**

Genki Kidoguchi[1], Yusuke Yoshida[1], Hirofumi Watanabe[1], Tomohiro Sugimoto[1], Sho Mokuda[1,2], Kunihiko Ando[1], Mayu Sato[1], Takeshi Suga[1], Michinori Ishitoku[1], Kei Araki[1], Yohei Hosokawa[1], Hiroki Kobayashi[1], Takaki Nojima[3], Tetsu Oyama[4], Shintaro Hirata[1]

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Conflict of interest: None

[Objective] Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (ACPA) positivity are risk factors for radiographic progression in rheumatoid arthritis (RA). However, 10-30% of RA patients do not have this seropositivity and are termed as seronegative RA. Few studies have investigated radiographic progression in seronegative RA. The aim of this study is to describe the incidence of radiographic progression in seronegative RA and to identify the risk factors contributing to its development. [Methods] We conducted a retrospective cohort study of patients with seronegative RA enrolled in the Three Arrow cohort, which was established at 10 referral sites in Hiroshima. The modified Total Sharp Score (mTSS) at baseline, week 24 and 52 were evaluated. Additionally, we categorized patients based on the trajectory of mTSS, and compared the baseline characteristics and disease activity throughout the 52-week among those groups using a linear mixed-effects model. [Results] A total of 43 patients were enrolled. The median age was 72 years old, and 58% were male. Ten patients (23%) exhibited a worsening mTSS from baseline at 52 weeks, with a median change of 1 [interquartile range: 0.6-2.6]. Based on the trajectory of mTSS change over 52 weeks, we identified three mTSS trajectory groups: stable (N=33 [76.7%]), worsening (N=4 [9.3%]), and transient worsening then stable (N=6 [14%]). Baseline disease activity was comparable among the three groups (CDAI: 23.0 vs 29.15 vs 25.05, p=0.219), and there were no significant differences in the therapeutic agents between the groups. However, the worsening group consistently exhibited higher CDAI throughout the 52-week period compared to the other two groups (p=0.020). [Conclusions] Even in seronegative RA patients, 23% experienced radiographic progression over the 52-week in our cohort. Persistent high disease activity was an important risk factor leading to joint destruction in those groups.

## ICW26-2

**Does Rheumatoid Factor Level Affect the Pharmacodynamics of Disease-Modifying Antirheumatic Drugs and the Efficacy of Tumour Necrosis Factor Inhibitors with Different Molecular Structures? In Vitro and Clinical Findings from the FIRST Registry**

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Conflict of interest: None

**Objective** To assess in vitro binding of rheumatoid factor (RF) and efficacy outcomes in patients (pts) with rheumatoid arthritis (RA) treated with biological disease-modifying antirheumatic drugs (bDMARDs) with or without a crystallizable fragment (Fc), stratified by RF level. **Methods** We included pts from the FIRST registry who started bDMARD treatment between January 2012 to May 2022 and were followed up for ≧1 year. Pts received certolizumab pegol (CZP; Fc-free bDMARD), or an Fc-containing bDMARD (infliximab [IFX], etanercept [ETA], adalimumab [ADA], golimumab [GLM]). We report clinical disease activity index (CDAI) remission at Month 12 stratified by RF level (≦Q3: RF <145.9 IU/mL; Q4: RF ≧145.9 IU/mL). Propensity score-based inverse probability of treatment weighting was performed to reduce the effect of selection bias. For in vitro analysis, CZP, IFX, ETA, ADA, GLM, tocilizumab, sarilumab and abatacept were coated on microtiter plates; sera from RF-positive/negative bDMARD-naïve pts were added and evaluated for IgM-RF binding by ELISA. **Results** 1,253 pts were included (≦Q3: 943; Q4: 310). CDAI remission was lower in pts with RF Q4 compared with RF ≦Q3 in ADA (≦Q3: 91/155 [36.9%]; Q4: 29/88 [24.9%]; p=0.02), GLM (≦Q3: 31/107 [29.4%]; Q4: 2/24 [8.3%]; p=0.03), and IFX (≦Q3: 23/90 [26.2%]; Q4: 2/14 [17.4%]; p=0.48) treated pts. In ETA-treated pts, CDAI remission was nominally greater in pts with RF Q4 compared with ≦Q3 (≦Q3: 38/138 [22.3%]; Q4: 17/54 [31.6%]; p=0.16). In CZP-treated pts, CDAI remission was similar between pts with RF ≦Q3 and Q4 (≦Q3: 131/325 [40.3%]; Q4: 44/112 [39.3%]; p=0.54). When sera of 24 RF-positive and 24 RF-negative pts were compared, ELISA showed that IgM-RF bound to all bDMARDs except CZP in RF-positive sera. There was little binding in RF-negative sera. **Conclusion** These data suggest RF may bind bDMARDs via the Fc, resulting in reduced efficacy in pts with high RF; higher efficacy may be expected with CZP even in RA pts with high RF levels.

## ICW26-3

**Well-controlled disease activity with drug treatment will not improve the frailty status of Rheumatoid Arthritis (RA) patients to robust state: A multicenter observational study (T-FLAG)**

Yoshifumi Ohashi[1,4], Nobunori Takahashi[1], Yasumori Sobue[3], Mochihito Suzuki[2,5], Hironobu Kosugiyama[2], Junya Hasegawa[2], Ryo Sato[2], Kenya Terabe[2], Shuji Asai[2], Shiro Imagama[2]

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Conflict of interest: None

[Objective] To examine predictive factors for improving the frailty status of RA patients to robust state. [Methods] Among 450 RA patients registered for an observational study using the Japanese frailty diagnostic criteria (J-CHS) from 2020 to 2022, 345 patients who were pre-frail or frail in 2021 were included. Based on J-CHS 2022, the patients were divided into 50 who improved to the robust state and 295 who did not improve. Predictors of improvement in robust state 1 year later were analyzed by multiple logistic regression analysis. After that, 225 patients were divided into the stable group with mean DAS28-ESR from 2020 to 2021 of less than 3.2, and 120 patients were divided into the unstable group with mean DAS28-ESR from 2020 to 2021 of more than 3.2. They were divided into the non-improved group (180 in the stable, 114 in the unstable group) and the improved group (45 in the stable, 6 in the unstable group), respectively, and the impact on J-CHS was investigated by multiple regression analysis. Two-year changes in the non-improved and improved groups of the stable group were examined. [Results] The predictive factor for improvement in the robust state (adjusted odds ratio, 95% confidence interval) was mean DAS28-ESR from 2020 to 2021 of less than 3.2 (4.01, 1.13-14.20). Follow-up mean DAS28-ESR influenced J-CHS score (T = 2.536, P = 0.013) only in the unstable group. The improved group in the stable group had lower HAQ-DI (non-improved vs. improved group, 2020: 0.32 vs. 0.16, 2021: 0.32 vs. 0.17, 2022: 0.32 vs. 0.21) and had higher grip strength (2020: 25.5 kg vs. 8.8 kg, 2021: 25.9 kg vs. 18.7 kg, 2022: 27.0 kg vs. 19.2 kg) than the non-improved group. Both groups of the stable group maintained clinical and functional remission over two years. [Conclusions] Maintaining well-controlled disease activity alone is insufficient to improve patients' frailty status after achieving treatment-to-target goals, suggesting the need for multifaceted approaches.

## ICW26-4

**Predictors of functional and pain improvement of RA patients who achieved low disease activity within 6 months: from the FIRST Registry**

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Conflict of interest: Yes

[Objective] To identify factors that associate with improvement of HAQ-DI and subjective pain of patients treated with biological and targeted-synthetic '(b/ts) disease modifying anti-rheumatic drugs (DMARDs) who achieved LDA. [Methods] Data from The FIRST Registry, a multi-institutional cohort of RA patients treated with b/tsDMARDs, established by the University of Occupational and Environmental Health, Japan, were extracted. Inclusion criteria: Cases that were enrolled in the FIRST Registry after JAKis were first approved in Japan, which is later than August 2013 Patients with LDA (CDAI < 10.0) at 6 months Exclusion criteria: Cases having both significant comorbidities and taking prednisolone > 15 mg/day Those who stopped treatment within 6 months Statistical analysis Logistic regression with outcome of functional remission (HAQ-DI <0.5) at 6 month was conducted using RA-related status at week 0, and concomitant use of MTX and GC as explanatory factors [Results] 1424 cases fulfilled the criteria, among whom 732 (51%) patients who achieved functional remission (HAQ-DI < 0.5). Seropositivity of RF or anti-CCP antibody and use of JAKi compared with use of TNFi were associated with functional remission. On the other hand, older age, longer disease duration, being female, past failure in 2 or more classes of b/tsDMARDs, higher HAQ-DI at week 0, higher disease activity at week 0, and use of glucocorticoid were associated with less likelihood of functional remission. [Conclusions] The results suggest the importance in T2T even among these patients who achieved LDA in relatively earlier phase in the treatment. Choice of drugs may impact the early HAQ improvment, though further analysis may be required. Early introduction of the drug might be a treatment option for the patients who have higher risks of the adverse events by glucocorticoid, such as severe osteoporosis.

## ICW26-5

**Comparison of the efficacy and safety of bDMARDs and their effect on glucocorticoid discontinuation in polymyalgia rheumatica complicated by rheumatoid arthritis from the FIRST Registry**

Yusuke Miyazaki[1], Shingo Nakayamada[1], Naoaki Okubo[1], Koshiro Sonomoto[2], Hiraoki Tanaka[1], Kentaro Hanami[1], Shunsuke Fukuyo[1], Satoshi Kubo[3], Ippei Miyagawa[1], Ayako Yamaguchi[4], Yasuyuki Todoroki[3], Yoshino Inoue[1], Yurie Satoh Kanda[1], Masanobu Ueno[1], Yoshiya Tanaka[1]

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Conflict of interest: Yes

[Objective] The study aimed to determine the efficacy and safety of bDMARDs in the treatment of polymyalgia rheumatica (PMR) complicated by rheumatoid arthritis (RA). [Methods] The study included patients with RA who initiated treatment with bDMARDs (n=5066) between Jan-

uary 2005 and February 2023 from the FIRST registry, along with a cohort of patients who received bDMARDs for RA with complicated PMR (TNF inhibitor (TNFi); n=84, IL-6 receptor inhibitor (IL-6Ri); n=101, CTLA4-Ig; n=40) were included in the analysis. The primary endpoint was the clinical PMR Activity Score (Clin-PMR-AS) after 26 weeks of treatment. Selection bias was minimized by propensity-score based inverse probability weighting (PS-IPTW). [Results] After adjusted PS-IPTW, there was no difference in patient background and the retention rate during 26 weeks among the three groups (p=0.76). Clin-PMR-AS significantly improved after 26 weeks in all three groups. The Clin-PMR-AS at 26 weeks was significantly lower in the IL-6Ri group than in the TNFi group (p=0.01) and the CTLA4-Ig group (p=0.03). The GC doses 26 weeks after introduction of bDMARDs were significantly reduced in the TNFi and IL-6Ri groups, but not in the CTLA4-Ig group. GC dose at 26 weeks was not significantly different among the three groups (p=0.13), however the proportion of patients who discontinued GC was significantly higher in the IL-6Ri group than in other groups (TNFi: IL-6Ri: CTLA4-Ig=20.1:36.7:27.5 (%), p=0.04). The multiple logistic regression analysis identified treatment with IL-6Ri as the only factor contributing to GC discontinuation. There was no difference in the incidence of serious adverse events among the three groups (p=0.84). [Conclusions] IL-6Ri potentially improves the disease activity of PMR and enable GC discontinuation better than TNFi and CTLA4-Ig.

## ICW26-6

**Concentrations of Methotrexate Polyglutamates in Patients with Rheumatoid Arthritis Treated with Low or High Dose-methotrexate in Combination with Adalimumab: Results from the MIRACLE Trial**

Hiroya Tamai[1], Kei Ikeda[2,3], Toshiaki Miyamoto[4], Hiroaki Taguchi[5], Shintaro Hirata[6], Yutaka Okano[7], Shinji Sato[8], Hidekata Yasuoka[9], Masataka Kuwana[10], Tomonori Ishii[11], Hideto Kameda[12], Toshihisa Kojima[13,14], Tsutomu Takeuchi[1,15], Yuko Kaneko[1]

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Conflict of interest: Yes

[Objective] Concentrations of methotrexate polyglutamates (MTX-PGs) in erythrocytes have been reported to be associated with efficacy and safety in patients with rheumatoid arthritis treated with MTX. We aimed to clarify the association of the concentrations of MTX-PGs with efficacy and safety in patients treated with reduced dose MTX at adalimumab initiation. [Methods] The multinational, randomized MIRACLE trial (NCT03505008) enrolled 300 MTX-naive patients. MTX was initiated and increased to the maximum tolerated dose (MTD). Patients who did not achieve remission according to simplified disease activity index (SDAI) at week 24 were randomized to the MTD group or the reduced dose group and started subcutaneous adalimumab 40 mg every other week. We measured the concentrations of MTX-PGs in erythrocytes with liquid chromatograph mass spectrometry at weeks 0, 4, 8, 12, 24, 36, and 48 and analyzed the association of the concentrations with efficacy and safety. [Results] As previously reported, MIRACLE trial showed that the efficacy of adalimumab with reduced dose of concomitant MTX was not inferior to that with MTD of MTX (remission rates at week 48: 44.3% vs 37.9%) with better safety profile (adverse events after week 24: 19.7% vs 35.3%). MTX-PG concentrations at week 48 were not different between patients who achieved SDAI remission and those who did not (95.1 nmol/L vs 98.6 nmol/L in the MTD group, p=0.743; 64.3 nmol/L vs 72.9 nmol/L in the reduced dose group, p=0.556). On the other hand, patients in the reduced dose group who experienced adverse events after week 24 tended to have higher concentration of total MTX-PGs than those who did not (140.3 nmol/L vs 106.9 nmol/L at week 24, p=0.050). [Conclusions] The MIRACLE trial demonstrated that while total MTX-PG concentrations were not relevant for SDAI remission by concomitant treatment with MTX and adalimumab, patients who experienced adverse events were exposed to higher MTX-PG concentrations.

## ICW27-1

**Discovery, characterization, and targeting of miR-126-3p in knee osteoarthritis reveal a protective role**

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Conflict of interest: None

**Objective:** Osteoarthritis (OA) is the most widespread chronic joint disease; despite this, its pathogenesis remains elusive and there are currently no disease-modifying treatments. MicroRNAs (miRNAs) are small non-coding RNAs that show promise as biomarkers, mechanistic drivers, and therapeutic agents in disease, including OA. Here we take an unbiased approach to first identify and then evaluate key miRNAs in knee OA. **Methods:** We used our custom pipeline to re-analyze two published miRNA-sequencing datasets reporting no validated differences in circulating miRNAs in OA patients versus controls. We then used primary knee OA specimens from our HFH OA Biobank and measured prioritized miRNA in plasma, tissues (infrapatellar fat pad, subchondral bone, synovium, articular cartilage, meniscus, and anterior cruciate ligament), and tissue culture supernatant. Next, we modulated miRNA levels using a mimic or inhibitor and measured changes in OA-associated markers. Last, we treated a surgical mouse model of OA with miRNA mimic or inhibitor and assessed knee joint changes by histological analysis. **Results:** In two independent datasets, we found circulating miR-126-3p is increased in knee OA compared to non-OA controls. Real-time PCR validation revealed that plasma miR-126-3p becomes elevated at Kellgren-Lawrence grade (KL) ≧ 2 knee OA. Across six human knee OA tissues, miR-126-3p levels were highest in fat pad, bone, and synovium, with fat pad also showing the highest secretion of miR-126-3p over time. Within these three tissues, miR-126-3p mimic led to downregulation of genes involved in inflammation, bone formation, and pain, while also increasing angiogenesis. In mice, miR-126-3p mimic reduced knee OA severity relative to both inhibitor and control groups. **Conclusions:** Our data suggest circulating miR-126-3p is a candidate biomarker for KL ≧ 2 knee OA while local tissue miR-126-3p plays a mechanistic role in mitigating knee OA severity, making it a potential therapeutic target.

## ICW27-2

**Transcriptome analysis of osteal macrophages identifies cell subset as a potential therapeutic target for postmenopausal osteoporosis**

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Conflict of interest: Yes

[Objective] Given the position of osteal macrophages in the bone microenvironment and their ability to potentially maintain bone homeostasis, the objective of this study was to explore their precise function in postmenopausal osteoporosis as a step toward the development of a newly therapeutic approach. [Methods] Osteal macrophages harvested from ovariectomized BALB/c female mice (OVX) after 4-week of surgery were

sorted with specific antibodies and then subjected to scRNA-seq and bulk RNA-seq analyses. Oxidative stressed- or OVX- macrophages were transferred onto calvarial bone to evaluate their pathological function. Anti-CD52, glutaminase inhibitor compound GIC968 and CB839 were used to depleted senescent osteal macrophages, and ferrostatin-1 to suppress the cellular increase of oxidative stress in OVX mice. [Results] Bulk RNA-seq analysis demonstrated that osteal macrophages in OVX mice upregulated a number of genes that are involved in inflammation, cell senescence and apoptotic process. scRNA-seq analysis revealed that osteal macrophages were clustered into 6 subsets and cell-subset distribution showed a 20-fold increase in subset 3 that shows a typical gene signature of cell senescence and inflammation in OVX-mice. There was correlation between postmenopausal condition and development of senescence in tissue macrophages, and estrogen supplementation suppressed macrophage senescence and the production of inflammatory cytokines in an in vitro oxidative stress model. Furthermore, transfer of oxidative stressed- or OVX- macrophages onto calvarial bone led to development of local inflammation and bone loss. Likewise, depletion of senescent osteal macrophages but not reducing the increased oxidative stress suppressed the excessive bone loss in postmenopausal mice. [Conclusions] Our results suggest the possibility of developing new therapeutic agents that target subset changes in osteal macrophages to prevent osteoporosis.

## ICW27-3

**Early miRNA Expression Changes Post-ACL Reconstruction: Molecular Insights and Gender-Associated Variations**

Amit Sandhu[1,2], Katrina Hueniken[1,2], Starlee Lively[1,2], Jason S Rockel[1,2], Anastasia Sanjevic[3], Kimberly Perry[1,2], Shgufta Docter[3], Tamara Wagner[1,2], Darrell Ogilive-harris[3], Tim Dwyer[3], Jaskarandip Chahal[3], Mohit Kapoor[1,2,4]

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Conflict of interest: None

Objective: Anterior cruciate ligament (ACL) reconstruction after ACL injury may reinstate knee stability, but it does not prevent post-traumatic osteoarthritis (PTOA). MicroRNA (miRNA) changes emerging shortly after ACL reconstruction remain insufficiently defined, potentially harbouring crucial early cues in PTOA evolution. Moreover their differential expression in genders also appears to exert influence on the disease's natural trajectory. This study aims to determine alterations in miRNA expression during the early stages after surgery and to identify a miRNA signature associated with KOOS scores six months post-surgery. Methods: Plasma samples were obtained from a cohort of 43 ACL reconstruction patients at baseline, 2 weeks, and 6 weeks post-surgery. The Knee injury and Osteoarthritis Outcome Score (KOOS) was used to assess patient-reported knee pain and function baseline (prior to surgery) and 6 months post-surgery. MiRNA sequencing was conducted, with batch correction. Associations between miRNAs and time-point, gender, and KOOS scores were explored. Results: Thirty-six miRNAs were significantly upregulated at two weeks post-ACL reconstruction. Five miRNAs displayed differential expression by gender; two miRNAs, hsa-miR-143-5p and hsa-miR-145-5p, exhibited sustained upregulation in female patients at 2 and 6 weeks post-surgery compared to males. Additionally, the analysis revealed a miRNA signature associated with change in KOOS pain scores from baseline to 6 months post-surgery, indicating downregulation of hsa-miR-196a-5p at pre-surgery baseline among patients with greater post-surgical improvement in pain. Conclusions: Overall, this study informs about miRNA expression changes following ACL reconstruction, offering insights into the molecular alterations post-surgery. It also highlights gender-specific miRNA variations. Understanding these changes could significantly enhance our knowledge of postoperative developments in ACL patients.

## ICW27-5

**A Cell and Transcriptomic Atlas of the Infrapatellar Fat Pad from Patients with Knee Osteoarthritis: Identification of an Obesity-Associated Transcriptomic Signature**

Pratibha Potla[1], Hayley Peters[1,2], Jason S Rockel[1], Keemo Delos Santos[1], Shabana Vohra[1], Starlee Lively[1], Kim Perry[1], Anthony Perruccio[1], Nizar N Mahomed[1], Raja Rampersaud[1], Rajiv Gandhi[1], Mohit Kapoor[1,2]

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Conflict of interest: None

**Objective:** Knee osteoarthritis (KOA) is the most common form of arthritis, defined by cartilage degeneration, synovial inflammation, fibrosis, and subchondral bone remodelling. Obesity is the greatest risk factor for developing this disease. The infrapatellar fat pad (IFP) is the largest FP within the knee however, its role in KOA is not well understood. Furthermore, the cell populations contributing to KOA remain to be fully characterized. This study aims to identify the distinct cell populations within the IFP that may contribute to KOA pathogenesis and how obesity impacts this process using single-nucleus RNA sequencing (snRNA-seq) and spatial transcriptomics. **Methods:** IFP was obtained from late-stage KOA patients [KL grades III/IV; n=15] during total knee replacement. Nuclei underwent snRNA-seq on an Illumina NextSeq 550 using the 150bp high output sequencing kit. Data was processed using Cell Ranger and clusters were annotated using canonical markers while differential gene expression testing determined a gene signature. IFP [n=10] were also spatially sequenced using Visium CytAssist techniques and analyzed using Seurat. **Results:** Clustering and spatial analysis identified fibroblasts, macrophages, adipocytes, and endothelial cells as major cell populations within OA IFP, each with distinct subsets with unique transcriptomic profiles located throughout the IFP. We also determined that there are transcriptomic differences within fibroblasts in obese BMI KOA-IFP compared to normal BMI. Our efforts are now focused on employing advanced bioinformatics to further characterize distinct differences subtypes in cells based on OA status. **Conclusions:** Using snRNA-seq and spatial sequencing, we have identified distinct cell subsets of fibroblasts, adipocytes, macrophages, and endothelial cells in IFP with KOA, and transcriptomic differences based on BMI. Our ongoing efforts will help characterize the role and function of these identified cell subsets in KOA pathogenesis.

## ICW28-1

**T-cell-instructed monocyte activation is a key feature in Ankylosing Spondylitis and provides novel therapeutic opportunities**

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Conflict of interest: None

[Objective] Ankylosing spondylitis (AS) is an incurable inflammatory disease with a strong genetic predisposition. Hyperactivity of monocytes and Th17 cells are two features of AS pathology. How monocytes are activated in AS is unclear, and here we asked whether T cells could be important activators of monocytes in AS. Additionally, it was also investigated whether AS risk genes ERN1 and ZC3H12C contribute to the T-cell-instructed monocyte activation in AS patients. [Methods] Human peripheral blood mononuclear cells (PBMCs), human primary monocytes and $CD3^+$ T-cells from 72 AS patients were used in this study. Small interfering RNAs (siRNA) or inhibitors were used to study the function of genes. The knockdown efficiency was determined by quantitative PCR (qPCR) and western blotting. Flow cytometry and enzyme-linked immunosorbent assay (ELISA) were used to quantify the production of pro-inflammatory cytokines. [Results] Activated T-cells potently stimulated monocytes from patients with AS to produce IL-1β and IL-23, which in turn acted back on T-cells to enhance Th17 responses. Antibody-mediated neutralisation of TNF-α and CD40L significantly reduced the production of IL-1β and IL-23 in patient-derived monocytes induced by T-cell activation. Silencing of the AS risk genes ERN1 (encoding IRE1α protein) or ZC3H12C downregulates the production of pro-inflammatory cytokines by T-cell-activated monocytes in AS patients. [Conclusions] We describe a novel and important mechanism contributing to monocyte activation in AS through T-cell-monocyte crosstalk, in which AS risk genes ERN1 and ZC3H12C

are involved.

## ICW28-2

**The molecular and metabolic mechanism in TCR-independently activated human CD8+ T cells in Ankylosing Spondylitis**

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Conflict of interest: None

[Objective] Genome-wide association study (GWAS) has identified multiple ankylosing spondylitis (AS) risk genes including HLA-B27 and ERN1. Recent studies show that $CD8^+$ T cell receptor (TCR) motif was associated with the pathogenesis of AS by identifying certain HLA-B*27-presented epitopes. $CD8^+$ T cells are known to be activated by proinflammatory cytokines TCR-independently. TCR-dependent activation of $CD8^+$ T cells is mainly regulated by mammalian target of rapamycin complex 2 (mTORC2), rather than mTORC1. Consequently, it is worth investigating whether TCR-independent $CD8^+$ T cell activation is mediated via mTOR pathway. If so, which mTOR complex plays the bigger role? [Methods] Human peripheral blood mononuclear cells (PBMCs), primary $CD8^+$ T cells and primary T cells were isolated from frozen leukocyte cones or fresh human peripheral blood. Small guide RNA and Cas9 protein or chemical inhibitors were used to study the function proteins. The knockout efficiency was detected by western blotting. The expression of IFN-γ and XBP1s were measured by flow cytometry or enzyme-linked immunosorbent assay (ELISA). [Results] $CD8^+$ effector memory T cells ($T_{EM}$) are the main cytokine producer in $CD8^+$ T cells under cytokine stimulation. Chemical inhibition of mTORC1 had a more potent reduction effect on cytokine-induced IFN-γ production than mTORC2. Both chemical inhibition and genetic knockout of IRE1α, an AS GWAS risk, as well as a downstream regulator of mTOR, potently supressed XBP1s expression and reduced the expression of cytokine-induced IFN-γ. [Conclusions] This study shows that TCR-independent $CD8^+$ $T_{EM}$ cells activation utilizes a metabolic mechanism which is distinct from TCR-dependent activation: mTORC1, rather than mTORC2, contribute more to this metabolic response. Our data also suggest that TCR-independent $CD8^+$ $T_{EM}$ cells activation is mediated via mTOR-IRE1α-XBP1s pathway. This metabolic mediated regulation of cytokine-induced $CD8^+$ $T_{EM}$ activation is likely relevant to AS.

## ICW28-3

**Tyk2 inhibitor suppresses neutrophil-mediated inflammation through inhibition of type1 interferon signaling in spondyloarthritis**

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Conflict of interest: Yes

Objective: Tyk2 inhibitor (Tyk2i) showed efficacy in psoriasis. However, the molecular mechanism is not fully understood. Because Tyk2 is involved with IL-12, IL-23, and Type1 Interferon (IFN) signaling, it is currently considered that the main pathway may be Th17 inhibition via IL-23. In this study, we studied the mode of action of Tyk2i utilizing an animal model of spondyloarthritis. Methods: Arthritis, psoriasis, colitis, and spondylitis were induced in the SKG mice which between 8-12 weeks of age received 6 mg curdlan administered intraperitoneally. Tyk2i (Bristol Myers Squibb-986202) (30 mg/kg qd) (n=10) or vehicle (n=12) were administered by gavage for 3-4 weeks. T helper cell subsets were analyzed by intracellular cytokine staining. Neutrophil subpopulations were analyzed by surface CXCR4 and intracellular IFIT1 expressions. Results: Tyk2i suppressed curdlan-induced SpA. Tyk2i was more effective if administered in the early (from the 3rd week) than in late (from the 6th week) phase of arthritis. Tyk2i inhibited the differentiation of IL-17+ IL-22+ Th17 cells (vehicle 5.59±1.37 vs Tyk2i 1.28±0.19) after 3 weeks Tyk2i treatment. However, suppression of arthritis started much earlier, even only 1 week Tyk2i treatment. Notably, Ly6G+ CD11b+ neutrophils were massively infiltrating into the inflamed joint, and Tyk2i rapidly suppressed neutrophil accumulation (vehicle 39.1±10.66 vs Tyk2i 1.5±0.92). Among neutrophil subpopulations, IFIT1+ neutrophils (G5b) decreased remarkably (vehicle 23.3±6.86 vs Tyk2i 1.5±0.64) suggesting the inhibition of type1 IFN signature by Tyk2i. CXCR4+ mature neutrophils (G5c) also decreased in the joint. Tyk2i also objectively and histologically suppressed psoriasis, colon inflammation, and spondylitis. Conclusion: Tyk2i rapidly suppressed neutrophil-mediated inflammation. Our results suggest that Tyk2i suppress SpA in two ways; suppression of Th17 through IL-23 and suppression of neutrophil activation and proliferation through Type1 IFN.

## ICW28-4

**Gut microbiome and metabolome association analysis in untreated ankylosing spondylitis patients**

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Conflict of interest: None

**Objective:** The objective of this study is to explore the relationship between changes in gut microbiota and metabolomics in patients with Ankylosing Spondylitis (AS) and their contribution to the immunopathogenesis of AS. **Methods:** Fecal microbiome data were collected from 40 untreated AS patients and compared with data from 40 matched healthy controls (HC) using 16S ribosomal RNA (rRNA) gene amplicon sequencing analysis. Additionally, we analyzed the plasma metabolic profile of both groups using the Liquid Chromatography Quadrupole Time-of-Flight (LC-QTOF) platform to identify the biological characteristics of untreated AS patients. **Results:** The results revealed a significant increase in the abundance of *Bacteroides, Dysgonomonas*, *Ruminococcus*, *Megamonas*, *Elusimicrobium*, and *unclassified Prevotellaceae* in AS patients. The pathways with the highest number of differentially expressed metabolites were bile secretion, neomycin, kanamycin, gentamicin biosynthesis, and arachidonic acid metabolism. Furthermore, we observed a positive correlation between Palmitoyl glucuronide, Leukotriene E3, and *Campylobacter*, *Anaeroglobus*, and *Dysgonomonas*. *Barnesiella* showed a significant association with most metabolites, underscoring its importance in the context of metabolomics ($P<0.01$). **Conclusion:** Our findings indicate that untreated AS patients exhibit disrupted gut microbiota and altered metabolites. The analysis of microbiome and metabolomics data revealed significant differences in flora and metabolites between untreated AS patients and the HC group. These preliminary findings provide valuable insights into the potential immunological mechanisms of AS, which warrant further exploration through comprehensive multi-omics studies and larger datasets.

## ICW28-5

**Unraveling Diverse Pathogenic Mechanisms in HLA-B27-Negative Axial Spondyloarthritis: Involvement of Interferon-Activated CD4+ T Cells and CD56bright NK Cells**

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Conflict of interest: None

[Objective] Axial spondyloarthritis (axSpA) is an autoimmune inflammatory condition primarily affecting the axial skeleton. Although the pres-

ence of the human leukocyte antigen B27 (HLA-B27) is a well-established genetic marker strongly associated with axSpA, the pathogenesis of HLA-B27-negative ax-SpA patients remains poorly elucidated. The objective of our study was to gain deeper insights into the pathogenesis of axSpA by conducting a comparative analysis between HLA-B27-positive and HLA-B27-negative cases. [Methods] We collected peripheral blood mononuclear cells from a cohort of 34 patients diagnosed with axSpA based on Assessment of SpondyloArthritis international Society criteria. The dataset, encompassing single-cell RNA-sequencing data and clinical profiles, was subjected to integrative analysis utilizing a generalized linear mixed model. [Results] In HLA-B27-negative cases, we observed a significant correlation between the proportion of interferon (IFN)-activated $CD4^+$ T cells and ASDAS-CRP ($P < 0.001$, OR = 2.19). In contrast, such a correlation was not evident in HLA-B27-positive cases ($P = 0.94$, OR = 1.02). Cell-to-cell interaction analysis further indicated a dynamic interplay between IFN-activated $CD4^+$ T cells and $CD56^{bright}$ NK cells. Notably, *CXCR6* expression was markedly elevated in $CD56^{bright}$ NK cells from HLA-B27-negative cases. These findings suggest a possible priming of $CD56^{bright}$ NK cells by IFN-activated $CD4^+$ T cells and their subsequent migration to inflammatory tissues, thus playing a role in the pathogenesis of spondylitis in HLA-B27-negative cases. [Conclusions] Our study underscores the presence of distinct immune phenotypes in HLA-B27-negative axSpA compared to their HLA-B27-positive counterparts. Investigating the molecular pathways underlying these aberrant immune responses in HLA-B27-negative axSpA and stratifying patients based on HLA-B27 status holds the promise of a more precise approach to diagnosis and treatment.

## ICW29-1

**The organ and system damage in systemic vasculitis: a single-centre retrospective study**

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Conflict of interest: None

Objectives: Systemic vasculitis (SV) is a rare and complex disease affecting multiple organs and systems, which can cause difficulties in diagnosis and often leads to significant morbidity and mortality. The study aims to determine the frequency of organ and system damage in SV. Methods: A single-centre retrospective study of 80 patients over 18 was conducted using the Almaty City Rheumatology Centre data. The medical records of patients from the southern region of Kazakhstan with SV for three years (2019-2021) were analyzed. Results: Of the 80 cases, the most prevalent conditions were IgA vasculitis (40%) and Takayasu arteritis (21.25%). Granulomatosis with polyangiitis (15%) was less common, while patients with Behcet's disease accounted for a slightly smaller proportion (11.25%). Three-quarters of the patients were from the city, while the remaining quarter were from rural areas. Females constituted 70% of the patients, and males, 30%. Disability was detected in 13% of patients with SV, and almost 60% were unemployed. The musculoskeletal system (65%), gastrointestinal tract (56.3%), skin and appendages (56.3%) and cardiovascular system (48.8%) were most often affected in patients. The genitourinary system (38.8%), lungs (17.5%), peripheral vessels (32.5%), visual organs (15%) and nervous system (10%) were also involved in the pathological process. Conclusion: In conclusion, the manifestation of vasculitis varied depending on the type, but the musculoskeletal system, digestive organs, skin and cardiovascular system were most often affected. A high percentage of unemployment was found among the patients, and there were cases of disability because of the involvement of vital organs and systems in the pathological process. Thus, patients with suspected vasculitis need increased awareness from primary care physicians and internal medicine doctors, leading to a detailed medical examination due to its unfavourable prognosis and the need for early treatment.

## ICW29-2

**Hydrogen gas inhalation alleviates cardiovascular lesions in a murine model of Kawasaki disease**

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Conflict of interest: None

[Objective] awasaki Disease (KD) is a syndrome primarily affecting young children, typically under the age of five and is characterized by the development of acute vasculitis. Through extensive research conducted on both murine and human subjects, it has been demonstrated that the heightened levels of reactive oxygen species (ROS) play a pivotal role in the development of KD especial the coronary artery lesions (CAL). [Methods] Hydrogen gas exhibits potent antioxidant properties that effectively regulate ROS production and the inflammatory response. In the current study, we used lactobacillus casei cell wall extract (LCWE)-induced vasculitis in mice as an animal model of KD and treated by hydrogen gas inhalation for developing therapeutic strategies for KD. [Results] We observed significant dilatation and higher Z score of LCA in D21 and D28 in mice after LCWE treatment compared to the control group ($p<0.05$) and significant resolution of LCA diameter ($p<0.005$) and Z score ($p<0.005$) after treatment with inhaled hydrogen gas. We further demonstrated that higher serum IL-6 expression in mice after LCWE treatment ($p<0.005$) and IL-6 significantly decreased after inhaled hydrogen gas therapy ($p<0.0005$). [Conclusions] In conclusion, from literature review this is the first report that hydrogen gas inhalation demonstrated effective prevent coronary artery dilatation in the KD murin model.

## ICW29-3

**Characteristics of the clinical phenotype of giant cell arteritis in clinical practice**

Satoshi Hama[1], Keisuke Izumi[1,2], Hiroki Tabata[1], Misako Higashida-Konishi[1], Tatsuhiro Ohshige[1,2], Hisaji Oshima[1], Yutaka Okano[1], Katsuya Suzuki[1]
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Conflict of interest: None

[Objective] This study aimed to determine the characteristics of the clinical phenotype of giant cell arteritis (GCA) in clinical practice [Methods] Consecutive patients with GCA who visited our department between 2006 April and 2023 September were included in our study. GCA was defined by positive findings on biopsy or imaging findings. We examined the following clinical features separately for cranial GCA and large vessel GCA (LV-GCA): age, gender, the presence of polymyalgia rheumatica (PMR) and malignancy, the days from symptoms to treatment, clinical finding such as fever, scalp tenderness and jaw claudication, temporal artery swelling or tenderness, and the worst blood test values (such as white blood cell count (WBC), and C-reactive protein (CRP), Erythrocyte sedimentation rate (ESR), IgG, LDH, ferritin) before the initial therapy. [Results] A total of 28 patients with GCA were identified. Among them, 18 patients (64.3%) presented cranial GCA, and 14 patients (50%) presented LV-GCA, and 4 patients (14.3%) presented both phenotypes. The positivity rate of fluorodeoxyglucose positron emission tomography (FDG-PET) was 75% in patients with LV-GCA compared to 20% in patients with cranial GCA. Whereas, the detection rate of temporal artery biopsy was 85.7% in patients who performed temporal artery ultrasound. The presence of cranial GCA, jaw claudication, temporal artery swelling and tenderness were more frequently in GCA patients without PMR than in those with PMR (cranial GCA; 84.6% vs. 46.7% (p=0.04), jaw claudication; 46.2% vs. 6.7% (p=0.02), temporal artery swelling; 76.9% vs. 20% (p=0.003), temporal artery tenderness; 69.2% vs. 6.7% (p=0.0006)). [Conclusions] We determined the characteristics of the clinical phenotype of GCA. Since cranial GCA patients have a low positivity rate on FDG-PET, this study suggested that temporal artery ultrasound may be useful in the GCA patients without PMR who have abnormal findings of temporal artery.

## ICW29-4

**Different clinical manifestations of ischemic stroke according to the disease activity in patients with Takayasu's arteritis**

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Conflict of interest: None

[Objective] Takayasu's arteritis (TA) is a rare idiopathic chronic large-vessel vasculitis that predominantly affects the aorta and its main branches. Ischaemic stroke is a relatively frequent manifestation in patients with Takayasu's arteritis, but the relationship between the clinical manifestation and disease stage has rarely been investigated. TA classically exhibits a pattern of expression consisting of an active inflammatory and a chronic "burnt-out" stage. We hypothesized that stroke manifestations in TA are different according to disease stage. [Methods] We analyzed a retrospective cohort of three hundred TA patients diagnosed with TA from March 2002 to March 2016, fulfilling the Sharma criteria. Clinical features were reviewed, including disease activity, angiographic classification, and carotid Doppler findings. Patients were subdivided into acute inflammatory and chronic "burnt-out" stages. The group with acute inflammatory stage was defined as satisfying three of four the following criteria: 1) an elevated ESR, 2) age < 40 years, 3) claudication of an extremity, 4) thickened arterial wall with mural enhancement on CT or MR angiography. [Results] Thirty-one patients (72.1%) were classified as a chronic stage. Those co-morbidities, including hypertension, diabetes mellitus, coronary heart disease, etc., showed no statistical difference between the active and chronic stages of TA groups. The active stage had more frequent common and internal carotid artery involvement than the chronic group. The chronic group showed a high incidence of silent ischemic lesions and posterior circulation ischemia. [Conclusions] These findings suggest that disease activity plays an important role in stroke manifestations in patients with TA. The chronic stage of TA has different clinical manifestations and mechanisms of ischemic stroke compared to the TA patients with the active stage.

## ICW29-5

**Anticoagulation in children with Kawasaki disease: our 3 decades of experience at Chandigarh, North India**

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Conflict of interest: None

**Objective:** To describe safety and efficacy of antiplatelet and anticoagulation therapy (aspirin and low molecular weight heparin (LMWH)/warfarin) in a cohort of Kawasaki disease (KD) patients with moderate to giant coronary artery aneurysm. **Methods:** Records of 1230 children with KD during 1994-2022 were analyzed. **Results:** Fourty-five (3.6%) children (32 boys; 13 girls) with KD, were put on aspirin and LMWH/warfarin. Median age of diagnosis was 18 months (range 1.5 months-12 years). Thirteen children (28.9%) were infants. Twenty-three patients (50%) received LMWH, while 10 (23.7%) received warfarin. Twelve patients received initially LMWH for 12-31 months duration followed by oral warfarin. Giant aneurysms were present in 41 patients while 4 patients had moderate-sized aneurysms. Thromboses developed in acute phase of disease in 5/38 (11.1%) and most common coronary artery affected was LAD. All patients were continued on oral aspirin (3-5 mg/kg/day) along with anticoagulation therapy and 6 patients also received a second antiplatelet agent (clopidogrel). Median duration of LMWH was 19 months (range: 3-42 months), and median warfarin duration was 46 months (range: 2-126 months). In 22 patients we were able to monitor factor Xa activity and median activity was 0.46 IU/mL (0.32-0.81). Median INR in patients receiving warfarin was 1.55 (0.99-2.73). There were no significant complications related to anticoagulation in any of the patients, although parents frequently complained of local bruising. Serial 2D-echocardiogram during follow-up showed remodeling of coronary arteries. None of the patients developed thrombosis or symptomatic stenosis during follow-up. Duration of follow-up was 1614 patient-months. **Conclusion:** Although the recommended INR in patients with KD and large aneurysm who are receiving anticoagulation therapy is 2-3, we maintained our patients on lower INR. Our results show that even on a much lower INR, these children have had no significant complications.

## ICW29-6

**Anti-EPCR antibodies found in Takayasu arteritis could connect vascular and intestinal inflammation**

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Conflict of interest: None

[Objective] The involvement of B cells has been clarified in Takayasu arteritis (TAK), and we identified two autoantibodies (Abs) in TAK. One of the Abs, anti-endothelial protein C receptor (EPCR) Abs were frequently detected in TAK complicated with ulcerative colitis (UC), and were also detected in primary UC. This study aimed to elucidate the pathogenic interplay of anti-EPCR Abs among intestinal and vascular inflammation. [Methods] 113 patients with UC and other 205 cases were included. The titer of anti-EPCR Abs was measured by cell-based assay, and its correlations with diseases, clinical course and phenotypes were evaluated. The expressions and functions of EPCR were evaluated in cellular components using primary cells and immune cells as well as in tissue using immunohistochemical staining (IHC). Repertoire analysis was performed using cells isolated from tissue and peripheral blood. [Results] Anti-EPCR Abs were detected in 75.5%, 6.7% and 0% in UC, Crohn's disease, and controls, respectively, and their titers were positively correlated with endoscopic severity. Although anti-EPCR Abs were found in patients with colonic inflammation, they remained positive after bowel resection, indicating extra-intestinal generation of Abs. IHC revealed strong expression of EPCR in the endothelium and interstitial tissue in normal colon. In contrast, such expressions were reduced in the inflamed lesion, indicating reduced EPCR-mediated anti-inflammatory activity in the disease. Repertoire analysis revealed the usage of the V and J genes for the Abs was consistent throughout the uninflamed tissue, inflamed lesions, and peripheral blood, confirming the systemic nature of aberrant B cell activation. [Conclusions] The inflammation in UC was not merely limited to the colon, and the systemic B cell responses were observed. Anti-EPCR Abs were found in both TAK and UC, and elucidating the common mechanisms how anti-EPCR Abs were generated would be critical to understand both diseases.

## ICW30-1

**Bone marrow-derived platelet-rich fibrin promotes rotator cuff healing in a rabbit degenerative model**

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Conflict of interest: None

[Objective] Although platelet-rich plasma (PRP) and peripheral blood-derived platelet-rich fibrin (P-PRF) are commonly applied in biological augmentation, there is no report on the therapeutic effect of bone marrow-derived PRF (BM-PRF) for degenerative rotator cuff tears (RCTs). This study aimed to evaluate the effects of PRP, P-PRF, and BM-PRF during RCR in a model of degenerative RCTs in rabbits. [Methods] Degenerative RCT models of 68 juvenile rabbits were created 2 weeks before beginning the study and were divided into 4 groups: the control, PRP, P-PRF, and BM-PRF groups. P-PRF and BM-PRF were prepared using a glass tube by centrifuging peripheral blood and bone marrow. These materials were administered for RCR between the rotator cuff and the footprint of the humerus. At 4, 8, and 12 weeks, rabbits were euthanized and histologically assessed. P-PRF and BM-PRF were also evaluated histologically. Statistical analyses were performed, and $P<.05$ was considered statistically significant. [Results] The continuity was significantly better in the BM-PRF group at 4 weeks ($P<.05$). Immunofluorescence staining demonstrated that VEGF-positive stained cells were significantly greater in the BM-PRF group than in the control group ($p < 0.01$). At 12 weeks, the percentage of COLI-positive stained area in the BM-PRF group was significantly greater than in the control group (37.9% ± 12.3% vs. 7.1% ± 5.5%, $p < 0.01$). The modified tendon maturing score was significantly greater in the BM-PRF group than in the control and PRP groups at 12 weeks ($p < 0.05$). BM-PRF showed 68 ± 52 cells/HPF, while no cells

were observed in P-PRF ($p < 0.05$). Of the cells observed in BM-PRF, 66% ± 14% were CD11b positive cells. [Conclusions] The rabbit model of degenerative RCTs repaired with BM-PRF enhanced tendon-bone continuity at 4 weeks and obtained preferable tendon-bone maturation at 12 weeks. RCR augmented with BM-PRF has the potential to improve clinical outcomes for RCTs.

## ICW30-2

**Bone marrow-derived platelet-rich fibrin improve repair of osteochondral defects in rabbits**

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Conflict of interest: None

[Objective] The therapeutic potential of the bone marrow-derived platelet-rich fibrin (BM-PRF) for osteochondral defects is unknown. This study aimed to compare the effect of peripheral blood-derived PRF (P-PRF) and BM-PRF on osteochondral defects. [Methods] Thirty-six New Zealand White rabbits were divided into 3 groups: the control, P-PRF, and BM-PRF groups (n = 12 in each). In the control group, a cylindrical osteochondral defect (4 mm in diameter and 3 mm in depth) was created on the patellar groove. In the P-PRF and BM-PRF groups, P-PRF and BM-PRF were prepared using a glass tube by centrifuging peripheral blood collected from the central ear artery and bone marrow aspirated from the iliac crest and transplanted into osteochondral defects in each. The knee joints were harvested at 4 and 12 weeks. The specimens at 12 weeks were scanned on micro-CT, and the subchondral bone volume was measured. In histological analysis, osteochondral defects were stained with Safranin O and evaluated by the Niederauer score at 4 and 12 weeks. In addition, Infrapatellar fat pad synovium was performed HE staining and evaluated by the Krenn score. Statistical analysis was performed, and $p < 0.05$ was considered a significant difference. [Results] Micro-CT showed that the subchondral bone volume in the PRF group was greater than the other groups at 12 weeks ($p<0.05$). The Niederauer score in the BM-PRF group was significantly higher than the control group at 12 weeks ($p<0.05$). The Krenn score in the BM-PRF group was significantly lower than the control group at 4 weeks ($p<0.05$). [Conclusions] The transplantation of BM-PRF into osteochondral defects decreased synovial inflammation in the early stage and led to healing with hyaline-like cartilage and a more robust tissue for osteochondral repair compared to the transplantation of P-PRF and defect only. These findings indicated that BM-PRF had an anti-inflammatory effect and accelerated the healing process of osteochondral defects.

## ICW30-3

**3BP2 deletion controls lupus via regulating B cell activation**

Shoichi Nawachi[1], Takayuki Katsuyama[1], Natsuki Kubota[1], Yuya Terajima[1], Kei Hirose[1], Kazuya Matsumoto[1], Kenta Shidahara[1], Takato Nakadoi[1], Yu Katayama[1], Yoshia Miyawaki[1], Eri Katsuyama[1,2], Mariko Narazaki[1], Yoshinori Matsumoto[1], Jun Wada[1]
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Conflict of interest: None

[Objective] 3BP2 is an adapter protein that mediates tyrosine kinase signaling. We have previously reported that 3BP2 is involved in cytokine production via Toll-like receptor (TLR) phosphorylation and innate immune regulation through SYK/SRC activation. Althogh abnormal activation of tyrosine kinase/TLR pathways in immune cells is known to be involved in the pathogenesis of Systemic lupus erythematosus (SLE), detailed mechanisms remain unclear. The objective of this study is to examine the role of 3BP2 in the pathogenesis of SLE and to establish genetic evidence that 3BP2 is an optimal therapeutic target for SLE. [Methods] We generated CD72KO/lpr 3BP2KO mice by crossing CD72 KO/lpr mice, which develop strong lupus phenotype due to abnormal B cell activation, with 3BP2 KO mice. First, we confirmed the expression of 3BP2 in lupus-prone mice. Histological evaluation of various organs, urinary protein quantification, and cell fractionation using splenocytes were examined. Furthermore, western blot and quantitative PCR were performed using B cells isolated from splenocytes to analyze the effect of 3BP2 deficiency on intracellular signals. [Results] To determine whether 3BP2 is involved in the pathogenesis of SLE, we examined 3BP2 expression in B cells of lupus-prone mice and found that 3BP2 expression was increased compared to wild-type mice. Deletion of 3BP2 resulted in a marked improvement in the urinary Alb/Cr ratio, glomerulonephritis and inflammatory cell infiltration in liver and lungs. In lupus-prone mice, the number of age (autoimmune)-associated B cells (ABCs) was increased, and 3BP2 deletion significantly reduced it. 3BP2 deletion regulated phosphorylation of Syk by stimulating BCR and TLR7 in B cells. In addition, IL-6 expression after stimulation was increased in B cells from lupus-prone mice, and 3BP2 deletion decreased it. [Conclusions] 3BP2 is involved in B cell activation in the pathogenesis of lupus, suggesting a possible new therapeutic target.

## ICW30-4

**Clinical Impact of High B-Cell-Activating Factor Levels in Patients with Rheumatic Disease Receiving Rituximab Treatment**

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Conflict of interest: None

[Objective] Rituximab (RTX) is used to treat various rheumatic diseases, leading to increased B-cell-activating factor (BAFF) levels. This single-center prospective study aimed to evaluate the clinical impact of high BAFF levels. [Methods] Patients not on biologics who were set to receive their first RTX therapy for rheumatic diseases between 2020 and 2022 were enrolled. The RTX therapy regimen consisted of two 500-mg intravenous infusions on days 1 and 15. Prior to each infusion, blood counts, routine biochemistry, and plasma cytokine levels were assessed. The increase in BAFF levels from day 1 to 15 was calculated. Clinical responses were evaluated based on the addition or tapering of current glucocorticoids (GCs), disease-modifying anti-rheumatic drugs, and non-steroidal anti-inflammatory drugs post-RTX within 6 months. Data analysis was conducted using the Kruskal-Wallis test, Spearman's rank correlation, and the generalized linear model. [Results] A total of 41 patients were included, diagnosed with antiphospholipid syndrome, Sjögren's syndrome, autoimmune thyroid diseases, and others. Initial BAFF levels (median 142.7 pg/mL; range 7.6 to 949.0) correlated with their elevation from day 1 to 15 (Spearman's rho = 0.45, $p = 0.003$). Combining belimumab reduced the BAFF increase ($p < 0.001$). Post-RTX, 4 patients (9.8%) needed more medications, whereas 8 (19.5%) could taper drugs. Factors associated with inferior clinical responses were higher initial BAFF levels ($p < 0.001$), elevated initial monocyte counts ($p = 0.043$), lower baseline GC doses ($p = 0.013$), and the absence of concurrent belimumab use ($p = 0.018$). An ROC curve identified a cut-off of 121.1 pg/mL for initial BAFF. Levels of IgG, complement, and IL-6 had no impact on outcomes. In multivariate analysis, higher initial BAFF levels independently predicted worse outcomes ($p < 0.001$). [Conclusion] Higher BAFF levels before RTX therapy predicted poorer clinical response, and belimumab treatment might improve it.

## ICW30-5

**Development of a rapid bead-based system for detecting diverse autoantibodies**

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Conflict of interest: Yes

[Objective] Autoantibody tests are clinically useful, because the disease phenotype and prognosis can be predicted from the type of autoanti-

body. However, rare autoantibodies cannot be measured in clinical tests, and the measurement process takes about one week. In order to detect diverse autoantibodies rapidly, we tried to develop in-house autoantibody detection system using magnetic beads. [Methods] Autoantigens were expressed in mammalian cell line and were immobilized on magnetic beads via a protein tag. Sera from patients who were suspected of idiopathic inflammatory myopathy were reacted with the antigen-binding beads, and after washing, fluorescent-labeled anti-human IgG antibodies were reacted. The titer of autoantibody was measured using FACS as median fluorescent intensity. [Results] Sera from 45 patients with suspected idiopathic inflammatory myopathy were tested, including 11 with anti-ARS antibody, 9 with anti-MDA5 antibody, 4 with anti-TIF1γ antibody, and 2 with anti-Mi-2 antibody. All cases that were positive in the clinical test could also be detected by the bead assay. It was possible to detect autoantibodies in serum in about 1 hour by preparing antigen-binding beads in advance, including anti-MDA5 antibodies, for which rapid detection is preferred. In the sera of 4 cases of anti-HMGCR antibody and 1 case of anti-SRP antibody measured by outsourcing, detection was possible by bead assay, except for 1 case in which the autoantibody titer was near the cutoff. Anti-OJ, anti-Ku, anti-NXP2, and anti-RuvBL1/2 antibodies were detected in cases in which autoantibodies could not be identified by clinical test and outsourcing. When several antigens were stored on beads at 4 degree, although variations in titer were observed from assay to assay, autoantibodies could be still detected after 2 months. [Conclusions] Although there are issues in accuracy control of quantitation, we established assay systems that can rapidly detect diverse autoantibodies.

## ICW30-6

**Polygenic risk score for predicting the development of autoimmune diseases using graph convolutional networks**

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Conflict of interest: None

[Objective] To develop a polygenic risk score (PRS) model specialized for autoimmune diseases using graph neural networks (GCN), in light of the suboptimal performance of linear PRS on HLA region SNPs. [Methods] Using the genotypic data of four autoimmune diseases (rheumatoid arthritis (RA), multiple sclerosis (MS), psoriasis (PSO), celiac disease (CEL)) and two non-autoimmune diseases (Atrial Fibrillation, Alzheimer's disease) from the UK Biobank. We constructed models on a cohort of 20,000 British Whites using 5-fold cross-validation and tested their performance on 10,000 non-British Whites. For RA, we also used the BioBank Japan and IORRA data. The performance of the GCN models were compared to those constructed by PRSice-2, PRScs, and a Simple Neural Net (SNN) using AUC. [Results] When constructed using SNPs from the HLA region, the GCN models consistently outperformed the conventional PRS models including PRSice-2, PRScs, and SNN models in all comparisons for each of the four autoimmune diseases with p-values <0.01. However, GCN was comparable to other methods for Alzheimer's and atrial fibrillation. When utilizing SNPs from all genomic regions, the GCN was superior to other models for the four autoimmune diseases, with the sole exception of the SNN model for RA. Visualization of the graph generated by the GCN revealed connected networks formed based on the count of HLA risk alleles (RA, *DRB1**04:01; MS, *DRB1**15:01; PSO, *B**57:01; and CEL, *DQB1**02:01). Furthermore, it was observed that networks associated with homozygous or heterozygous risk alleles exhibited a high true positive rate, while networks related to null alleles showed a high true negative rate: for RA, null allele networks had a 78% true negative rate and 0% true positive rate, while homozygous allele networks had a 45% true positive rate and 0% true negative rate. [Conclusions] PRS with GCN improved polygenic prediction of autoimmune diseases.

## ICW31-1

**Complications After Orthopedic Surgeries in Patients with Rheumatoid Arthritis Treated with Janus Kinase Inhibitors: a Retrospective Observational Study**

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Conflict of interest: None

[Objective] The current study compared the outcome after orthopedic surgeries in patients with RA receiving JAKi versus biologic disease-modifying anti-rheumatic drugs (bDMARDs). [Methods] This was a retrospective observational study of Japanese patients with RA. Sixty-two patients with RA using JAKi preoperatively underwent orthopedic surgeries. Using propensity score matching, these 62 patients were matched with 62 patients using bDMARDs preoperatively. The number of adverse events was counted. We also examined whether the drug-withholding period in the JAKi-treated group was associated with the occurrence of major postoperative adverse events, namely inflammatory flares and delayed wound healing (DWH). [Results] JAKi-treated patients had a higher incidence of postoperative flares than bDMARDs-treated patients (29% vs 12.1%, p=0.01). The incidences of postoperative complications other than flares were not significantly different between the two groups. Among the JAKi-treated group, a longer perioperative drug-withholding period (more than 11 days) was associated with a higher incidence of postoperative flares (p=0.04). The incidences of DWH and SSI were not associated with the duration of the JAKi withholding period. [Conclusions] JAKi-treated patients had a higher incidence of postoperative flares than bDMARDs-treated patients. A perioperative JAKi withholding period of more than 11 days was associated with postoperative flares.

## ICW31-2

**Comparison of efficacy and safety between anti-IL-6 receptor inhibitors and JAK inhibitors in RA patients with inadequately response to bDAMRDs, from real world practice in FIRST Registry**

Yusuke Miyazaki[1], Shingo Nakayamada[1], Koshiro Sonomoto[2], Hiroaki Tanaka[1], Kentaro Hanami[1], Shunsuke Fukuyo[1], Satoshi Kubo[3], Ippei Miyagawa[1], Ayako Yamaguchi[4], Yasuyuki Todoroki[3], Yoshino Inoue[1], Yurie Satoh Kanda[1], Msanobu Ueno[1], Yoshiya Tanaka[1]

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Conflict of interest: None

[Objective] This study aimed to establish a suitable bDMARd or tsDMARD) in RA patients with inadequate response to bDMARDS by analyzing the efficacy and safety of IL-6 receptor inhibitors (IL-6Ris) and JAK inhibitors (JAKinibs), which are often used for such therapies. [Methods] We analyzed b/tsDMARDs selected as the first- to third-line drugs in 2,291 RA patients. Among the patients unresponsive to one or more bDMARDs (bDMARD-IR), 259 and 279 patients who received IL-6Ris and JAKinibs, respectively, were selected, and the efficacy and safety of these drugs were compared via propensity score-based inverse probability of treatment weighting (PS-IPTW). [Results] TNF inhibitors were commonly selected as the first-line (n=1179/2291), IL-6Ris as the second-line (n=305/890), and IL-6Ris (n=183/457) and JAKinibs (n=117/457) as the third-line b/tsDMARDs. No differences in 26-week (w) continuation rate were shown between the two groups after PS-IPTW adjustment. The CDAI remission rate at 26w was higher in the JAKinibs group than the IL-6Ris group (p=0.01). The rate of infections was higher in the JAKinibs group (p=0.01). CDAI trajectories were analyzed using a mixed growth model and were categorized into four groups. In the IL-6Ris group,

patients with less prior use of bDMARDs were more likely to belong to the group responsive to treatment. In patients unresponsive to one bDMARD, there was no difference in CDAI remission rates at 26w between the JAKinibs and IL-6Ris groups (p=0.21). The CDAI remission rates at 26w were higher in the JAKinibs group than the IL-6Ris group in patients unresponsive to two bDMARDs. (p=0.01) and three or more bDMARDs (p=0.01). [Conclusion] IL-6Ris are superior drugs for the second-line or subsequent therapies for bDMARD-IR patients based on the balance between efficacy and safety, however JAKinibs might be suitable for patients unresponsive to multiple bDMARDs.

## ICW31-3

**Comparative Efficacy and Safety of JAK Inhibitors and Abatacept for Rheumatoid Arthritis: A Multicenter, Inverse Probability Weighting Analysis**

Kento Ichikawa[1], Yosuke Kunishita[2], Kayo Harita[3], Chikara Honda[1], Naoki Suzuki[2], Kana Higashitani[2], Yuki Iizuka[2], Yuji Uzawa[4], Chiharu Hidekawa[2], Takaaki Komiya[4], Natsuki Sakurai[2], Yuichiro Sato[5], Masaki Mitsuhashi[6], Naoki Hamada[2], Yuji Yoshioka[2], Naomi Tsuchida[7], Ayaka Maeda[2], Lisa Hirahara[2], Daiga Kishimoto[3], Kaoru Minegishi[2], Ryusuke Yoshimi[2,8], Yohei Kirino[2], Tadanobu Okubo[6], Shigeru Ohno[3], Shohei Nagaoka[4], Hideaki Nakajima[2]

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Conflict of interest: None

[Objective] To evaluate real-world efficacy and safety of approved JAK inhibitors (JAKis) including tofacitinib (TOF), baricitinib (BAR), peficitinib (PEF), upadacitinib (UPA) and filgotinib (FIL) for rheumatoid arthritis (RA) comparing with abatacept (ABT). [Methods] A multicenter retrospective case-control study of the patients who were newly administered with JAKis and ABT between July 2019 and July 2022. Patient background and clinical findings, including gender, age at onset and starting drugs, disease activity of RA, and laboratory data were collected using medical records. Disease activity was evaluated at the time of starting drugs, at 3, 6, and 12 months after starting drugs, and every year thereafter. The log-rank test was used to compare the continuation rates between JAKis and ABT. An inverse probability of treatment weighting method (IPTW) was adopted to adjust the differences of the patients' characteristics. [Results] A total of 488 patients (JAKis, 333; ABT, 155) were enrolled, 101, 93, 64, 50, 25, and 155 were used TOF, BAR, PEF, UPA, FIL and ABT. The mean observational period was 0.98 years. There was no significant difference in the 1-year continuation rates with JAKis and ABT after adjustment by IPTW (JAKis, 65.4%; ABT, 61.0%, p=0.69). The cumulative incidence probability of herpes zoster was 5.3% and 2.0% (p=0.053). For JAKis patients, the discontinued rates due to ineffectiveness, adverse events, and other reasons were 46.3%, 27.3%, 26.4%. Conversely, for ABT, 72.1%, 9.8%, and 18.0%. [Conclusions] After minimizing selection bias, JAKis exhibited a safety profile similar to ABT. herpes zoster incidence probability in JAKis was high but not significantly different from that of ABT in our cohort.

## ICW31-4

**Tofacitinib in Rheumatoid arthritis - is a well tolerated drug with minimal adverse events - a real world study of 563 patients**

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Conflict of interest: None

[Objective] JAKis (Janus kinase inhibitors) have changed the way we approach rheumatoid arthritis, With the ease of oral tablets and the introduction of generic cheap alternatives it has been increasingly used in our country. While there has been growing concerns on the occurrence of major adverse cardiovascular events it needs to be evaluated in real life scenario [Methods] All rheumatoid arthritis patients records who were prescribed tofacitinib from Jan 2021 to December 2022 with minimum of 6 months follow-up were retrieved and analysed. Patients demographics, before and after lab investigations, before and after steroids intake and drug details were noted. [Results]: There were a total of 563 patients who were included for the analysis, In this there were 489 females and 74 males. The mean age of the study population was 49.9 (11.1) years, and the mean disease duration was 4.2 (4.6) years. The mean duration of tofa intake was 18.1 (3.73) months. In this analysis, 65 of them already had biologicals. In the 563 at the time of analysis 347 (61.6%) were still on tofacitinib and remaining 216 (38.3%) had stopped tofacitinib. The reason for stopping was Better 109 (50.2%), Not responding 52 (23.9%), Poor compliance 27 (12.4), Adverse events 23 (10.6%), pregnancy 5 (2.3%). In comparing with before and after tofacitinib there was significant reduction in ESR, CRP, RF and also significant gain in weight. However, there is no significant change in the steroid doses. On analyzing the adverse events there were more fatigue (23%), minor infection (14.9%), headache (13.6%), cough (12.4%), alopecia (10%), itching (8.5%), APD (7%), UTI (5.8%), Herpes Zoster (2.1%), while major adverse events like CAD, Pneumonia, pulmonary Koch's was seen in less than 1%. [Conclusions] In this analysis we found thatTofacitinib in Rheumatoid arthritis is effective with significant reduction in inflammatory markers and minimal major adverse events.

## ICW31-5

**Comparison of risks of malignancy and MACEs associated with JAK and IL-6 inhibitor treatment: a multicenter cohort study**

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Conflict of interest: None

[Objective] The ORAL Surveillance trial showed a potentially higher incidence of malignancy and major adverse cardiovascular events (MACEs) associated with tofacitinib than those associated with tumor necrosis factor inhibitors (TNFis). However, few studies have compared the safety of non-TNFis or other Janus kinase inhibitors (JAKis). This study was aimed at comparing the incidence rates (IRs) of malignancies and MACEs in rheumatoid arthritis (RA) patients treated using interleukin-6 inhibitors (IL-6is) or JAKis. [Results] We retrospectively analyzed 427 RA patients who were treated using an IL-6i (n=273) or a JAKi (n=154). We determined the IRs of malignancy and MACEs, and the standardized incidence ratio (SIR) of malignancies and investigated factors related to malignancy and MACEs. After adjusting the clinical characteristic imbalance by propensity score matching (PSM), we compared the IRs of adverse events between the JAKi and IL-6i groups. [Results] After PSM, the observational period was determined to be 605.27 patient-years (PY), and the median observational period was determined to be 2.28 years. The IRs in the JAKi treatment were: malignancy, 2.94/100PY; MACE, 2.56/100PY. The IRRs of JAKi-treated patients versus IL-6i-treated patients were 2.13 (95% confidence interval (CI): 0.67-7.42) for malignancy and 3.03 (95%CI: 0.77-15.21) for MACE, with no significant differences between both groups. Multivariable Cox regression analyses revealed that older age and JAKi use were independent risk factors for malignancy, while older age, hypertension, and JAKi use were risk factors for MACEs. The overall malignancy SIR was significantly higher in the JAKi-treated group compared to the general population (2.10/100PY, 95%CI: 1.23-2.97). [Conclusions] The IRs of malignancy and MACE in RA patients after PSM were comparable between IL-6i-treated and JAKi-treated patients. However, the SIR of malignancy in JAKi treatment was significantly higher than in the general

population.

## ICW32-2

**The multi-trait genome-wide association meta-analysis for Systemic Sclerosis Identified a Risk Locus Shared Across Multiple Autoimmune Diseases**

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Conflict of interest: None

[Objective] We previously identified three novel risk loci (*FCRL/FCGR*, *TNFAIP3*, *PLD4*) for SSc in the largest-ever East Asian GWAS. We also identified three additional novel risk loci (*EOMES*, *ESR1*, *CD40*) by meta-analyzing with the largest European datasets. We also observed significant genetic correlations among SSc, SLE, and RA, highlighting shared genetic architecture among these traits. This study aimed to identify novel susceptibility regions for SSc by taking advantage of common genetic architectures underlying autoimmune diseases across populations. [Methods] The multi-trait analysis of genome-wide association summary statistics (MTAG) was conducted using the largest SSc, SLE, and RA summary statistics for both Japanese (14,189 cases and 420,233 controls) and European populations (35,155 cases and 98,922 controls) followed by a trans-ancestry meta-analysis. Genome-wide significant (GWS) SNPs were curated based on the direction of effect size among the traits and p-values of SSc, the local genetic correlations among the traits using LAVA, and posterior probability of replicability in SSc using MAMBA. [Results] We identified eight GWS loci in the Japanese dataset, including all five known risk loci and three novel risk loci, among which *IKZF1* was a novel risk locus and was associated across the traits. *TNFSF4* was another locus robustly shared across the traits and reported its association with SSc for the first time in Asians. In Europeans, twenty-three GWS loci including four novel risk loci were identified. One of the novel risk SNPs was positioned in an intergenic region between *IL-2* and *IL21*. The trans-ancestry meta-analysis identified thirty-nine GWS loci and nineteen novel loci including *CD28-CTLA4*, *BANK1*, *CSF2*, *WDFY4*, *ARID5B*, and *CLEC16A loci*. [Conclusions] Our largest MTAG for SSc identified novel susceptibility loci shared across autoimmune diseases among multiple populations. Our approach can also provide a reasonable method of post-MTAG variant processing.

## ICW32-3

**Impact of Rituximab vs. Cyclophosphamide on Nailfold Capillary Abnormalities in Patients with Systemic Sclerosis**

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Conflict of interest: Yes

[Objective] The effectiveness of rituximab (RTX) on fibrotic conditions including skin sclerosis and interstitial lung disease in patients with systemic sclerosis (SSc) have been elucidated, however, little is known regarding impact on capillary involvements. Herein, we aimed to determine whether RTX has efficacy against capillary abnormalities compared to intravenous cyclophosphamide (IVCY). [Methods] Patients with SSc who met the 2013 ACR/EULAR classification criteria and who started treatment with RTX or IVCY between April 2018 and April 2023 were enrolled. Capillaries were morphologically evaluated using a nailfold video capillaroscopy (NVC) at baseline (BL) and 6 months after. Nailfold capillary abnormalities were evaluated based on previous reports by evaluating enlarged capillary, giant capillary, and hemorrhage in eight fingers excluding the thumb and using the NVC score. Cases whose score ameliorated by ≧5 points were defined as "improved". [Results] RTX group included 11 patients (10 women), of whom 6 had anti-Scl-70, 4 had anti-RNA polymerase III, and 1 patient was negative for both. IVCY group included 13 patients (10 women), of whom 6 had anti-Scl-70, 3 had anti-RNA polymerase III, and 4 were negative for both. In RTX and IVCY groups, the mean age was 52.8 ± 16.4 years vs. 57.0 ± 16.5 years (p=0.48). In RTX group, the mean NVC score was 19.3 ± 17.5 at BL vs. 25.3 ± 19.1 after 6 months (p<0.01). In IVCY group, the mean NVC score was 25.2 ± 12.4 at BL vs. 13.2 ± 11.7 after 6 months (p<0.01). The mean NVC score worsened in RTX group, whereas improved in IVCY group. Regarding nailfold capillary abnormalities, "improved" was observed in only 1 patient (9.1%) in RTX group, while in 9 patients (69.1%) in IVCY group. (p<0.01) [Conclusions] RTX was less effective in improving nailfold capillary abnormalities than IVCY in patients with SSc, which may be due to differences in target molecules.

## ICW32-4

**The association of nailfold capillary densities with exercise-induced pulmonary hypertension in Systemic sclerosis**

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Conflict of interest: None

[Objective] Exercise-induced pulmonary hypertension (ExPH) is a recently introduced concept in the 2022 European Society of Cardiology/European Respiratory Society guidelines. It highlights the significance of promptly identifying and addressing pulmonary arterial hypertension (PAH). Our investigation focused on understanding the attributes of ExPH patients with Systemic sclerosis (SSc). [Methods] Nineteen SSc patients experiencing exertional fatigue symptoms participated in the study, undergoing exercise right heart catheterization (ExRHC). We conducted a comparative analysis of clinical features among ExPH, established PAH, and Non-PAH groups. [Results] The mean age of the participants was 65.8 years, and all patients exhibited Raynaud's phenomenon (RP). The mean disease duration from RP was 12.1 years, and 42.1% (8/19) of patients had interstitial lung disease. Among these patients, 6 were diagnosed with PAH, 9 with ExPH, and 4 with Non-PAH. Notable differences were observed between PAH and Non-PAH, particularly in %DLco (Non-PAH vs PAH = 85.5 vs 36.7, p = 0.01), 6-minute walking distance (m) (Non-PAH vs PAH = 505 vs 205, p = 0.01), and Tricuspid regurgitation pressure gradient (TRPG) (mmHg) (Non-PAH vs PAH = 21.3 vs 36.3, p = 0.02) as assessed by echocardiography. However, no significant differences were found in these parameters between ExPH and Non-PAH. Of note, palpitations during exertion were significantly more common in ExPH compared to Non-PAH (Non-PAH vs ExPH = 88.9% vs 25.0%, p = 0.02). Additionally, capillary density (/mm) observed through nailfold videocapillaroscopy was notably lower in the ExPH group (Non-PAH vs ExPH = 8.0 vs 4.8, p = 0.01). [Conclusions] The %DLco and TRPG, commonly employed for established PAH screening, may not be sufficient for ExPH detection. Our study indicates that evaluating nailfold capillary density and monitoring symptoms such as exertion-induced palpitations could prove valuable for early PAH identification.

## ICW32-5

**Peripheral blood phenotype characteristics of patients with systemic sclerosis (SSc) who benefit from Rituximab (RTX)**

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Conflict of interest: None

Objective: To investigate the effectiveness of RTX for skin sclerosis

and interstitial lung disease (ILD) in SSc and to delineate the clinical characteristics of cases responded to RTX Methods: We compared 32 SSc patients (pts) receiving RTX with 32 pts on SoC, adjusting for background differences using PS-IPTW. Primary outcomes at 24 weeks were mRSS and %FVC changes. Secondary outcomes studied immunophenotypes in pts with improved skin sclerosis or ILD. Result: Age, sex (female), and disease duration were 61.2 years, 71.9%, and 6.1 years in RTX group (RTX), and 60.6 years, 87.5%, and 7.2 years in SoC group (SoC), respectively. mRSS was 13.0 in RTX and 14.0 in SoC. 16 pts (50.0%) improved in mRSS after RTX (mean 16.0 to 12.0, p=0.047), compared to 8 pts (25.0%) in SoC (14.0 to 12.5, p=0.331). We examined potential predictors of treatment response to skin sclerosis in RTX but did not identify any factors within the pts' clinical background that contributed to the improvement in mRSS. When examining the lymphocyte phenotype by FCM, we found that higher counts of class-switched memory (CSM) B cells, IgM memory B cells, and Th1 cells were associated with a positive response to RTX (p=0.04, p=0.04, p=0.03). On the other hand, there was no association between immunophenotype and treatment response in the SoC. Calculating the cut-off values by ROC, CSM B cells 15.2 cells/μl, IgM memory B cells 3.4 cells/μl, and Th1 cells 147.4 cells/μl were estimated, respectively, and the improvement in skin sclerosis was greater in the cases with cut-off values or higher. Notably, 87.5% of pts with Th1 cell counts above this threshold exhibited improvement. Regarding FVC improvement in pts with ILD (13 vs. 19), the RTX % FVC change was +1.6% and the SoC -0.3% at 24 weeks, with no significant improvement in either group. Conclusion: RTX has shown clinical effectiveness against skin sclerosis. Prediction of the efficacy of RTX might be feasible by assessing peripheral blood lymphocyte phenotypes.

## ICW32-6

**Single-cell RNA sequencing discovers immune cell abnormalities underlying scleroderma renal crisis**

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Conflict of interest: Yes

[Objective] The purpose of this study is to clarify the abnormalities of immune cells in scleroderma renal crisis (SRC), and to get a closer look at their involvement in the pathogenesis. [Methods] Peripheral blood samples from 21 systemic sclerosis (SSc) patients (4 with SRC, 17 without SRC) and 6 age-matched healthy donors (HD) were collected. None of them were medicated with glucocorticoids or immunosuppressants. Kidney tissue was also obtained from one patient in active renal crisis. Droplet-based method from 10x Genomics was used for single cell isolation of blood samples. CITE-seq, a method to measure transcriptome and multiple surface proteins simultaneously at single cell level, was performed. Datas were integrated using SCTransform, based on the Seurat methodology. Differential gene expression analysis, Differential abundance (DA) analysis and pseudotime analysis were conducted to identify immune dysregulation in SRC. [Results] DA analysis revealed an increase in a sub-population of monocyte, expressing specific genes in patients with SRC compared to patients without SRC or HD. It was considered to be SRC-specific, because the same population was not found in samples derived from patients with other autoimmune disorders. By differential gene expression analysis, characteristics of SRC-specific monocytes were estimated. Longitudinal analysis showed an increase in this distinct monocyte subpopulation during the onset of SRC and its subsequent decrease after treatment. Analysis of kidney tissue revealed an increase in macrophages with an inflammatory phenotype derived from the SRC-specific monocytes. [Conclusions] Our findings highlight the important role of a specific monocyte population in the pathogenesis of SRC. Unique changes in gene expression of these cells could be a potential therapeutic target for SRC.

## ICW33-1

**IFN-alpha promotes the functional damage of peripheral CD-56dimCD57+ NK cells in systemic lupus erythematosus patients by up-regulating HIF-1alpha-mediated mtROS production**

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Conflict of interest: None

[Objective] Our previous study found that the peripheral CD-56$^{dim}$CD57$^{+}$ NK cell was significantly reduced, and exhibited increased apoptosis and impaired cytotoxicity in response to activated CD4$^{+}$ T cells in systemic lupus erythematosus (SLE). Our present study aimed to investigate the effects of interferon-α (IFN-α) on CD56$^{dim}$CD57$^{+}$ NK cell in SLE patients and explore the specific mechanism. [Methods] After collecting the peripheral blood of healthy control (HC) and SLE patients, the levels of functional molecules, cytotoxicity to K562 cells, hypoxia-inducible factor (HIF)-1α and mitochondrial reactive oxygen species (mtROS) in CD-56$^{dim}$CD57$^{+}$ NK cell were detected by flow cytometry. Serum IFN-α was determined by ELISA. And the levels of apoptosis, functional molecules, HIF-1α and mtROS of CD56$^{dim}$CD57$^{+}$ NK cells treated with $H_2O_2$ or ROS scavenger N-acetyl cysteine (NAC) or IFN-α and HIF-1α inhibitor were detected by flow cytometry. [Results] Compared with HC, the levels of granzyme, perforin, CD107a, CD16 and cytotoxicity to K562 cells were significantly decreased, and the level of mtROS was significantly increased in peripheral CD56$^{dim}$CD57$^{+}$ NK cells from SLE patients. Moreover, $H_2O_2$ treatment significantly increased the apoptosis and down-regulated the perforin expression of CD56$^{dim}$CD57$^{+}$ NK cells from HC. Meanwhile, NAC significantly decreased the apoptosis and restored perforin expression of CD56$^{dim}$CD57$^{+}$ NK cells from SLE patients. The levels of serum IFN-α and HIF-1α in CD56$^{dim}$CD57$^{+}$ NK cells were increased in SLE patients. And IFN-α stimulation increased mtROS production and apoptosis, but decreased cytotoxic molecules expression of CD56$^{dim}$CD57$^{+}$ NK cells, which could be restored by HIF-1α inhibitor. [Conclusions] The high level of serum IFN-α in SLE patients may promote the production of mtROS by up-regulating HIF-1α to induce apoptosis and impair cytotoxic activity of CD56$^{dim}$CD57$^{+}$ NK cells.

## ICW33-2

**Tissue-Resident Memory T cell differentiation and pathological relevance in Systemic Lupus Erythematosus**

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Conflict of interest: None

[Objective] Tissue-Resident memory T (Trm) cells are a novel cell subset involved in local immunity. Trm cells were identified in affected organs of autoimmune diseases. However, the mechanism of differentiation and their involvement in the pathogenesis of autoimmune diseases remain unclear. We investigated (1) the characterization of Trm cells in RA/SLE patients, and (2) the differentiation mechanisms and functions of human Trm cells in vitro. [Methods] The percentage of peripheral blood CD8$^{+}$CD69$^{+}$103$^{+}$ T cells (Trm-like cells) in RA/SLE patients was compared. The study included 40 RA patients, 26 SLE patients, and 10 healthy donors (HDs). The patients were enrolled in our RA cohort (FIRST Registry) or SLE cohort (LOOPS registry) and consented to a comprehensive immunophenotyping study (FLOW study). Naive CD8$^{+}$ T cells (CD45RA$^{+}$CCR7$^{+}$) isolated from the peripheral blood of HDs were then cultured under various stimuli and assessed for cell surface molecules, cytokines/serine protease production, and transcription factors by flow cytometry and PCR. [Results] (1) Trm-like cells in the peripheral blood were significantly increased in RA/SLE patients compared to HDs (p<0.001). (2) In SLE patients, Trm-like cells expressed higher levels of Blimp-1, correlated with anti-ds-DNA antibody titer (rs=0.468, p=0.016) and inversely correlated with CH50 (rs=-0.397, p=0.045). (3) Trm-like cells were induced from

naive CD8$^+$ T cells by TCR+TGF-β1+IL-15 stimuli in vitro ($p<0.001$). (4) Trm-like cells produced high IFN-γ and granzyme B levels and survived for more than 15 days in vitro. (5) The addition of JAK inhibitors prevented differentiation into Trm-like cells and reduced the production of granzyme B. [Conclusions] Trm cells were present in the peripheral blood of SLE patients and were associated with disease activity. Trm-like cells differentiate upon IL-15+TGF-β1 stimulation and induce inflammation and tissue damage, suggesting that Trm cells are potential therapeutic targets in SLE.

## ICW33-3

**Role of IFNg producing CD4+T cells induced in IMQ-induced SLE model mice**

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Conflict of interest: Yes

[Objective] In our previous study, imiquimod (IMQ) administration significantly increased splenic IFNγ producing CD4+ T cells in C57BL/6 wild-type (WT) mice, which suggested their involvement in pathogenesis of IMQ induced lupus mice model. The aim of this study to identify the detailed role of IFNγ producing CD4+ T cells in the development of lupus using IFNγ-deficient (KO) mice. [Methods] After administration of IMQ in C57BL/6 WT mice and KO mice, 1) lupus phenotype was evaluated by measuring serum anti-dsDNA IgG antibody titer and staining of C3 and IgG in kidney. We also evaluated 2) CD4+ T cell subsets, 3) Cytokine production from in vitro stimulated CD4+ T cells, and 4) B cell subsets in spleen by flowcytometry (FCM). 5) Splenic CD4+ T cells of WT-IMQ or WT-Control mice were co-cultured with splenic naïve B cells of WT-Control mice for 3 days, and then B cell differentiation was evaluated by FCM. 6) After 7 days of co-culture described in 5), IgG levels in culture supernatant were measured by ELISA. [Results] 1) Serum anti-dsDNA antibody titer was significantly decreased, and C3 and IgG deposition tended to be attenuated in KO mice compared with WT mice. 2) There was no significant difference in PD-1+CXCR5+ Tfh cells and PD-1+CXCR5- Tph cells between them. 3) IL-17 producing CD4+ T cells were significantly increased in KO mice compared with WT mice. 4) Plasmablasts were significantly increased, and plasma cells tended to be decreased in KO mice compared with WT mice. 5) Differentiation into CD19+CD11c+ age associated B cells from naïve B cells tended to be increased after co-cultured with CD4+ T cells of WT-IMQ mice compared with WT-Control mice. 6) IgG levels tended to be increased after co-cultured with CD4+ T cells of WT-IMQ mice compared with WT-Control mice. [Conclusion] These results raised the possibility that IMQ induced IFNγ producing CD4+ T cells may be involved in autoantibody formation of SLE via enhanced differentiation of antibody secreting cells.

## ICW33-4

**Clinically inactive SLE resting naïve B cells retains abnormal transcriptome and epigenome**

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Conflict of interest: None

[Objective] B cells, the progenitors of autoantibody producing plasma cells, are a key pathogenic cell type in systemic lupus erythematosus (SLE). We previously reported that resting naïve B cells from active patients have already shown the specific transcriptional and epigenetic changes that differentiate them from naïve B cells from healthy donors. However, it is unclear to what degree these changes are due to disease activity. [Methods] SLE diagnosis and activity were defined by the 2019 EULAR/ACR classification and the SELENA-SLEDAI index such as active (SLEDAI≧5) or inactive (SLEDAI<5) disease. Resting naïve B cells from active lupus patients, inactive lupus patients, and healthy donors were compared by transcriptome and epigenome. [Results] Transcription and chromatin accessibility were analyzed by RNA (healthy 17, inactive 15, active 12) and ATAC sequencing (healthy 10, inactive 10, active 7) of RNA and DNA isolated from sorted resting naïve B cells. The 3 groups were clearly separated by principal component analysis. Intriguingly, CD40 and cytokine (IL-12, IL-10 and TNFα) signaling and germinal center light zone gene sets were all enriched in inactive patients in addition to shared interferon signature in SLE by gene set enrichment analysis. Epigenetically, more differentiated accessible regions (DAR) were detected in inactive patients than active patients almost not accompanied by increased gene expression, suggesting these open regions may be epigenetic memory. Page Rank analysis revealed naïve B cells from inactive patients preferred TCF- and MEF-family transcription factor compared to STAT- and IRF-family upregulated in active patients. [Conclusions] These results indicate that distinct signaling programs are active in resting naïve B cells from inactive patients. Understanding these pathways and their epigenetic regulation may potentially provide new therapeutic approaches to maintain long term remission.

## ICW33-5

**Gut Commensal Translocation as a Trigger for Autoantibody Production in Systemic Lupus Erythematosus**

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Conflict of interest: Yes

[Objective] While the gut microbiome has been spotlighted as a causative factor in lupus pathogenesis, the underlying mechanisms remain elusive. The present study aimed to elucidate whether specific gut commensals could translocate across the mucosal barrier, and contribute to autoantibody production via molecular mimicry. [Methods] Bacterial translocation was evaluated by non-selective culture of mesenteric lymph nodes (MLNs) in B6SKG mice, a spontaneous lupus model characterized by impaired T cell receptor signaling and gut dysbiosis. The pathogenic potency of cultured bacteria and its antigen was investigated by *in vivo* experiments, enzyme-linked immunosorbent assay (ELISA), immunoblotting and epitope mapping. [Results] While the frequencies of bacterial translocation were not different between B6SKG and wild-type mice, the profile of cultured gut commensals was altered. *Lactobacillus. murinus* (*L. murinus*)-translocated B6SKG mice showed significantly higher titers of anti-dsDNA antibody, and the injection of heat-killed *L. murinus* replicated autoantibody production. Immunoblotting of *L. murinus* lysates with B6SKG mice sera detected a common protein band, identified as peptide ABC transporter (ABCT) by mass spectrometry. Recombinant ABCT partly neutralized anti-dsDNA antibodies by ELISA inhibition assay, and *in vivo* immunization with ABCT accelerated autoantibody production. Notably, SLE patients showed elevated titers of anti-ABCT antibodies. Epitope mapping of ABCT revealed shared binding sites between B6SKG mice and SLE patients. Part of the binding sequences was predicted as MHC class II-restricted epitopes, and located on the protein's surface in the three-dimensional model structure. [Conclusions] A gut symbiont translocating in MLNs promoted the production of lupus autoantibodies via its mimicry antigen in genetically predisposed hosts. Commensal-induced molecular mimicry as well as bacterial translocation may serve as pathogenic environmental factors of autoimmunity.

## ICW33-6

**Elucidation of the involvement of a novel age-associated CD4$^+$ T cell subset in the pathogenesis of systemic lupus erythematosus**

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Conflict of interest: Yes

[Objective] Aging is one of the risk factors for developing autoimmune diseases, but the precise role of immune senescence in the pathogenesis of autoimmune disorders remains unclear. We have identified and characterized a novel CD4$^+$ T cell subset, "Age-associated helper T (ThA)" subset, which increased with age and in autoimmune diseases. [Methods] A total of 354 samples of flow cytometry data and 1562 RNA-seq data from nine CD4$^+$ T cell subsets were obtained from healthy controls (HC) and patients with systemic lupus erythematosus (SLE), rheumatoid arthritis, and idiopathic inflammatory myositis. We conducted differential expression analysis and variance partitioning analysis to assess the subset's functions and impacts on the pathogenesis of SLE. ThA cells were isolated from PBMCs to perform *in vitro* functional and gene regulatory analyses. [Results] The proportion of ThA cells was positively correlated with age in HC and autoimmune patients. ThA cells from autoimmune disease patients characteristically expressed *CXCL13*, a potent chemoattractant of B cells, compared to HC. *In vitro* experiments showed that ThA cells induced B cell antibody production and that type I interferon enhanced CXCL13 production in ThA cells. We have also identified transcription factors that regulate the *CXCL13* expression of ThA cells. Intriguingly, variance partitioning analysis revealed that gene expression variation in SLE-ThA cells had the most considerable impact on disease activity compared to other CD4$^+$ T cell subsets. The expression levels of *CXCL13* in SLE-ThA cells correlated with disease activity score, SLEDAI-2K, and were associated with serum anti-Sm antibody levels. Moreover, calcineurin inhibitors significantly affected gene variation in SLE-ThA. [Conclusions] ThA cells play a crucial role in the pathogenesis of SLE. Further analysis of ThA cells will shed light on the link between aging and autoimmune diseases, including SLE, potentially discovering new drug targets.

## ICW34-1

**Femoral nerve approaches the anterior acetabulum at hip osteoarthritis. A comparative study using magnetic resonance imaging improving nerve visualization**

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Conflict of interest: None

[Objective] Femoral nerve palsy after total hip arthroplasty may result from a retractor due to the closeness of the femoral nerve (FN) and anterior acetabulum (AA), however, there is little information on the distance between the FN and AA in hip osteoarthritis (OA). This study aims to evaluate the distance between the FN and AA in hip OA and test the hypothesis that the FN is closer to the AA with an atrophic iliopsoas muscle in an OA hip compared to a normal hip. [Methods] Forty-one patients with unilateral hip OA underwent magnetic resonance imaging. Three measurement levels were defined, and the minimum distance between the FN margin and AA rim was measured on axial T1-weighted images on the OA and normal sides at each level, with reference to an advanced neurography view. Three observers also measured the cross-sectional area (CSA) of the iliopsoas muscle at each level bilaterally. Distances and CSAs were compared between the OA and normal side. Multiple regression analysis was performed to identify variables associated with the distance in OA. [Results] The mean minimum FN to AA distances in OA were 19.4 mm at the top of the anterior inferior iliac spine (AIIS), 24.3 mm at the bottom of the AIIS, and 21.0 mm at the tip of the greater trochanter. These distances were significantly shorter than in normal hips at the top and bottom of the AIIS, with mean differences of 1.6 and 5.8 mm, respectively ($p=0.012$, $p<0.001$). CSAs of the iliopsoas in OA were significantly smaller at all levels (all $p<0.001$), with reductions of 10.5% to 17.9%. The CSA of the iliopsoas at the bottom of the AIIS was associated with the FN to AA distance at the same level ($p = 0.026$). [Conclusions] The hypothesis of a shortened FN to AA distance in OA is applicable to the bottom of the AIIS level. To minimize the risk of femoral nerve palsy, a retractor placed around the AIIS and the tip of the greater trochanter level of the AA should be within 19 mm in length in OA hip surgery.

## ICW34-2

**JAK inhibitor suppresses STAT3 activation in synovial tissues from the hip joint in the early stage of rapidly destructive coxopathy**

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Conflict of interest: None

[Objective] Interleukin-6 signaling activates signal transducer and activator of transcription 3 (STAT3), resulting in matrix metalloproteinase (MMP)-3 production. The hip joints with rapidly destructive coxopathy (RDC) show rapid chondrolysis, probably by increased levels of MMP-3 in the synovial fluid in the affected hip joint. Constitutive activation of STAT3 is observed in synovial tissues from the joint with rheumatoid arthritis in contrast to no apparent activation in synovial tissues from the joint with osteoarthritis. Currently, no information is available on STAT3 activation in the RDC synovial tissues. This study aimed to investigate STAT3 activation in the synovial tissues with joint destruction in the early stage of RDC. This study also investigated the effect of tofacitinib on STAT3 activation in the synovial tissues from the hip joint with RDC. [Methods] Synovial tissues within 7 months from the disease onset were obtained from four RDC patients with femoral head destruction and high serum levels of MMP-3. The tissues were incubated with or without tofacitinib. Immunohistochemical examination was performed to detect STAT3 phosphorylation with anti-phospho-STAT3 antibody. [Results] RDC synovial tissues demonstrated the synovial lining hyperplasia with an increase of CD68-positive macrophages and CD3-positive T lymphocytes. STAT3 activation was found in the synovial tissues. The majority of phospho-STAT3-positive cells were the synovial lining cells and exhibited negative expression of macrophage or T cell marker. Treatment with tofacitinib resulted in a decrease in phospho-STAT3-positive cells, especially with high intensity, indicating effective suppression of STAT3 activation in RDC synovial tissues. [Conclusions] Inhibitory effect of tofacitinib could work through the Janus Kinase/STAT3 axis in the synovial tissues in the early stage of RDC. Thus, STAT3 may be a potential therapeutic target for prevention of joint structural damage in RDC.

## ICW34-3

**Oral delivery of delta-9-tetrahydrocannabinol provides symptom and disease modification in mouse models of knee osteoarthritis**

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Conflict of interest: None

**Objectives:** Osteoarthritis (OA) is a joint disease that affects cartilage and synovium. Some OA patients use cannabis to alleviate pain. $\Delta^9$-tetrahydrocannabinol (THC), a prominent phytocannabinoid, can signal in joint cells. We investigated the effects and signalling mechanisms of THC on pain and joint degeneration in pre-clinical models of knee OA. **Methods:** Destabilization of the medial meniscus (DMM) and monosodium iodoacetate (MIA; 0.5 mg) mice were given THC (0, 5, or 10 mg/kg) orally 5 days/week for 9 or 3 weeks, respectively. Von Frey tests were used to evaluate pain. DMM mouse joints were assessed for cartilage degeneration/synovitis (OARSI scoring) and Ki67/αSMA expression [immunohistochemistry (IHC)]. FLS and chondrocytes from human OA synovium and cartilage were treated with 0-10μM THC for 48h. Flow cytometry was

used to detect Annexin V$^+$ cells. RNA sequencing was performed on THC-treated (1μM) OA FLS and chondrocytes to determine differentially expressed genes (DEGs) and DEG-enriched pathways. **Results:** 10 mg/kg THC provided the most significant pain reduction in DMM and MIA mice (n=15/group). In DMM mice, all THC doses reduced cartilage degeneration, with 10 mg/kg THC reducing synovitis (n=9-10/group) and decreasing αSMA but not Ki67 synovial expression (n=6/group). *In vitro*, THC increased Annexin V$^+$ OA FLS and chondrocytes at 2.5 μM (n=5). RNA sequencing identified 73 DEGs in OA FLS and 21 DEGs in OA chondrocytes after 1μM THC treatment (n=4). Extracellular matrix (ECM) organization and cholesterol biosynthesis pathways were enriched in upregulated and downregulated genes, respectively, in both cell types. **Conclusions:** 10 mg/kg THC reduced pain, cartilage degeneration, synovitis, and synovial αSMA expression in DMM/MIA mouse knee joints. THC treatment of human OA FLS and chondrocytes modified gene expression associated with ECM organization and cholesterol biosynthesis. Next studies will focus on identifying signalling mechanisms of THC in joint cells.

## ICW34-4

**Mid-term results of revision total hip arthroplasty with KT plate and allograft**

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Conflict of interest: None

[Objective] We have been using KT plate and allograft for revision of cup loosening with bone loss after total hip arthroplasty (THA). We investigated the mid-term results of this procedure. [Methods] Thirty-six hips (6 males, 7 hips; 25 females, 29 hips) who underwent revision THA using KT plate and allograft between 2003 and 2017 and were followed up for at least 5 years were included in the study. Primary diseases were 31 osteoarthritis, 2 osteonecrosis of femoral head, 2 giant cell tumor of bone, and 1 rheumatoid arthritis. The mean age at revision was 66.5 (36-83) years, and mean follow-up was 10.7 (5-20) years. The degree of bone loss, the method and size of bone graft, breakage or migration of KT plate, postoperative complications, and JOA score were investigated. [Results] The degree of bone loss was Paprosky classification type 1: 4, type 2: 16, and type 3: 16 hips. The method of bone graft (chip/bulk) was 9/27 hips each. The maximum thickness of the bone graft averaged 17.5 mm (6-32 mm). Breakage of KT plate occurred in 4 hips (11.1%), and displacement of >3° or cephalad migration of >3 mm occurred in 3 hips. Two of the 7 hips had chipped graft, and the other 5 hips had bulk graft, but the hooks on the KT plate were not hooked to the teardrop sufficiently and were not associated with the thickness of the grafted bone ($p = 0.16$). Postoperative complications were dislocation in 5 hips (13.8%) and infection in 2 hips (5.6%). Re-revision THA was performed in 5 hips (13.8%; 1 KT plate breakage, 2 dislocations, 2 infections). The cumulative survival rate was 97.2% with the endpoint of revision THA due to KT plate migration, and the mean JOA score significantly improved from 61.7 points (16-98) preoperatively to 83.2 points (56-97) at the last follow-up ($p<0.001$). [Conclusions] The mid-term results of revision THA with KT plate and allograft were excellent. It is important to use a bulk bone graft in the loading area and to firmly attach the hooks to the teardrop.

## ICW35-1

**Sarcopenia and Osteoporosis in patients with psoriatic arthritis: a single-center retrospective study**

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Conflict of interest: None

[Objective] In this study, we collected data on sarcopenia and osteoporosis in patients with PsA at our institution and evaluated the associations and risk factors. [Methods] The data in this study were extracted from 320 patients with PsA meeting CASPAR criteria diagnosed between January 2010 and December 2021 at Nippon Life Hospital. The 156 patients who had undergone body composition measurements with dual-energy X-ray absorptiometry were included. The data were collected, including sex, age, BMI, the duration of psoriasis, the duration of PsA, RF, ACPA, grip power, skeletal muscle mass Index (SMI), ASDAS-CRP, DAPSA, DAS28-CRP, prednisolone usage, MTX usage, MTX dose, biologics usage, osteoporosis treatment, T-score (lumber and femur). [Results] Overall, the rate at which SMI met sarcopenia criteria was 23.7%. Only BMI was significantly different between patients with and without Sarcopenia. There was also a correlation between SMI and BMI. Multivariate analysis of the determinants of SMI showed that age, gender, BMI, and grip strength were significantly involved. Furthermore, the patients with DXA measured within 1 year of the time the SMI was measured were evaluated (N=127). Regarding gender differences, T-score was lower in females and significantly different in Femur. Although the proportion of women in each group was similar, with and without Sarcopenia, the sarcopenia group had a significantly lower BMI, a significantly lower T-score in all regions, and significantly more cases of osteoporosis treatment. Correlations were observed between SMI and T-score, and between BMI and T-score. Multivariate analysis of the determinants of T-score for each site showed that SMI was significantly involved for the lumbar spine and the femoral neck, and BMI and RF positivity for the total hip. [Conclusions] In patients with PsA, SMI, T-score, and BMI are correlated with each other and should be taken into account in clinical practice.

## ICW35-2

**Nail Involvement as an Independent Risk Factor for Left Ventricular Diastolic Dysfunction in Psoriatic Arthritis Patients**

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Conflict of interest: None

[Objective] Asymptomatic left ventricular diastolic dysfunction (LVDD) is associated with incident heart failure. Although early cardiovascular involvement and higher prevalence of LVDD have been found in patients with psoriatic arthritis (PsA), few studies have related this to nail psoriasis (NP). This study aims to investigate the effect of NP on cardiac function and explore the risk factors of LVDD among PsA patients. [Methods] A total of 116 PsA patients without clinical evidence of cardiovascular disease were recruited from June 2016 to December 2022 at the Rheumatology Department in Huashan Hospital, Fudan University. All underwent conventional echocardiography Doppler imaging. [Results] There were 80 patients (69.0%) with NP and 36 patients (31.0%) without NP. The left atrial diameter, left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left ventricular posterior wall thickness, left ventricular end-diastolic volume, stroke volume and left ventricular mass index in patients with NP were significantly higher than those in patients without NP. The incidence of LVDD was significantly higher in NP group than in non-NP group (37.5% vs 13.8%). Compared with non-LVDD group, patients with LVDD were older, had a longer disease duration, a higher prevalence of hypertension and type 2 diabetes mellitus. Multivariate Logistic regression analysis showed that NP (OR 7.556, 95%CI 1.328-42.993, P=0.023), age (OR 1.125, 95%CI 1.046-1.210, P=0.003) and hypertension (OR 4.788, 95%CI 1.078-21.274, P=0.04) were independent predictors of LVDD. The AUROC of LVDD diagnosed by NP, age and hypertension was 0.867 (95%CI 0.796-0.939, P<0.001). [Conclusions] Subclinical left ventricular diastolic dysfunction was common in patients with PsA, especially in those with nail lesions. Therefore, it is important to closely monitor the cardiac function of PsA patients with nail psoriasis in order to identify individuals at high risk for cardiovascular disease.

## ICW35-3

**Metabolic and Inflammatory Profiles of Entheses in Psoriasis and Psoriatic Arthritis Patients: Insights from Multispectral Optoacoustic Tomography**

David Simon[1,2], Koray Tascilar[2], Rita Noversa De Sousa[2], Sara Bayat[2], Lukas Sollfrank[3], Arnd Kleyer[1,2], Michael Sticherling[3], Adrian P Regensburger[4], Ferdinand Knieling[4], Markus F Neurath[5], Georg Schett[2], Maximilian Waldner[5], Filippo Fagni[2]
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Conflict of interest: Yes

[Objective] The aim of this study was to use multispectral optoacoustic tomography (MSOT) to evaluate and compare metabolic and inflammatory changes at the entheses in patients with psoriasis (PsO), psoriatic arthritis (PsA), and healthy controls (HC). [Methods] This cross-sectional study was conducted with PsA and PsO patients who had not received bDMARD treatment, as well as HC individuals. The participants underwent clinical, ultrasonographic, and MSOT examinations of six different entheses. MSOT measurements included hemoglobin (Hb), oxygen saturation (SO2), collagen, and lipid levels, which were quantified, and mean differences between groups were calculated using linear mixed-effects models. MSOT-measured analytes were compared between entheses with and without clinical and ultrasound anomalies. [Results] The study included ninety participants (30 PsO, 30 PsA, 30 HC). A total of 540 entheses were clinically assessed, and 540 ultrasound and 830 MSOT scans were conducted. Both PsA and PsO patients exhibited significantly increased levels of MSOT-measured oxygenated Hb (PsA: p=0.005; PsO: p=0.001) and SO2 (PsA: p<0.001; PsO: p=0.001) and decreased collagen signals (PsA: p<0.001; PsO: <0.001) when compared to HC, with more pronounced changes observed in PsA. There were significantly lower collagen levels (p=0.01) and increased lipids (p=0.03) in tender entheses compared to non-tender ones. Erosions and enthesophytes observed on ultrasound were associated with significant MSOT-measured differences in SO2 and lipid signals, respectively (both p=0.003). [Conclusions] Patients with PsA and PsO exhibit a similar metabolic pattern at the entheses, which is further exacerbated in the presence of inflammation. These findings support the idea of a psoriatic disease spectrum characterized by common immuno-metabolic tissue changes.

## ICW35-4

**Precision medicine using different biological DMARDs based on the serum IL-22 concentration in psoriatic arthritis**

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Conflict of interest: Yes

[Objective] This study evaluated the possibility of strategic treatment based on the serum cytokine concentration (IL-6,7,12,17A/F,21,22,23, IFN-γ, TNF-α). Immunological characteristics of each subgroup were clarified by evaluating the relationship among treatment response, peripheral blood immune phenotypes, and serum cytokine profiles. [Methods] 68 patients were included. We identified the cytokines that predict the achievement of DAPSA-REM for TNF/IL-17A-i, developed a treatment strategy, and evaluated the effectiveness for up to 12 months. Immunophenotyping was performed for T, B, NK cells, DCs, and monocytes. The association between treatment response, cytokine profiles, and immune phenotypes was assessed. [Results] Low serum IL-22 concentration was identified as a predictive factor for achieving DAPSA-REM for IL-17A inhibitors. PsA was classified into IL-22 low and IL-22 high types. The increase of IL-17A is common to both types. TNF-α was increased only in the IL-22 high type. By strategic use of TNF (IL-22 high) and IL-17A-i (IL-22 low), DAPSA-REM was achieved in 90% and MDA in 80% in the strategic treatment group (standard treatment: DAPSA-REM 66%. MDA 41%). IL-22 was positively correlated with TNF-α and IL17A, but the correlation was stronger between IL-22 and TNFα. There was no correlation between IL-17A and TNF-α. Compared to HC, abnormal differentiation of CD4+/CD8+ T cells, NK cells, dendritic cells, monocytes, and increased activated CD4+/CD8+ T cells are common in PsA. The non-classical/classical monocyte ratio was significantly higher in the IL-22 high type and was positively correlated with IL-22 and TNF-α. Neither TNF/IL17 inhibitors had any effect on the immune phenotype. [Conclusions] The possibility of serum cytokine-based precision medicine was demonstrated. The analysis of treatment response, cytokines, and immunophenotyping revealed the possible presence of a subgroup with increased monocyte and TNF-α in addition to the common immune phenotypes.

## ICW35-5

**Utility of a multi-biomarkers panel on predicting disease activity in patients with psoriatic arthritis - a derivation and validation study**

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Conflict of interest: None

[Objective] To investigate the correlation of serum protein biomarkers and disease activity in patients with PsA. [Methods] 176 patients fulfilled the CASPAR (ClASsification criteria for Psoriatic ARthritis) were recruited in this cross-sectional study. Disease activity was measured by the clinical Disease Activity in Psoriatic Arthritis (cDAPSA). 45 protein biomarkers, cartilage and bone turn-over markers level were assessed. The patients were randomly divided into a derivation-cohort and a validation-cohort at a ratio of 7:3. Least absolute shrinkage and selection operator (LASSO) was used to select biomarkers which were associated with moderate/high disease activity in the derivation cohort. Receiver operating characteristic (ROC) curve, GiViTI calibration belt were used to assess the performance of the model in both cohorts. [Results] The cohort [age: 55.5 (44.0-62.75) years, male: 80 (45.5%)] had moderate disease activity [DAPSA: 15.9 (8.3-26.9); PASI: 3.2 (0.5-6.8)]. 101 PsA patients (57.4%) had moderate/high disease activity. Biomarker levels associated with moderate/high disease activity included SAA (Serum amyloid A), IL8 (Interleukin 8), IP10 (Interferon gamma-induced protein 10), M-CSF (Macrophage colony-stimulating factor), SCGF-β (Stem cell growth factor), SDF-1α (Stromal cell-derived factor 1α). The model's equation including the 6 biomarker levels was applied to the validation-cohort. The area under the ROC curve (AUC) for discriminating moderate/high disease activity was 0.802 and 0.835 for the derivation-and-validation-cohorts, respectively. The multi-biomarkers panel model had higher-AUC when compared with that of CRP (AUC=0.727, $p$=0.022). The P-values of calibration charts in the two sets were 0.902 and 0.123. [Conclusions] The multi-biomarkers panel had excellent performance in discriminating patients with moderate/high disease activity from those with low disease activity/remission.

## ICW36-1

**Study on the mechanism of lactate regulating the function of Tph cells in rheumatoid arthritis patients through protein lactylation modification**

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Conflict of interest: None

[Objective] Our previous study results found that the serum lactate level was significantly increased in RA patients compared with healthy people, and it was positively correlated with the disease score. Not only is lactate a metabolite, it can also influence epigenetics by regulating gene transcription by modification of histone lactylation. The aim of this study is to investigate the effect of lactate on the function of Peripheral helper T (Tph) cells in RA patients and the specific mechanism. [Methods] Peripheral blood samples of RA patients were collected, and after stimulation with lactate, the proportion of Tph cells, activation level, ability to secrete cytokines and differentiation into Tph cell subtypes in the peripheral blood

of all tested RA patients were determined by flow cytometry. And the metabolic capacity of Tph cells was measured by quantitative real-time PCR and flow cytometry. Then the lactylation levels was detected in healthy humans and RA patients by Western blot, and the lactylation levels of Tph cells in RA patients were detected after stimulation with lactate. [Results] The proportion of Tph cells in peripheral blood of RA patients after lactate stimulation was significantly higher than that of the control group; Meanwhile, lactate could promote the differentiation of Tph cells from RA patients into Tph1 type; However, lactate stimulation had no significant effect on the metabolic capacity of Tph cells from RA patients. Tph cells from RA patients showed a state of lactylation in relatively healthy people, and the lactylation levels of Tph cells from RA patients was also significantly increased after lactate stimulation. [Conclusions] Lactate up-regulated the proportion of Tph cells in RA patients, and promoted the differentiation of Tph cells to Tph1 type; Lactate promoted the lactylation level of Tph cells in RA patients and may promote the function of Tph cells in RA patients through protein Lactation modification.

## ICW36-2

**Study on the mechanism of SLAMF8 overexpression inducing the residence of immune cells in the synovium in rheumatoid arthritis**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease, at present, the pathogenesis of RA is not completely clear. SLAMF8 is a member of the lymphocyte activation signaling molecule family, and the SLAMF8 gene level is increased in the synovial membrane of RA joints. So our study aimed to elucidate the mechanism of SLAMF8 involved in the occurrence and development of RA. [Methods] Microarray datasets in RA or osteoarthritis (OA) were downloaded from the Gene Expression Omnibus (GEO) database, we constructed the protein-protein interaction (PPI) network, cytoscape was used to construct the co-expressed network and cytoHubba was used to screen hub genes. Synovial tissues from RA patients and OA patients were collected for immunohistochemical of SLAMF8, similarly, synovial tissues from the mouse were collected for immunohistochemical of SLAMF8. We tested the expression of SLAMF8 in different cells by immunofluorescence, adhesion assay was used to detect the adhesion of SLAMF8-expressing RA-FLS cells to PBMC. [Results]: We compared PBMC, FLS cells and synovial tissue samples and found that synovial tissue may be the medium of connection between PBMC and FLS cells. Further analysis of the four synovial datasets revealed 54 differentially expressed genes, and PPI analysis identified SLAMF8 as a key molecule, histochemical results showed SLAMF8 levels increased in RA patients of synovial tissue compared with OA patients, SLAMF8 was similarly elevated in CIA model mice compared with healthy mice. We found that SLAMF8 was mainly expressed in $CD4^+$T cells by immunofluorescence confocal, and SLAMF8 acts as an adhesion molecule that allows immune cells to reside in the synovial membrane. [Conclusions] This work establishes SLAMF8 is highly expressed in the synovial membrane as an adhesion molecule that allows immune cells to reside. We propose that SLAMF8 may be a potential target in the treatment of RA.

## ICW36-3

**Endoplasmic reticulum stress coupling mitochondrial stress enhances MSC-based therapy for rheumatoid arthritis**

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Conflict of interest: None

[Objective] Allogeneic mesenchymal stem cell (MSC) transplantation has been used in the clinical treatment of many immune-related diseases. In recent years, the modification of MSC in vitro to enhance its immunotherapy effect has attracted the attention of researchers. Endoplasmic reticulum stress (ERS), a multiple cause of misfolded or unfolded protein aggregation, was involved in cell function-regulation. Previous study verified that ERS-MSC exhibited stronger immunoregulatory effect. This study aimed at exploring the therapeutic effect of ERS-MSC on rheumatoid arthritis (RA) *in vivo*, together with its therapeutic mechanism preliminarily. [Methods] Collagen-induced arthritis (CIA) mouse model was constructed, then MSC and ERS-modified MSC were injected into CIA mouse to observe the therapeutic effect. T cell subsets was detected by flow cytometry and the transcriptional level of soluble factors was also evaluated. Then analysis of key transcription factors involved in soluble factor regulation via QPCR and Western Blot. We also analyze the effect of ERS on mitochondrial membrane potential, mitochondrial stress and mitochondrial dynamics. [Results]: *In vivo* research confirmed that ERS-modified MSC exhibited better therapeutic effect on CIA model compared to MSC group, and inhibited Th1/Th2 ratio mainly by upregulating COX2. During mechanism exploration, we found that ERS integrated mitochondrial stress was involved in COX2/PGE2 axis regulation through PERK-elf2α-ATF4 pathway. [Conclusions] ERS integrated mitochondrial stress co-enhanced MSC-based therapy for RA through PERK-elf2α-ATF4 pathway by upregulation of COX2/PGE2 axis.

## ICW36-4

**Mitochondrial Dysfunction Promoted CD4+PD-1+T Cell Senescence and Cytotoxic Activity in Rheumatoid Arthritis by Disrupting PD-1 signaling**

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Conflict of interest: None

**Objective:** Programmed cell death protein 1 (PD-1)-expressing T cells are expanded in individuals with established rheumatoid arthritis (RA). However, little is known about their functional role in the pathogenesis of early RA. In this study, we explored the mechanism of $CD4^+PD\text{-}1^+$T cell dysfunction in RA patients from the perspective of mitochondrial function and cellular senescence. **Methods:** The co-stimulatory molecule expression, cytokine secretion ability, and cytotoxic activity of $CD4^+PD\text{-}1^+$T cells and $CD4^+PD\text{-}1^-$T cells were analyzed by flow cytometry. Senescence Assay Kit was used to detect the cellular senescence state. MitoSOX, MitoTracker, and JC-10 were used to detect cell mitochondrial function. $CD4^+PD\text{-}1^+$T cells were treated with Mitoquinone to detect the impact of mitochondrial ROS (mtROS) on cell senescence, cytokine release, and cytotoxic activity. To demonstrate the function of $CD4^+PD\text{-}1^+$T cells in vivo, we compared the severity of joint inflammation in collagen-induced arthritis (CIA) mice by adoptive transfer of $CD4^+PD\text{-}1^+$T cells and $CD4^+PD\text{-}1^-$T cells respectively. **Results:** 1. The increased frequency of $CD4^+PD\text{-}1^+$T cells in RA patients and CIA mice was associated with disease activity and joint inflammation. 2. RA $CD4^+PD\text{-}1^+$T cells displayed cellular senescence characteristics. 3. RA $CD4^+PD\text{-}1^+$T cells exhibited cytotoxic activity. 4. Mitochondrial dysfunction promoted $CD4^+PD\text{-}1^+$T cell senescence and cytotoxicity. 5. PD-1 signal has no significant effect on $CD4^+$ T cell cytotoxic activity but promotes cell senescence. 6. MtROS interferes with PD-1 signal mediated suppression of $CD4^+PD\text{-}1^+$T cell inflammation and cytotoxicity activity. 7. The severity of joint inflammation aggravated after the transfer of $CD4^+PD\text{-}1^+$T cells in CIA mice. **Conclusion:** Our study indicated that mitochondrial ROS promote $CD4^+PD\text{-}1^+$T cell senescence and cytotoxic activity in RA patients by disrupting PD-1 signaling.

## ICW36-5

**The significance of MS4A4A expression on peripheral blood monocytes from patients with rheumatoid arthritis and its relationship to the pathogenesis**

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Conflict of interest: None

[Introduction] Membrane Spanning 4-Domains A4A (MS4A4A) is a four-transmembrane protein expressed on M2 macrophages and is highly expressed on peripheral blood monocytes of RA patients in a disease-specific manner based on a cross-sectional study. Since MS4A4A expression is particularly high on non-classical monocytes, we aimed to identify the clinical characteristics of the RA patient population with high MS4A4A positivity (MS4A4A$^{high}$) on non-classical monocytes. [Methods] The cut-off value for MS4A4A$^{high}$ was defined as the mean +1SD (38.01 + 17.77) of the MS4A4A positivity rate on healthy non-classical monocytes, and the MS4A4A$^{high}$ group was defined as those above the cutoff value. MS4A4A$^{high}$ positivity rate, clinical information (age, gender, treatment, SDAI, DAS28- ESR) and serum cytokine were analyzed. [Results] Of 79 RA patients, the age of the MS4A4A$^{high}$ group (N=42, 37 women) was 65 years [49.75, 78.5] (median [range]), methotrexate, glucocorticoid and b/tsDMARDs use rate were 74% (31/42), 14% (6/42) and 36% (15/42), disease duration, SDAI, and DAS28-ESR were 11.24±11.61, 9.28±10.44, and 2.99±1.38 (mean±SD), respectively. There was no significant correlation between MS4A4A$^{high}$ group and clinical information, but there was a significant correlation between serum IL-4 (r=0.32, p= 0.044), IL-10 (r=0.42, p=0.0058), and IFN-γ (r=0.42, p=0.0058) concentrations. [Conclusion] Due to the nature of the cross-sectional analysis, there were number of cases with low disease activity and no correlation was found between MS4A4A positivity and disease activity. However, the correlation with serum IL-4, IL-10, and IFN-g suggested the accelerated M2 macrophage differentiation *in vivo* from nonclassical monocytes in MS4A4A$^{high}$ group indicating as a biomarker related to disease activity. The expression of MS4A4A on peripheral blood monocytes may be a potential biomarker for disease activity.

## ICW36-6

**Seroconversion of anti-cyclic citrullinated peptide antibody and its relationship with an immune response to vimentin**

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Conflict of interest: Yes

[Objective] Anti-citrullinated protein antibodies (ACPA) are a constellation of partially cross-reactive autoantibodies and a hallmark of rheumatoid arthritis (RA), whereas its presence is clinically evaluated with the positivity of anti-citrullinated peptide antibody (CCP). Previous studies have indicated that epitope spreading with an increase in the recognition of citrullinated antigens precedes the onset of RA. Here we hypothesize that seroconversion of anti-CCP may occur in some patients with the clinical diagnosis of seronegative RA and evaluate its significance. [Methods] Sixty patients fulfilling the 2010 ACR/EULAR criteria for RA but negative for anti-CCP were included. Anti-CCP was re-evaluated with an interval of 80 [IQR 49-111] months. The presence of anti-citrullinated vimentin (cVIM) was assessed by enzyme-linked immunosorbent assay (Orgentec) and the HLA-DRB1 alleles were genotyped by PCR-SBT method. [Results] Out of the 60 enrolled subjects, five displayed anti-CCP level fluctuations, moving from undetectable to positive (12.2 [IQR 12.2-12.6] (<4.5) U/mL). Sera in the period of anti-CCP-negative were available in three of the five subjects, positive for anti-cVIM in all the three. Among five subjects with anti-CCP seroconversion, one, three, and one patients had 0, 1, and 2 shared epitope alleles, respectively. Clinically, these subjects exhibited difficult-to-treat and progressive joint destruction despite standard treatment including abatacept therapy. Anti-cVIM was detected (72.6 [IQR 25.7-106.4] (<20) U/mL) in nine out of the remaining 55 cases with persistently negative for anti-CCP. [Conclusion] Seroconversion of anti-CCP occurs in a certain proportion of patients with the clinical diagnosis of seronegative RA and may be related with an immune response to vimentin. Our findings suggest the heterogeneity of ACPA in terms of its production, epitope spreading, and pathogenicity. Clinically, anti-cVIM may have diagnostic and prognostic potentials.

## ICW37-1

**Association between lymphadenopathy regions and clinical presentation in idiopathic multicentric Castleman's disease and TAFRO syndrome**

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Conflict of interest: Yes

[Objective] To determine the association between the number of lymph node regions and clinical presentation in idiopathic multicentric Castleman's disease (iMCD) and TAFRO syndrome. [Methods] Cases of iMCD and TAFRO syndrome occurring between 1995 and 2022 were collected from 10 centers and classified into 4 groups according to the number of enlarged lymph nodes: none type: patients with no swollen lymph nodes; localized type: one lymph node region, regional type: two lymph node regions or more and the lesion is localized to one side across the diaphragm; multiple type: patients with lesions on both sides of the diaphragm in the thoracic and abdominal regions. We explored whether variations in the number of lymph node regions were linked to variations in the severity and clinical features of patients with iMCD and TAFRO syndrome, taking into consideration the presence or absence of TAFRO signs. [Results] A total of 321 patients were studied: iMCD-NOS (not otherwise specified): 76 (24%), iMCD-IPL: 141 (44%), iMCD-TAFRO: 78 (24%), and TAFRO syndrome (TAFRO-without iMCD): 26 (8.1%). The median age at onset was 49 years, and the proportion of women was 43%. Patients were classified according to the number of enlarged lymph node regions: none type (n = 26), localized type (n = 48), regional type (n=52), and multiple type (n=195). In the group without TAFRO signs (n=217), no significant difference was detected between the number of enlarged lymph node regions and clinical symptoms, while in the group with TAFRO signs (n=104), the rate of dialysis induction was significantly higher in patients with fewer enlarged lymph node regions (p=0.023). The group with TAFRO signs had a worse life expectancy (p=0.003, log-rank test). [Conclusions] This study showed that a lower number of enlarged lymph node regions is associated with a higher rate of dialysis induction in patients with TAFRO signs. These findings have implications for the clinical management of iMCD and TAFRO syndrome.

## ICW37-2

**Effectiveness and safety of tocilizumab in patients with polymyalgia rheumatica in clinical practice**

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Conflict of interest: None

[Objective] The objective of this study is to evaluate the efficacy and safety of tocilizumab, an interleukin-6 receptor antibody, in patients with polymyalgia rheumatica (PMR) in clinical practice. [Methods] We reviewed consecutive patients with PMR in Keio University Hospital from May 2012 to October 2022 and included those treated with tocilizumab in the analysis. Patients complicated with active giant cell arteritis were excluded. We collected clinical data, including PMR-activity score (AS), prednisolone dose, recurrence, and adverse events. Recurrence was defined as worsening of symptoms that required intensification of treatment, including initiation or increase in glucocorticoid, immunosuppressant, and/or tocilizumab. [Results] Forty-eight patients with PMR who were treated with tocilizumab were identified. Tocilizumab was administered 8 mg/kg intravenously every 4 weeks or 162 mg/body subcutaneously every 2 weeks. The median observation period from tocilizumab initiation to the last visit was 43 months. The median age at tocilizumab initiation was 76 years, 35 (73%) were female, and 39 (81%) had experienced recurrences before tocilizumab initiation with a median prednisolone dose of 7.3 mg/day. PMR-AS significantly improved after tocilizumab initiation from 0.42 to 0.05 at the last visit (p<0.001), and the median prednisolone dose was significantly decreased from 9.0 mg/day to 0.0 mg/day at the last visit (p<0.001) with 34 patients (71%) achieving glucocorticoid-free. While

tocilizumab administration interval was prolonged in 15 patients (31%) with 10 patients (21%) achieving withdrawal, 18 patients (38%) experienced recurrences with a median prednisolone dose of 0.0 mg/day during tocilizumab treatment. A total of 10 adverse events including six fracture, three infection, and one diverticular bleeding were recorded. [Conclusions] Tocilizumab is a useful treatment option with glucocorticoid sparing effects in patients with PMR in real world.

## ICW37-3

**Treatment responsiveness and prognostic predictors in idiopathic multicentric Castleman's disease and TAFRO Syndrome**

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Conflict of interest: None

[Objective] Idiopathic multicentric Castleman's disease (iMCD) is a rare inflammatory disorder characterized by multiple enlarged lymph nodes and associated inflammatory reactions, yet its precise pathogenesis remains elusive. iMCD comprises two distinct subtypes: iMCD-TAFRO, presenting with TAFRO signs, and iMCD-NOS, which lacks these signs, suggesting potential differences in pathogenesis. This study aimed to investigate treatment responses in iMCD, as well as TAFRO syndrome. [Methods] We collected cases of iMCD-NOS, iMCD-TAFRO, TAFRO syndrome, unicentric Castleman's disease (UCD), and suspected iMCD occurring from 1987 to 2022 across 11 institutions, including our hospital. Patient data, disease type, treatment protocols, disease progression, and treatment responses were systematically compiled and analyzed. [Results] A total of 214 cases were included, comprising iMCD-NOS (63%), iMCD-TAFRO (25%), suspected iMCD (1.9%), UCD (1.4%), and TAFRO syndrome (8.9%). Notably, the iMCD-NOS, iMCD-TAFRO, and TAFRO syndrome groups exhibited significant improvements in key parameters (PS, Hb, Alb, and CRP) as early as three months after initiating PSL treatment. In patients with iMCD-NOS, iMCD-TAFRO, and TAFRO syndrome (125 cases in total) followed up to 24 months after commencing treatment, the CHAP score was calculated at 24 months post-PSL initiation, categorizing patients into two groups: <2 points (96 cases) and >2 points (29 cases). Although no significant differences were observed in terms of age, clinical diagnosis, or baseline Hb levels, it was noteworthy that the time from PSL administration to TCZ administration was significantly longer in the group with a CHAP score of 2 or more points compared to the group with a CHAP score of less than 2 points. [Conclusions] Early identification of cases necessitating TCZ intervention and prompt suppression of IL-6 may prove pivotal in improving the prognosis of these diseases.

## ICW37-4

**IgG4-related disease administered dupilumab**

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4-RD) is a fibroinflammatory disease affecting various organs. Glucocorticoids (GC) are used as first-line therapy, and GC maintenance therapy is often used to reduce recurrence, leading to GC-related adverse events (AEs). Various molecularly targeted therapies are under development to reduce GC-related AEs. Dupilumab (DUP) is a monoclonal antibody blocking the IL-4 receptor alpha for refractory bronchial asthma, chronic sinusitis, and atopic dermatitis; however, the efficacy and safety of DUP for patients complicated with IgG4-RD is under discussion. Here, we report IgG4-RD patients administered DUP. [Methods] The patients classified as IgG4-RD by ACR/EULAR classification criteria and treated with DUP from January 2020 to April 2023 were included, and their medical records were reviewed retrospectively. Laboratory tests, imaging findings, GC dose, and IgG4-RD responder index (IgG4-RI) were examined at baseline, three, and six months after the initiation of DUP. A paired t-test was performed as the statistical analysis. [Results] Ten patients (8 females) met the inclusion criteria. The age at the baseline was 56 [41-73] (median [range]) years old. Five patients concomitantly used GC at the baseline, and the dose of GC was 6 [3-20] mg/day (prednisolone equivalent). The serum IgG4 levels were 320 [101-543], 242 [93-479], and 115 [66-278] mg/dL at the baseline, three months, and six months, respectively, and the serum IgG4 levels were significantly lower than that at three months (p=0.039), at six months (p=0.0004), respectively. IgG4-RI was 7 [3-15], 3 [0-9], and 3.5 [1-6], respectively, and significantly decreased with three months (p=0.00034) and six months (p=0.0034). GC dose did not change significantly. No AEs associated with DUP were identified during the observation period. [Conclusions] DUP lowers serum IgG4 levels and IgG4-RI in patients with IgG4-RD. DUP can be effective and safe for IgG4-RD with comorbidities for DUP indications.

## ICW37-5

**Peripheral blood CD8 effector memory T cells re-expressing CD45RA is a predictor of disease flare in IgG4-related disease (IgG4-RD)**

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Conflict of interest: None

[Objective] IgG4-RD is characterized by a good initial response to glucocorticoid (GC), however, one-third of IgG4-RD patients experience relapse during GC tapering. This study aimed to investigate the long-term treatment outcome of IgG4-RD. [Methods] 74 patients with IgG4-RD who had been treated with GC for at least 1 year were enrolled. Comprehensive immunophenotyping was performed by flow cytometry. Definition of relapse was emerging or worsening of existing organ function disorders, organ swelling or mass-forming lesions, and the increase in GC dose the addiction a new immunosuppressant. [Results] Treatment with GC led to a swift reduction in disease activity within a year. Relapse was observed in 20 patients and frequently transpired when the GC dose was tapered to 5 mg or less of PSL. There were fatalities at a rate of 4 per 100 patient-years, primarily attributed to adverse events, such as infections, linked to GC treatment. A comparison of clinical data between patients who relapsed and those who did not showed that hypocomplementemia at baseline could be a factor for disease flare, but not significant. In order to identify predictive factors for disease flares, we conducted an assessment of immunophenotypes. Univariate analysis revealed associations with disease relapse for CD8 effector memory T cells re-expressing CD45RA (TEMRA), helper1 T cells, and double-negative B cells. However, multivariate analysis showed that solely the proportion of CD8 TEMRA was the predictive marker for disease flare. Notably, patients with a higher percentage of CD8 TEMRA faced a nearly threefold higher risk of relapse compared to those with a lower percentage. On the other hand, the percentage of CD8 TEMRA did not decrease following GC treatment. Furthermore, these CD8 TEMRAs expressed fractalkine receptors. [Conclusions] Pre-treatment CD8 TEMRA percentage was linked to relapse. This cell population expressing fractalkine could potentially be a therapeutic target for IgG4-RD.

## ICW37-6

**Mind-Body Interventions in the Management of Fibromyalgia: Effects on Pain Perception, Psychological Well-being, and Quality of Life**

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Conflict of interest: None

**Objective** Fibromyalgia is a complex chronic pain condition. This study aims to investigate the impact of mind-body interventions, specifically mindfulness-based stress reduction (MBSR) and yoga, on pain perception, psychological well-being, and quality of life in individuals with fibromyalgia. **Methods** A randomized controlled trial was conducted with 150 fibromyalgia patients, divided into three groups: MBSR, yoga, and a control group receiving standard care. Pain perception was assessed using the Visual Analog Scale (VAS), psychological well-being using the Hospital Anxiety and Depression Scale (HADS), and quality of life using the Fibromyalgia Impact Questionnaire (FIQ) and the Short Form-12 (SF-12). The interventions were administered over a 12-week period. Statistical analyses included ANOVA, repeated measures ANOVA, and post-hoc tests, with 95% confidence intervals. **Results** Both the MBSR and yoga groups showed a significant reduction in pain perception compared to the control group. The MBSR group reported a mean VAS score reduction of 3.5 points (95% CI -4.02 to -2.98), and the yoga group reported a mean reduction of 2.9 points (95% CI -3.42 to -2.38). Improvements in psychological well-being were observed, with the MBSR group experiencing a significant reduction in anxiety and depression scores on the HADS (anxiety score decrease of 4.2, 95% CI -4.61 to -3.79; depression score decrease of 4.0, 95% CI -4.35 to -3.65). The yoga group also showed reductions in anxiety and depression scores, although they were slightly smaller. In terms of quality of life, both intervention groups reported significant improvements in FIQ and SF-12 scores compared to the control group. **Conclusions** This study shows that MBSR and yoga effectively reduce pain and improve well-being in fibromyalgia patients, offering holistic treatment options. Integrating these interventions can enhance patient outcomes. More research is needed for long-term effects and mechanisms.

## ICW38-1

**Leveraging Machine Learning and Cytokine Profiles for Precision Diagnosis of Seronegative Rheumatoid Arthritis**

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Conflict of interest: None

**Objective:** Seronegative Rheumatoid Arthritis (RA) poses a diagnostic challenge due to the absence of traditional rheumatoid factor and anti-citrullinated protein antibodies. This study assesses the diagnostic accuracy of machine learning models in distinguishing seronegative RA from other rheumatic conditions and healthy controls, utilizing novel biomarkers, and cytokine profiles. **Methods:** A well-defined cohort of 320 patients, including 85 seronegative RA, 120 other rheumatic disease patients, and 115 healthy controls, underwent extensive examination. The dataset integrated clinical, laboratory markers, cytokine profiles, and synovial fluid analysis. Seven machine learning algorithms underwent rigorous stratified ten-fold cross-validation. Diagnostic performance was assessed in terms of sensitivity, specificity, and AUC-ROC. **Results:** The stacked ensemble method outperformed other models with a sensitivity of 91.2% (95% CI: 86.7% - 94.1%) and specificity of 89.6% (95% CI: 85.1% - 93.2%). The AUC-ROC for seronegative RA diagnosis was 0.93 (95% CI: 0.89 - 0.96), indicating excellent discrimination capability. Cytokine profiles significantly improved performance, yielding an AUC-ROC of 0.95 (95% CI: 0.91 - 0.98). **Conclusions:** Machine learning, especially the stacked ensemble, holds promise for early seronegative Rheumatoid Arthritis diagnosis. Cytokine profiles enhance diagnostic accuracy, aiding in prompt intervention and improved patient outcomes. Further validation studies in diverse cohorts are needed for clinical applicability.

## ICW38-2

**Predicting Cost-Related Medication Non-Adherence in US Adults with Chronic Arthritis: A Machine Learning Approach**

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Conflict of interest: None

**Objective**: Cost-related medication non-adherence (CRN) arises from financial barriers, causing patients to miss doses and risk health issues. Accurate prediction of CRN is essential for targeting resources to high-risk individuals. This study aims to use machine learning to predict CRN in a nationally representative sample of US adults with chronic arthritis. **Methods**: Data from the National Health Interview Survey collected between 2013 and 2018 were analyzed. Logistic regression (LR), tuned random forest (TRF), and tuned neural network (TNN) classifiers were employed to predict CRN using various demographic and health-related factors. Feature importance plots were utilized to assess the significance of each input in predicting CRN. Additionally, model performance was evaluated using five-fold cross-validation, and the results were visualized using receiver operating characteristic (ROC) curves. **Results**: The study included 23,952 participants with chronic arthritis, among whom 4,632 (19.33%) experienced CRN. The LR classifier identified advanced age as having the smallest odds ratio, while a high comorbidity burden had the largest odds ratio (Figure 1a). Similarly, the TRF classifier indicated that advanced age was the most influential factor, followed by having private or Medicare coverage (Figure 1b). The TNN classifier identified the absence of a high-deductible health plan (HDHP) as the most significant predictor of not having CRN; on the other hand, a lapse in health coverage emerged as the most influential factor in predicting the presence of a CRN (Figure 1c). All three classifiers demonstrated comparable prediction powers, with areas under the curve (AUC) of 76%, 71%, and 73% for LR, TRF, and TNN classifiers, respectively (Figure 2). **Conclusions**: Our classification models exhibited promising performance with AUC values close to three-fourths. This study highlights the potential of machine learning classifiers in identifying patients at higher risk of CRN.

## ICW38-3

**Cost-Related Medication Non-Adherence Among US Adults with Chronic Arthritis: Trends, Comparisons, and Disparities**

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Conflict of interest: None

**Background**: Cost-related medication non-adherence (CRN) is when patients cannot adhere to prescribed medication regimens due to high costs or inadequate insurance coverage, leading to adverse health effects. We investigated CRN in a nationally representative US sample of adults with chronic arthritis. **Methods**: Using National Health Interview Survey (NHIS) data from 2013 to 2018, we calculated CRN proportions for chronic arthritis, cancer, diabetes, and heart disease. We analyzed gender and racial/ethnic subgroups among those receiving at least one prescription drug, applying 95% confidence intervals and $p<0.05$ for significance. Analysis was conducted using Stata and Python. **Results**: The study included 163,579 participants without chronic arthritis and 26,534 with chronic arthritis (17,840 females). Chronic arthritis group breakdown: 19,047 non-Hispanic Whites, 3,917 African Americans/Blacks, 2,497 Hispanics, 625 Asians, and 421 from other racial/ethnic groups. From 2013 to 2018, CRN decreased in individuals with chronic arthritis (21.26% to 17.83%, $p<0.05$) and without (14.72% to 10.76%, $p<0.05$). Chronic arthritis patients consistently had higher CRN rates than those without, similar to cancer and diabetes patients (Figure 1). Gender disparities widened over time, with females with chronic arthritis more likely to experience CRN (Figure 2). African Americans/Blacks and Hispanics showed trends of increased CRN risk compared to non-Hispanic Whites and Asians, but differences were not statistically significant (Figure 3). **Conclusion**: CRN rates are declining but remain high in chronic arthritis patients, similar to cancer and diabetes groups. Gender disparities persist and may worsen over time. Concerns arise regarding potential racial/ethnic disparities in CRN risk. Further research and targeted policies are needed to ensure equitable access to affordable medications for individuals with chronic arthritis in the United States.

## ICW38-4

**Enhancing Cardiovascular Risk Prediction in RA Patients with Cardiothoracic Ratio Derived from Deep Learning**

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Conflict of interest: None

[Objective] To investigate whether incorporating cardiovascular indices from chest radiographs into existing cardiovascular risk prediction scores enhances the predictive accuracy for major adverse cardiovascular disease (MACE) in patients with rheumatoid arthritis (RA). [Methods] Patients aged 20 and above with RA, enrolled in the Institute of Rheumatology, RA cohort, and with chest radiograph data from April 2000 to September 2022 were included. Observations began at the earliest radiographic date and censored at the occurrence of MACE, loss to follow-up, 10 years post-observation initiation, or September 2023, whichever came first. Cardiothoracic ratio (CTR), tracheal bifurcation angle, and aortic calcification were extracted using deep learning. Associations of these indices with MACE was assessed using a time-dependent Cox regression model. Patients were randomly assigned to Derivation or Validation cohort at 1:1 ratio. Using the coefficient from the Penalized Cox regression model in the Derivation cohort, scores for each CTR tertile were added to the existing scores (modified Systematic Coronary Risk Evaluation (mSCORE) or Expanded Cardiovascular Risk Prediction Score for RA (ERS-RA)). Subsequently, the predictive accuracy in the Validation cohort was assessed using AUC. [Results] Of a total of 3468 patients selected, with a mean age of 58.4 and 87.0% being female, 314 patients experienced MACE. Only CTR was associated with MACE as an independent risk factor among the cardiovascular indices (CTR, $p < 0.0001$). With Derivation cohort data, additive percentages for each CTR tertile were +0, +0.3, +2.6 for mSCORE, and +0, +1.0, +8.7 for ERS-RA. In the Validation cohort, including CTR in the existing scores improved the accuracy of mSCORE (AUC 0.685 vs. 0.713; $p = 0.006$) and ERS-RA (AUC 0.675 vs. 0.714; $p = 0.002$). [Conclusions] The predictive accuracy for MACE in patients with RA is enhanced by incorporating CTR into the existing cardiovascular risk prediction scores.

## ICW38-5

**4-year follow-up observational study of difficult-to-treat rheumatoid arthritis (D2T RA): contributing factors for resolving D2T RA**

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Conflict of interest: None

**Objective**: We reported clinical characteristics of patients with difficult-to-treat rheumatoid arthritis (D2T RA) in 2019, and in this study, we followed them and elucidate their long-term clinical course. **Methods**: We followed the patients who were categorized as D2T RA in 2019 and collected clinical course and long-term outcomes until 2023. We divided the patients with D2T RA into two groups; patients who achieved remission or low disease activity, i.e. escape from D2T RA or not. We compared clinical characteristics between the two groups and investigated contributing factors for resolution of D2T RA. We also performed sub-analysis depending on the reasons for D2T RA. **Results**: Among 173 patients who were identified as D2T RA in 2019, 150 were included in the analysis after excluding patients with loss to follow-up or lack of enough data. Among the 150 patients, 67 (45%) resolved D2T RA, 75 (50%) remained D2T RA, and 8 (5%) died during the follow-up. Patients who resolved D2T RA were significantly younger at the latest visit (66 vs 71 years, p=0.02), had a higher proportion with treatment change including dose or interval modification of biological disease modifying anti-rheumatic drugs (84 vs 59%, p=0.002), a higher proportion of interleukin-6 receptor inhibitor (IL-6Ri) use (36 vs 20%, p=0.04), and a fewer proportion of prednisolone use (15 vs 39%, p<0.001). In the multi-drug resistance group, 39% of patients resolved D2T RA. Proportion of IL-6Ri tended to be higher in the resolving group (45 vs 19%, p=0.06), but proportion of JAK inhibitors was comparable (35 vs 39%, p=1.00). High rheumatic disease comorbidity index was an independent risk factor for death (odds ratio 2.72, 95% confidential interval 1.37-5.36, p=0.004). **Conclusion**: About 45% of patients with D2T RA achieved remission or low disease activity during the 4-year follow-up of D2T RA, indicating further change or modification of treatment could be one solution for resolving D2T RA in clinical practice.

## ICW38-6

**Prediction for patients with difficult-to-treat (D2T) RA by machine learning, from the FIRST registry**

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Conflict of interest: None

**Objective**: The aim of this study was to establish a model to predict future progression to D2T RA by background factors in csDMARDs-IR RA patients who will receive b/tsDMARDs for the first time. **Methods**: RA patients with inadequate response to csDMARDs were enrolled in prospective multicentre cohort FIRST registry (N=5,066). The study included the patients who initiated first b/tsDMARDs treatment between August 2013 and August 2022. The primary endpoint was the rate of progression of D2T RA defined by EULAR. The predictive model for D2T RA progression was established based on patient characteristics using the Lasso technique (Least Absolute Shrinkage and Selection Operator). Patients were categorized into high- and low-D2T RA risk groups by ROC regression analysis. The impact of the choice of first b/ts DMARDs on the progression of D2T RA was examined using Post-Double-Selection (PDS) Lasso analysis between groups. **Results**: 1270 patients (mean follow-up period of 26.8 months) were included, of whom 173 (13.6%) progressed D2T RA after a mean of 27.0 months. Thirty variables were employed with Lasso regression to formulate a predictive model for D2T RA progression. In this model, the sensitivity, specificity, positive and negative predictive values were 53.3%,79.6%,24.1% and 91.5%, respectively. The predictive performance of the model was a risk ratio of 2.29 [1.19-4.42]. In the high-risk D2T RA group, 30.4% of TNFi-, 14.4% of IL-6Ri-, 28.0% of CTLA4-Ig-, and 11.1% of JAKi-treated patients developed D2T RA. PDS Lasso analysis revealed that JAK inhibitors were significantly associated with a lower rate of D2T RA progression in the high-D2T RA risk group (vs. others OR: 0.90 [0.84-0.95]). Conversely, in the low-D2T RA risk group, the first b/tsDMARDs class showed no significant impact on D2T RA progression. **Conclusions**: The model to predict D2T RA progression was established. In the high-D2T RA risk group, the choice of first b/tsDMARDs may influence the higher incidence of D2T RA.

## ICW39-1

**Early resolution of urinary cellular casts predicts improvement in renal function in ANCA-associated glomerulonephritis**

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Conflict of interest: None

[Objective] To clarify clinical usefulness of monitoring urinary cellular casts after induction therapy in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis. [Methods] Consecutive patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) who had new-onset biopsy-proven ANCA-associated glomerulonephritis from 2009 to 2022 in our hospital were included. The change in urinary casts was recorded, and patients were classified into two groups according to resolution of all urinary cellular casts one month after induction therapy. Clinical characteristics at induction therapy initiation, renal histology, and renal function at one year after induction therapy were compared between the two groups. [Results] A total of 22 patients (6 GPA

and 16 MPA) with new-onset ANCA-associated glomerulonephritis were included in the analysis. All patients had urinary cellular casts before induction therapy. At one month, all casts disappeared in 12 patients (55%, early resolution group). No significant difference was found in the positivity of MPO-ANCA (91.7 vs 90.0%, p=1.00), eGFR levels at baseline (57 vs 30 ml/min/1.73m$^2$, p=0.11), the prednisolone dose used for induction therapy (50 vs 55 mg/day, p=0.17), cyclophosphamide use (75 vs 70%, p=1.00), and rituximab use (17 vs 20%, p=1.00) between the two groups, except for baseline urinary protein levels (0.4 vs 1.1 g/day, p=0.02). Proportion of interstitial fibrosis and tubular atrophy was significantly lower in the early resolution group (5 vs 40%, p<0.01), whereas that of cellular crescents did not show significant difference (10 vs 23%, p=0.08). At one year, eGFR was significantly improved in the early resolution group than in the non-early resolution group (59 vs 46 ml/min/1.73m$^2$, p=0.02). [Conclusions] Resolution of urinary cellular casts at one month after induction therapy predicts good renal function at one year in patients with new-onset ANCA-associated glomerulonephritis.

## ICW39-2

**Dental infection is associated with early relapse in patients with ANCA-associated vasculitis**

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Conflict of interest: None

[Objective] Infection is known as a factor associated with relapse of systemic vasculitis. The objective of this study is to investigate the association between dental infection which requires tooth extraction and early relapse of ANCA-associated vasculitis (AAV). [Methods] This study included patients with AAV admitted to our department and received remission induction therapy and dental evaluation between January 2011 and July 2022. Patients with dental infections that require tooth extraction were defined as the dental infection (DI) group. Our primary outcome was defined as either an AAV relapse or any cause of mortality within one year after achieving remission. Outcomes were reported as both proportions and incidence rates calculated as events per 100 person-years (100PY). We employed a Cox proportional hazard model, adjusting for variables such as age, sex, and the type of AAV, to identify the association of dental infection with relapse and mortality within one year after remission. [Results] 94 cases (60 females) with a mean age of 72.2 years (standard deviation: SD, 9.7) were enrolled in this study. Thirty-eight cases were diagnosed with microscopic polyangiitis, 36 with granulomatosis with polyangiitis, 15 with eosinophilic granulomatosis with polyangiitis, and 5 with unclassifiable AAV. Dental infections that require tooth extraction were observed in 41 cases (43.6%). Relapse within 1 year occurred in 26.4% (11/41, 35/100PY) in the DI group and 7.5% (4/53, 10.0/100PY) in the control group. Multivariate analysis revealed that dental infection that required tooth extraction was significantly associated with the risk of AAV relapse (adjusted HR 3.58, 95%CI 1.10-11.7, p=0.035). [Conclusions] This study has demonstrated an association between dental infection and early relapse of AAV. 43.1% of the patients had a dental infection that required tooth extraction, suggesting that dental referral is important when starting the treatment of AAV.

## ICW39-3

**The profile of multiple cytokines and chemokines to distinguish large vessel vasculitis from small vessel vasculitis**

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Conflict of interest: None

[Objective] The disease entity of primary systemic vasculitis consists of three types: large vessel vasculitis (LVV), medium vessel vasculitis, and small vessel vasculitis (SVV). Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is the primary type of SVV. We aimed to differentiate LVV from AAV by the serum cytokines and chemokines (proteins) profile to assume the underlying pathophysiological differences between both vasculitis. [Methods] Multiplex cytokine/chemokine bead assays were performed using preserved serum supernatants before immunosuppressive treatments from 43 patients with LVV and 71 patients with AAV newly diagnosed from March 2010 to July 2023 in Nagasaki University Hospital. Serum samples from 101 healthy donors defined the normal protein levels. We compared the patterns of serum levels of multiple proteins between LVV and AAV. [Results] Among measured 35 serum proteins, patients with LVV had significantly high levels of serum macrophage-derived chemokine (MDC), granulocyte-macrophage colony-stimulating factor (GM-CSF), and C-X-C motif chemokine ligand 1 (CXCL1). Patients with AAV had significantly higher levels of 28 proteins, including granulocyte colony-stimulating factor (G-CSF), interleukin (IL)-6, IL-10, and tumor necrosis factor-α. LASSO regression demonstrated a positive coefficient of G-CSF for AAV and positive coefficients of GM-CSF and MDC for LVV. A random forest model exhibited CXCL1 as the most important contributor to distinguishing LVV and AAV. The t-distributed neighbor embedding (t-SNE) and the uniform manifold approximation and projection (UMAP) for dimension reduction of 35 serum proteins demonstrated that patients with LVV had a distinctive distribution pattern from that of AAV in two dimensions. [Conclusions] The profiles of multiple proteins of LVV and AAV are distinctive from each other. The cytokines and chemokines associated with macrophages and neutrophils contributed to distinguishing LVV and AAV.

## ICW39-4

**A Novel '5F' Risk Score Model for Predicting Mortality in ANCA-Associated Vasculitis Patients: Development and External Validation**

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Conflict of interest: None

[Objective] This study aims to develop and externally validate a mortality risk prediction model for ANCA-associated vasculitis. [Methods] Total 215 cases of primary AAV were included in the follow-up cohort, and 142 patients with ANCA-associated vasculitis were included in the development cohort to build a mortality risk prediction model. The Lasso regression was used to screen the predicted factors, and the Cox proportional hazards regression model was used to develop predicted model. For model evaluation, C statistic refers to the model discrimination index, the Brier score is the model calibration index. The bootstrap method was used for internal verification, and external verification was performed in an independent cohort of patients with different admission times. [Results] A combined risk score, the '5F' risk score model, was used to predict mortality risk: disease onset age > 65 years (one score), male gender (one score), infection during induction treatment phase (one score), serum creatinine >= 150mol/L (two scores), albumin < lower limits of normal (35g/L, one score). According to the '5F' risk score model, patients were divided into two risk groups: low, 0 to 3, and high, 4 to 6. High-risk patients had significantly higher mortality rates than low-risk patients in both the discovery and validation cohorts (P < 0.05). In terms of discrimination and calibration, the model performed well in internal verification (C statistic > 0.87 and Brier score < 0.09) and reasonably well in external validation (C statistic > 0.72 and Brier score < 0.19). [Conclusions] The '5F' risk score model could aid in to predicting survival in AAV patients, as well as guiding treatments and further clinical research on risk-based treatment.

## ICW39-5

**The validity of glucocorticoid tapering strategy for ANCA-associated vasculitis in the real-world practice: Analysis by propensity score matching using the J-CANVAS registry**

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Conflict of interest: None

[Objective] To investigate the real-world practice of glucocorticoid tapering strategy in the treatment of microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) and to compare it with the guidelines for ANCA-associated vasculitis published by BSR/BHRP (British Society for Rheumatology and British College of Rheumatologists). [Methods] A retrospective cohort study was conducted using the J-CANVAS registry. Patients with MPA and GPA were selected from the registry and sham-randomized into two groups by propensity score matching (PSM) based on the pace of prednisolone (PDN) dose reduction. Based on BSR/BHRP guideline, patients with PDN dose reduced to 15 mg/day or less (≧7.5 mg/day) at 12 weeks after initiating treatment were assigned to BSR group, and with PDN dose greater than 15 mg/day at the same point were assigned to B-SLOWER group. Patients with PDN dose reduced to less than 7.5 mg/day at 12 weeks were excluded. The primary outcome was the relapse-free period for both groups, and the secondary outcome was the infection-free period for both groups. [Results] A total of 680 patients were enrolled in the J-CANVAS registry, 463 of whom were included in the study. Of the 463 patients, 168 patients (36.3%) were assigned to BSR group and 295 patients (63.7%) to B-SLOWER group. There was no statistically significant difference in relapse-free and infection-free periods between the two groups, but there was a trend toward shorter infection-free periods in the B-SLOWER group ($p$=0.184). [Conclusions] In real-world practice, PDN reduction is often slower than recommended by BSR/BHRP, but slow PDN tapering does not reduce the risk of relapse and may even increase the risk of infection.

## ICW39-6

**Association of nailfold Videocapillaroscopy abnormalities with disease severity in ANCA-associated Vasculitis**

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Conflict of interest: None

[Objective] This study aimed to evaluate nailfold videocapillaroscopy (NVC) as a useful tool for assessing the disease activity of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). [Methods] We enrolled 51 Patients with AAV from 2018 to 2021 in Osaka Medical and Pharmaceutical University. They were diagnosed with AAV according to the Chapel Hill consensus definition. We scored NVC findings semi-quantitatively, and compared them between AAV patients and controls. We also examined the association of NVC findings with disease activity indicators, histopathological findings of skin biopsies, and high-resolution computed tomography (HRCT) scores in AAV. [Results] Out of 51 patients, 35 had microscopic polyangiitis, 7 had granulomatosis with polyangiitis, and 9 had eosinophilic granulomatosis with polyangiitis. The median age was 74 years, and 49% patients were women. 70.6% (36/51) of patients with AAV showed a microangiopathy pattern in NVC. The scores for microhemorrhage, capillary loss, neoangiogenesis, and tortuosity were significantly higher in the AAV group than in the control group. These NVC abnormalities correlated with the severity of small vasculitis, including, skin, lung, and kidney involvement. First, the scores of microhemorrhage significantly correlated with perivascular inflammatory cell infiltrations in the upper dermis of the purpura and tended to correlate with the total ground-glass opacity and consolidation scores on HRCT. Second, the scores of capillary loss correlated with the chest BVAS and the renal BVAS. Also, they had a significant positive correlation with serum creatinine levels. Third, the scores of neoangiogenesis were significantly higher in patients with rapid progressive glomerulonephritis (RPGN) than those without RPGN. [Conclusions] NVC abnormalities are significantly associated with disease severity in AAV. This result suggests that NVC is a useful tool for assessing the disease activity in AAV.

# Workshop

## W1-1

**An abnormal increase of CD26 (-) CD28 (-) cytotoxic effector CD4 and CD8 T cell populations in patients with systemic lupus erythematosus**

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Conflict of interest: None

[Objective] CD26 is a T cell costimulatory molecule, and $CD26^+$ T cells are increased in various autoimmune diseases. In contrast, we previously showed that CD26 (-) T cells were markedly increased in SLE, reflecting abnormal expansion of CD28 (-) cytotoxic subsets of both CD8 and CD4 T cells. In this study, we investigated their potential involvement in the pathology of SLE. [Methods] We conducted CD26-based T cell subset analyses utilizing PBMCs from 57 SLE patients and 31 healthy controls, and analyzed correlation of available clinical information with the proportion of CD26 (-) CD28 (-) T cell populations. [Results] Abnormal increase of these populations was observed in both active and inactive groups. The effect of treatment on these populations varied from patient to patient, and elevated level of these cells might be found in some inactive stage SLE patients with difficult to control symptoms. The patients could be separated into two groups, one being in active stages with low serum levels of complement CH50, and the other with high CH50 serum levels. [Conclusions] Our data suggest that analysis of these populations in SLE may be a useful tool to classify this markedly heterogenous disease, and selective depletion of these populations may be a novel therapeutic approach for SLE.

## W1-2

**Interaction between programmed cell death-1 and its ligand co-expressing in B cell regulates autoantibody formation in Toll-like receptor agonist imiquimod induced lupus phenotype**

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Conflict of interest: None

[Objective] To analyze the functional role of programmed cell death-1 (PD-1) in mouse model of SLE induced by TLR7 agonist imiquimod (IMQ). [Methods] 1) After C57BL/6 (WT) and PD-1 knock out (KO) mice were treated with IMQ for 8 weeks, anti-double strand (ds) DNA IgG in sera and histology in kidney were evaluated. 2) Cytokines production from in vitro-stimulated splenic $CD4^+$ T cells isolated from IMQ-treated WT and KO mice was examined by FCM. 3) PD-1 and PD-L1 expression in B cells were analyzed before and after treatment of IMQ. 4) IgG production from in vitro-stimulated B cells of WT and KO mice was measured by ELISA. 5) Effect of PD-L1-Fc on IgG production from B cells was evaluated. [Results] 1) Anti-dsDNA IgG tended to be higher, and pathological change in kidney was enhanced in KO mice compared with WT mice. 2) There was no significant difference in cytokines from $CD4^+$ T cells between WT and KO mice. 3) Expression of PD-1 and PD-L1 was significantly up-regulated after IMQ treatment. 4) IgG production was significantly elevated in KO mice compared to WT mice. 5) PD-L1-Fc had no effect on IgG production from B cell. [Conclusions] Interaction between PD-1 and PD-L1 co-expressing in B cell might play a role in regulation of autoantibody formation in IMQ induced lupus phenotype.

## W1-3

**Pathogenic relevance of transcription factor T-bet in lupus model mice induced by Toll-like receptor 7 agonist imiquimod**

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Conflict of interest: Yes

[Objective] To investigate the involvement of transcription factor T-bet in imiquimod (IMQ) induced SLE model mice. [Methods] 1) After the administration of IMQ for 8 weeks in C57BL/6 wild-type (WT) mice and T-bet knockout (KO) mice, lupus phenotype was evaluated by measuring serum anti-dsDNA IgG, urinary protein, and by immunofluorescent staining of C3 and IgG in kidney. 2) After administration of IMQ for 8 weeks, expression of surface antigens on splenic CD4+ T- and B-cells were evaluated by flowcytometry (FCM). 3) After splenic CD4+ T-cells were isolated from untreated or IMQ-treated WT or KO mice, then stimulated in vitro, cytokine production from them was evaluated by FCM. [Results] 1) Although there were no differences in titer of anti-dsDNA IgG and urinary protein between WT and KO mice, deposition of C3 and IgG in kidney tended to be decreased in KO mice compared with WT mice. 2) CXCR5+PD-1-Tph cells were significantly reduced, while there were no differences in B cells between them. 3) IFNγ-producing CD4+ T-cells were decreased in KO mice compared to WT mice. [Conclusions] Our results suggested the possibility that T-bet might have an important role in IMQ induced lupus model through the differentiation and the function of CD4+ T- and B-cells.

## W1-4

**Association between pregnancy outcomes and maternal and umbilical cord blood immune cell profiles using mass cytometry in pregnancies complicated with systemic lupus erythematosus (SLE)**

Ayako Kitada[1,2], Takehiro Nakai[1], Atsushi Nomura[2,3], Hiroto Tsuboi[1], Hirofumi Toko[1], Saori Abe[1], Haruka Miki[1], Hiromitsu Asashima[1], Yuya Kondo[1], Isao Matsumoto[1], Masato Okada[2]

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Conflict of interest: None

Objective: To clarify the association between pregnancy outcomes and immune cell profiles in SLE-complicated pregnancies using mass cytometry (CyTOF). Methods: We included 7 pregnant women with SLE and 5 pregnant healthy controls (HC) at St. Luke's Hospital between Aug 2020 and Dec 2022. 1) Immune cell profiles in maternal peripheral blood of third trimester and cord blood were compared between pregnant women with SLE and pregnant HC. 2) In SLE-complicated pregnancies, the associations between pregnancy outcomes and changes in immune cell profiles were analyzed. Results: 1) In maternal blood, $CD8^+$T cell significantly increased while central memory $CD4^+$T cell significantly decreased in SLE group than in HC. In cord blood, $CD8^+$T cell significantly increased while $CD4^+$T cell significantly decreased in SLE group than in HC, resulting in similar trend of maternal blood. 2) Adverse pregnancy outcomes (APO) group (N=3) showed a higher trend of classical monocyte frequency in maternal blood compared to without APO group (N=4). Gestational age/birth weight significantly and negatively correlated with dendritic cells/live cell ratio in maternal blood. Conclusion: Maternal/cord blood immune cell profiles were different in pregnant women with SLE compared with HC, which might correlate with APO.

## W1-5

**Hyperlipidemia in lupus mice promotes neutrophil extracellular trap (NET) formation induced by steroid pulse**

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Conflict of interest: None

[Objective] We have reported that steroid pulse to lupus mice induces NET formation and that prenylcysteine oxidase 1 abundant in VLDL is involved in this induction. This study aimed to determine the effect of hyperlipidemia on this phenomenon. [Methods] Imiquimod (IMQ) was applied to congenic Apo E mutant mice that develop hyperlipidemia to induce lupus (n=7). Four of them were given methylprednisolone (mPSL) on Days 39-41. Three were given PBS instead. BALB/c mice were treated similarly as controls. Peripheral blood was labeled with SYTOX green and Gr-1, and circulating NET-forming neutrophils were detected by flow cytometry. [Results] There was no difference in anti-dsDNA antibody titer in Day 35 plasma between IMQ-applied Apo E mutant and BALB/c mice. SYTOX green high positive cells in Gr-1 low positive cells were increased in mPSL-administered Apo E mutant lupus mice compared with controls, indicating an increase in circulating NET-forming neutrophils. The increase was observed in Day 56 blood but not in Day 49 blood. The effects were smaller in BALB/c mice. [Conclusions] Hyperlipidemia did not affect anti-dsDNA antibody production by IMQ, while it promoted NET formation induced by steroid pulse to lupus mice. The effect appeared after a certain period of steroid pulse.

## W1-6

**Anti-phosphatidylserine/prothrombin complex antibodies induce neutrophil extracellular traps**

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Conflict of interest: None

[Objective] Antiphospholipid syndrome (APS) is an autoimmune disease characterized by thrombosis. Anti-phosphatidylserine (PS)/prothrombin (PT) complex antibodies (aPS/PT) are strongly associated with thrombosis. Although the mechanism by which aPS/PT promote thrombosis remains unclear, it was reported that IgG derived from APS patients has the ability to induce neutrophil extracellular traps (NETs), which are involved in thrombogenesis. This study asked if aPS/PT could bind to neutrophils and induce NETs. [Methods] Human peripheral blood neutrophils were primed with histone to express PS, allowed to react with PT to form PS/PT complexes, and made to bind with aPS/PT. NET formation was evaluated by flow cytometry (FCM) and morphologically. [Results] NET formation was significantly increased in neutrophils with aPS/PT binding on the cell surface compared to neutrophils without aPS/PT binding. Although NET-forming neutrophils were equivalent between neutrophils with and without histone priming in FCM, it was noted that abundant NETs were formed when neutrophils were primed with histone followed by aPS/PT binding under morphological observation. [Conclusions] aPS/PT can bind to neutrophils and induce NETs. aPS/PT-induced NETs may be involved in the thrombogenesis in patients with APS.

## W2-1

**Factors affecting the efficacy of hydroxychloroquine for cutaneous lupus erythematosus and the cutaneous manifestations of systemic lupus erythematosus**

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Conflict of interest: Yes

[Objective] To investigate the factors affecting the efficacy of hydroxychloroquine (HCQ) for CLE and the cutaneous manifestations of SLE. [Methods] Post-marketing surveillance (PMS) was performed in 1142 patients who received a HCQ dosage of 4.9±1.2 mg/kg/day. PMS data of CLE or SLE with cutaneous manifestations were analyzed. Treatment efficacy was assessed at 52 weeks using a 7-point scale, and the responses, "remarkably improved" and "improved", indicated good treatment efficacy. [Results] HCQ was effective in 49.3% of the 460 patients (75 with CLE and 385 with SLE). On univariate analysis, diagnosis (CLE: 60.0%; SLE: 47.3%), disease duration (years) (<1: 60.0%; 1>= and <5:

51.3%; 5>=: 45.8%), smoking history (never: 50.9%; current: 30.8%), complications (no: 56%; yes: 43.9%), PSL (mg/day) (<5: 29.4%; 5>= and <7.5: 47.8%; 7.5>= and <30: 47.8%; 30>=: 63.3%), and HCQ dosage (low dosage: 37.9%; approved dosage: 53.3%) were associated with treatment efficacy ($p<0.05$). On multivariate analysis, the odds ratio (95%CI) for CLE, current smoking habit, and low HCQ dosage was 2.547 (1.119-5.798), 0.315 (0.139-0.716), and 0.547 (0.295-1.017), respectively. [Conclusions] The efficacy of HCQ for CLE and the cutaneous manifestations of SLE was lower in SLE patients and current smokers.

## W2-2

**Factors affecting the efficacy of hydroxychloroquine for non-cutaneous manifestations of systemic lupus erythematosus**

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Conflict of interest: Yes

[Objective] To investigate the factors affecting the efficacy of hydroxychloroquine (HCQ) for non-cutaneous manifestations of SLE. [Methods] Post-marketing surveillance (PMS) was performed in 1142 patients who received a HCQ dosage of 4.9±1.2 mg/kg (RBW)/day. PMS data of SLE patients with non-cutaneous manifestations were analyzed. Treatment efficacy was assessed at 52 weeks using a 7-point scale [Results] HCQ was effective in 37.8% of the 872 patients. On univariate analysis, disease duration (years) (<1: 60.7%; 1>= and <5: 32.6%; 5>=: 35.0%), smoking history (never: 39.1%; current: 25.9%), PSL (mg/day) (<5: 22.1%; 5>= and <7.5: 35.3%; 7.5>= and <30: 35.8%; 30>=: 61.4%), and HCQ dosage (low dosage: 29.5%; approved dosage: 40.4%) were associated with treatment efficacy ($p<0.05$). On multivariate analysis, the odds ratio (95% CI) for disease duration (years) 1>=, <5, and 5>=; current smoking habit; PSL < 5 mg/day; and low HCQ dosage was 0.422 (0.240-0.742), 0.500 (0.304-0.822), 0.413 (0.215-0.793), 0.360 (0.170-0.764), and 0.587 (0.379-0.909), respectively. [Conclusion] The efficacy of HCQ for non-cutaneous manifestations of SLE was lower in patients with a disease duration 1>= year, current smoking habit, PSL <5 mg/day, and low HCQ dosage.

## W2-3

**Consideration of Appropriate Dosage of Hydroxychloroquine in Japanese**

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) is an important drug recommended for use in Japanese guideline. It is widely indicated for the prevention of disease flare-ups in patients with SLE. However, it can cause retinopathy side effects. In Japan, there is currently no clear statement on volume adjustment other than the package insert. [Methods] We examined the effect of HCQ on relapse prevention by volume using approximately 100 patients who started HCQ administration between December 2015 and March 2019, with a change of 4 or more SLEDAI points defined as a relapse. [Results] The mean observation period was 51.3 months. Excluding 21 patients who discontinued treatment due to side effects within 1 month of treatment, 4 (23.5%) of 17 patients who received less than the indicated dosage experienced relapse, and 15 (24.2%) of 62 patients who received the indicated dosage experienced relapse. The difference between the two groups was not significant when compared by log-rank test. [Conclusions] It is believed that the accumulated dose is related to the occurrence of retinopathy, and it is undesirable to use high doses for a long period of time. Based on the results of the present study, it is possible that dosing at less than the labeled dose may be sufficient in preventing relapse.

## W2-4

**Clinical effects of hydroxychloroquine dosage on systemic lupus erythematosus**

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Conflict of interest: None

[Objective] Hydroxychloroquine (HCQ) dose of < 5 mg/kg of real body weight (rBW) is recommended to prevent HCQ retinopathy. We investigated the effects of HCQ dosage on systemic lupus erythematosus (SLE). [Methods] Patients with SLE continued HCQ for ≧ 1 year were included. We retrospectively collected the clinical and serological data from the medical records. [Results] Of 169 who continued HCQ for ≧ 1 year, 49 and 120 patients were prescribed HCQ ≧ 5 mg/kg of rBW (HD) and < 5 mg/kg of rBW (LD), respectively. In HD, values of anti ds-DNA antibody and C3 were 10.3 IU/mL (IQR: 6.5 - 23.5) and 78 mg/dL (IQR: 63.5 - 94.3) at the start (T0) and 8.9 IU/mL (IQR: 6.4 - 17.7), 83 mg/dL (IQR: 72 - 91.5) at 12 months (T12), respectively ($p = 0.01$ and 0.01), but not significantly improved in LD. In LD, PSL dosage decreased from 8 mg (IQR: 5 - 10) at T0 to 6 mg (IQR: 4 - 8) at T12 ($p < 0.001$) and from 9 mg (IQR: 5 - 15) to 7 (IQR: 4.7 - 9) in HD ($p < 0.001$). The changes in PSL dosage from T0 to T12 were -2 mg (IQR: -5 - 0) and -2 mg (IQR: -7 - 0) in LD and HD ($p = 0.37$) and SLEDAI-2K score were 0 (IQR: -4 - 0.25) and 0 (IQR: -4 - 2) in LD and HD, respectively ($p = 0.44$). [Conclusions] HD improved the serological findings but had similar effects on PSL dosage and SLEDAI-2K score as LD.

## W2-5

**Status of ophthalmological screening for hydroxychloroquine retinopathy by prefecture using the Japan Medical Data Base of Insurers**

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Conflict of interest: Yes

[Objectives] To clarify the implementation status of screening for hydroxychloroquine (HCQ) retinopathy screening in Japan. [Methods] Using the Japan Medical Data Base of Insurers from 2015 to 2023, we investigated rate of ophthalmological consultations and tests nationwide and by prefecture in patients with SLE or CLE. [Results] Among 2,567 patients prescribed HCQ, 599 (23.3%) patients discontinued the treatment. The observation period was one year for 1,680 patients (65.4%) and five years for 256 patients (10.0%). The rate of ophthalmological consultations was 88.0% (2258/2567) nationwide and 62.5% to 100% by prefecture at baseline, 76.3% (1282/1680) nationwide (0 to 100% by prefecture) at year 1, and 78.5% (201/256) nationwide (0 to 100% by prefecture) at year 5. The nationwide implementation rate of optical coherence tomography (OCT) and visual field testing (VFT) was 70.4% (1808/2567) and 56.5% (1450/2567) at baseline; 58.7% (986/1680) and 44.3% (745/1680) at year 1; and 67.6% (173/256) and 55.1% (141/256) at year 5, respectively. [Conclusion] Prefectural differences in the status of screening for HCQ retinopathy were observed. Although the screening rate at year 1 had not declined, a decrease in the rate of OCT and VFT, which are important for screening, was observed.

## W2-6

**Examination of the clinical characteristics of patients with systemic lupus erythematosus in our hospital who have not yet received hydroxychloroquine**

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Conflict of interest: None

[Objective] In the clinical practice guidelines for SLE, HCQ is positioned as a basic drug for the treatment of SLE. However, there are still many cases which HCQ cannot be administered. [Methods] Among the 115 SLE patients attending Yodogawa Christian Hospital in October 2023, 1) whether HCQ was administered or not, 2) patient background, 3) treatment, and 4) the reasons HCQ was not administration were examined retrospectively. [Results] There were 69 patients (60%) receiving HCQ. The average dose of HCQ was 4.16 mg/body weight. Comparing cases which HCQ was introduced (n = 69) or not (n = 46), 88% vs. 85% were women, age was 45 years vs. 58 years, and disease duration was 10 years vs. 18.5 years. Patients who had not taken HCQ tended to be older and had a longer disease duration. In addition, the oral prednisolone dose was 4 mg/day vs. 5 mg/day, and glucorticoid (GCs)-free cases were 8 vs. 1. Among patients who had not used HCQ, 19 cases (41%) were treated with GCs alone. The most common reason for not using HCQ was "unable to obtain consent" at 30%. [Conclusions] Patients who have not used HCQ tend to have a longer disease duration, are older, and still depend on GCs treatment, suggesting that there are many cases which HCQ has not been introduced at the patient's request.

## W3-1

**Serum CA19-9 levels in systemic sclerosis-associated interstitial lung disease**

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Conflict of interest: None

[Objective] To assess the utility of serum CA19-9 levels as a biomarker in systemic sclerosis-associated interstitial lung disease (SSc-ILD). [Methods] SSc patients who were admitted to Tokyo Women's Medical University Hospital from 2010 to 2021 were enrolled. ILD was diagnosed by chest CT. Patients were classified into limited and extensive groups based on chest CT and pulmonary function test (PFT). We assessed differences in CA19-9 levels between these groups, and correlations between CA19-9 levels and ILD area or PFT. Moreover, cutoff values of KL-6 and CA19-9 were calculated to detect a wide range of groups, and their discriminatory ability was compared by the De Long test. [Results] Of 56 patients, 40 had ILD; 17 were classified into the extensive group. CA19-9 was significantly higher in the extensive group compared to the limited group. KL-6 and ILD area correlated with CA19-9, but PFT did not. The AUC values for KL-6 and CA19-9 were 0.89 and 0.74, respectively (p=0.12). The Extensive group met either (1) KL-6 ≧ 518 U/mL or (2) KL-6 < 518 U/mL and CA19-9 ≧ 19.8 U/mL. [Conclusions] Serum CA19-9 levels were suggested as a useful diagnostic marker for identifying the extensive group, and its ability was further enhanced when combined with serum KL-6 levels.

## W3-2

**A model for predicting progression of Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)**

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Conflict of interest: None

[Objective] SSc-ILD is the leading cause of morbidity and mortality, while it is difficult to predict the progressive pulmonary fibrosing phenotype in clinical practice. In this study, a single-center prospective registry of SSc-ILD patients was used to generate the predictive score model of progressive pulmonary fibrosis (PPF). [Methods] Baseline characteristics that predicted the PPF event were identified using univariate and multivariate analyses, and a prediction score model was created by combination of identified predictors. [Results] Of 121 patients with SSc-ILD, 34 (28%) developed PPF during median of 23 months of follow-up. Anti-topoisomerase I antibody, KL-6 > 820 IU/mL, and percent predicted forced vital capacity < 70%, and UIP pattern were considered independent predictors for the PPF event. A predictive risk score was created based on the number of predictors (anti-topoisomerase I antibody, KL-6, and UIP pattern). ROC curve analysis found that this model performed excellent in limited disease (optimal cut-off 0.5 and area under the curve of 0.81); the odds of PPF in patients with the scores of 0, 1, 2 and 3 were 0%, 20.5%, 66.7%, and 100%, respectively. [Conclusions] We successfully generated the model for predicting progression of SSc-ILD.

## W3-3

**Safety and Efficacy of Nintedanib in the Treatment of Connective Tissue Diseases-Associated Interstitial Lung Disease. A retrospective survey in our department**

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Conflict of interest: None

[Objective] This study aims to assess the safety and efficacy of nintedanib (NTB) in connective tissue diseases-associated interstitial lung disease (ILD). [Methods] Patients prescribed NTB were extracted from medical records. Drug continuation rates, maximum tolerated doses, and adverse events (AEs) were evaluated, and were compared between patients with systemic sclerosis (SSc) and the others. KL-6 levels before and after NTB therapy were compared. [Results] 39 cases (female; 27, the mean age; 63.5±12.5 years) were involved. Underlying diseases included SSc; 16, rheumatoid arthritis; 7, inflammatory myositis; 6, ANCA-associated vasculitis; 4, mixed connective tissue disease; 4, and Sjögren's syndrome; 2. AEs included diarrhea; 14, nausea; 6, and liver injury; 6. Diarrhea was the most common reason for discontinuation (6/13). Continuation rates (10/16 vs. 16/23, p=0.645) and AEs rates were similar between SSc group and the others. The proportion who could continue 300 mg/day tended to be lower in SSc group (2/16 vs. 9/23, p=0.086). KL-6 levels were significantly decreased in 20 patients who continued NTB for more than 6 months (890.9±530.9 U/mL vs. 619.5±374.5, p=0.01). [Conclusions] NTB was associated with frequent AEs, but showed the significant improvement of ILD biomarker.

## W3-4

**Evaluating the risk of digital ulcers in systemic sclerosis through the measurement of radial and ulnar artery diameters using vascular ultrasonography**

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Conflict of interest: None

[Objective] To evaluate the risk of digital ulcers (DUs) in systemic sclerosis (SSc) through the measurement of radial artery (RA) and ulnar artery (UA) diameters using vascular ultrasonography (US). [Methods] In this study, we examined the medical records of SSc patients who underwent vascular US between August 2022 and August 2023 at our hospital. The association between the occurrence of DUs and US findings was assessed by logistic regression analysis. [Results] We included 32 female patients with SSc. The median age and disease duration were 69 years and 9.7 years, respectively. Among these patients, 16 (50%) were on vasodilator medications, and 22 (69%) had a history of DUs. The median vessel diameter was 1.07 mm for the UA, 1.64 mm for the RA, and 2.88 mm for the sum of them. The diameters of RA, UA, and the sum significantly influenced the occurrence of DUs (odds ratio; 95% confidence interval, 22.6; 1.44-352.6, 29.8; 1.56-563.3, 13.0; 1.60-105.7, respectively). The cutoff value for the sum diameter of RA and UA, demonstrating the most significant association, was 2.76 mm (AUC 0.857). [Conclusions] Screening tests using vascular US of RA and UA are suggested to be useful for considering the treatment strategy for DUs in SSc.

## W3-5

**A case of systemic sclerosis complicated with severe interstitial pneumonia and pulmonary hypertension who survived 2 years after double lung transplantation with improvement of respiratory condition**

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Conflict of interest: None

[Background] There are limited reports on the outcomes after lung transplantation in patients with systemic sclerosis-associated lung disease (SSc-ILD) in Japan. [Case] A 39-year-old woman came to our department in X-10 because of cough, Raynaud's phenomenon and skin stiffening. She had positive anti-Scl-70 antibody and ILD. Comorbid pulmonary hypertension was ruled out. Although she was treated for SSc-ILD with glucocorticoids, intermittent intravenous cyclophosphamide, and mofetil mycophenolate, in X-7 she developed eRVSP 45.3 mmHg and was started on tadalafil. Her respiratory distress further worsened in X-5, and home oxygen therapy (HOT) was introduced. She was suspected of chronic thromboembolic pulmonary hypertension (CTEPH) and warfarin was added. For young, treatment-resistant SSc-ILD and CTEPH, we registered her for lung transplantation in X-4. Although her respiratory condition continued to worsen, she was able to receive a brain-dead double lung transplantation in X year. Her FVC showed improvement from 56.1% to 82.8%. At X+2 years, she has maintained HOT withdrawal and is doing well with no PH relapse. [Clinical Significance] Lung transplantation may be an option for young patients with refractory SSc-ILD/PH to improve their survival rate and ADL.

## W3-6

**Clinical characteristics of patients with the physical frailty asscociated with systemic sclerosis**

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Conflict of interest: None

[Objective] To clarify the clinical characteristic of cases with the physical frailty in SSc. [Methods] Patients with SSc fulfilled the 2013 ACR/EULAR classification criteria and visited our hospital between April 2021 and September 2023 were included. Physical frailty phenotype (PFP) was recognized as the frailty, pre-frailty or no-frailty based on the definition of Japan Center for Health and Safety of Working People (J-CHS). Clinical information was retrospectively collected and compared among 3 groups. [Results] Forty-nine SSc was included. Mean age was 63.7 ± 13.3, 78% was female. Thirty five (71%) were pre-frail and 5 (10%) frail and 9 (18%) were no-frailty. When clinical characteristic was compared among 3 groups, higher HAQ-DI ($p<0.001$), age at SSc diagnosis ($p<0.05$) and longer duration of SSc ($p<0.01$) were extracted. As for the SSc organ involvements, the PFP was associated with dysphagia ($p<0.03$) and bloating ($p<0.03$), EAT-10 total score ($p<0.01$), F-scale total score ($p<0.05$), fecal incontinence, social functioning, psychological health, constipation and total score on the UCLA GIT-2.0 ($p<0.05$, $p<0.05$, $p<0.02$, $p<0.02$, $p<0.05$, respectivly). [Conclusions] The physical frailty may be correlated with disease duration of SSc and associated with gastrointestinal involvement.

## W4-1

**Epidemiological characteristics of polymyositis and dermatomyositis before and after the COVID-19 pandemic**

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Conflict of interest: None

[Objective] This study aimed to clarify the epidemiological characteristics of PM/DM patients before and after the COVID-19 pandemic. [Methods] We retrospectively examined PM/DM diagnosed in our department from 2017 to 2022 by year of onset for age, sex, specific antibodies, and presence of interstitial pneumonia (IP) from medical records. [Results] 80 patients were identified, 26 PM, 54 DM, age 57.4±15.7 years, male to female ratio 25:55, IP at onset, 63.8%, autoantibodies were ARS: MDA5: TIF-1γ: other: negative 30:20:10:5:15. The number of patients with PM/DM increased significantly in the three years from 2020 to 2022 compared to the previous three years ($p=0.0422$, Student t-test). ARS antibody-positive patients increased for three consecutive years, TIF-1γ antibody-positive patients in 2020 & 2021, and MDA5 antibody-positive patients in 2022-no increase in the percentage of IP. The percentage of patients with IP was 90% in ARS/MDA5 antibody-positive patients and 40% in specific antibody-negative patients, while all TIF-1γ antibody-positive patients had no interstitial pneumonia. [Conclusions] This study found that PM/DM cases in our department increased significantly in the past three years after 2020, especially among patients with positive for ARS, MDA5, and TIF1γ antibodies.

## W4-2

**Characteristics and outcomes of idiopathic inflammatory myopathy: a single-center retrospective cohort study**

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Conflict of interest: None

[Objective] Myositis-specific antibody (MSA) assays such as anti-MDA5 antibody have been covered by insurance in Japan since October 2016, enabling early evaluation of antibodies useful for predicting clinical course and selecting therapy. We evaluated the clinical characteristics and outcomes of idiopathic inflammatory myopathy since October 2016. [Methods] This was a retrospective, single-center study in 91 patients with diagnosed polymyositis (PM) or dermatomyositis (DM) between October 2016 and September 2021. [Results] Of all patients, 63.7% had DM, 65.9% had interstitial lung disease, 19.8% had malignancy, and 17.6% died during the observation period. The most common MSA was anti-ARS antibody, followed by anti-MDA5 antibody and anti-TIF-1γ antibody. All anti-MDA5 antibody-positive patients were treated with combined immunosuppressive therapy and showed no significant difference in survival curves compared with anti-ARS antibody-positive patients. [Conclusions] Previously, anti-MDA5 antibody-positive patients were considered to have a poor prognosis, but with the widespread use of combined immunosuppressive therapy, there was no difference in outcome between patients with anti-MDA5 antibody and those with other antibodies.

## W4-3

**Clinical characteristics of anti-mitochondrial antibody-positive myositis experienced in our hospital**

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Conflict of interest: None

Purpose: Anti-mitochondrial antibodies (AMA) are frequently detected in primary biliary cholangitis (PBC) and are widely used in the diagnosis of PBC. In inflammatory myositis (IM), inflammation is induced in striated muscles by an autoimmune mechanism. Among them, AMA-positive cases have been reported, but the frequency is low among all myositis. Therefore, the purpose of this study was to analyze data on AMA-positive myositis treated at our hospital and to clarify its characteristics. Methods: Thirteen cases of AMA-positive IM were extracted. The medical history, symptoms, laboratory findings, treatment of the patients were investigated retrospectively from medical records. Results: age 31-77 (median 49) years. Females 12. Polymyositis 11. CK 369-5640 (median 1652)

U/mL at onset, PBC 4, autoimmune hepatitis (AIH) 4, cardiac disease 4, interstitial pneumonia 4, no malignancy. Infiltrating T cells in myositis lesions were CD4-dominant. Treatment: prednisolone (PSL) dose 20-60 (median 45) mg/day, high-dose intravenous immunoglobulin therapy in 5, tacrolimus in 8, statin in 2. Outcome: 12 patients recovered, 1 died. Summary: Except one case, the AMA-positive myositis was polymyositis, but infiltrating T cells were predominantly CD4. Most of the cases were complicated by PBC or AIH.

## W4-4

**Evaluation of Progressive Pulmonary Fibrosis (PPF) in Anti-MDA5 Antibody-Positive Polymyositis/Dermatomyositis Complicated by Interstitial Lung Disease**

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Department of Rheumatology, Osaka Medical and Pharmaceutical University, Osaka, Japan

Conflict of interest: None

Objective: This study explores the characteristics of patients meeting the progressive Pulmonary Fibrosis criteria in those with anti-MDA5 antibody-positive PM/DM. Methods: We examined 17 consecutive cases of anti-MDA5 antibody-positive PM/DM with interstitial lung disease admitted to our institution between July 2016 and October 2022. The median age was 60 years, with a female predominance of 70.6%. We analyzed clinical backgrounds, treatment regimens, respiratory symptoms, pulmonary function test results, and chest HRCT findings to identify factors associated with PPF progression. Results: Among the 5 cases meeting PPF criteria, 4 also met the criteria for PF-ILD with progressive fibrosis. The duration to meet PPF and PF-ILD criteria was 0.3 (0.04-0.4) years and 0.2 (0.03-0.4) years, respectively. In the PPF group, there was a trend toward higher pre-treatment anti-MDA5 antibody titers and serum ferritin levels (P=0.07,0.19, respectively) and lower FiO2 (P=0.15) compared to the non-PPF group. Moreover, the use of steroid pulse therapy was significantly more frequent in the PPF group (P=0.04). Conclusion: This study suggests a potential link between adverse prognostic factors before treatment and the progression of PPF in anti-MDA5 antibody-positive PM/DM-ILD.

## W4-5

**Interstitial lung disease related to anti-MDA-5 antibody-positive dermatomyositis: clinical analysis of 27 cases**

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Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Nagano, Japan

Conflict of interest: None

[Objective] To investigate the clinical feature of patients with interstitial lung (ILD) related to anti-MDA-5 antibody-positive dermatomyositis (MDA5-DM) depending on the prognosis. [Methods] Clinical information in 27 patients with MDA5-DM was statistically analyzed between patients who died (PD) and those who survived (PS). [Results] ILD was observed in all patients, including 19 PS and 8 PD, who died ascribable to ILD deterioration, (8 females, 74 ± 12 years). PD significantly had higher frequency of skin ulcers, white blood cell counts, serum level of ferritin and CRP, and anti-MDA5 antibody titers, and lower respiratory functions than PS. Corticosteroids concomitantly with tacrolimus or cyclosporine were initially administered in all, while an intravenous infusion of cyclophosphamide was given in 26 patients. Rituximab (RTX) was additionally administered in 11 patients with resistant to initial treatment, including 6 PS (PS-RTX) and 5 PD (PD-RTX). Of those, 4 were alternatively treated with baricitinib. Longer periods up to initiating treatments were observed in PD-RTX than in PS-RTX. [Conclusions] Suggestive prognostic factors of refractory MDA5-DM ILD were significantly observed in PD. Early treatments are necessary for achieving a favorable prognosis.

## W4-6

**A retrospective study Study of Factors Influencing Glucocorticoid Free in Anti-MDA5 Antibody-Positive Dermatomyositis**

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Conflict of interest: None

[Objective] Various prognostic factors about anti-MDA5 antibody-positive dermatomyositis (MDA5-DM) have been reported. However, little is known regarding the factors of achieving clinical remission in the patients. In this study, we investigated contributing factors to glucocorticoid (GC)-free remission in MDA5-DM patients. [Methods] We included MDA5-DM patients who visited our institution. Clinical remission was defined as patients who did not experience recurrence or worsening of clinical symptoms and were able to achieve discontinuation of GC use. We retrospectively analyzed the characteristics of the remission and non-remission groups. [Results] A total of 28 MDA5-DM patients were enrolled, with a median age of 52.5 years, and 46.4% were male. The remission group had 10 patients and the non-remission group had 18 patients. The remission group had significantly lower initial CK levels (p=0.05), shorter time to antibody conversion (p=0.03), and lower prevalence the reverse Gottron's sign (p=0.05). Age, gender, and the presence of ILD at disease onset did not predict remission. [Conclusions] Initial CK levels, the presence of the reverse Gottron's sign, and the time to conversion of anti-MDA5 antibodies to negative may be potential factors contributing to achieving GC-free remission.

## W5-1

**Ultrasound synovial findings in patients with rheumatoid factor and anti-CCP antibodies positive/negative**

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Conflict of interest: None

[Objective] In rheumatoid arthritis (RA), the presence of autoantibodies such as rheumatoid factor (RF) and anti-citrullinated peptide antibodies (anti-CCP antibodies) is known to affect not only diagnosis but also treatment response. Therefore, we evaluated the ultrasound synovial findings in the hand and foot in cases where RF and anti-CCP antibodies were positive or negative. [Methods] 818 patients with RA were included performed ultrasound examination. Gray scale (GS) and power Doppler (PD) scores were evaluated using a semi-quantitative method, and each was compared based on RF positive/negative and anti-CCP antibody positive/negative. We also investigated the combination of RF±/anti-CCP antibody±. [Results] GS and PD scores were significantly higher in the RF positive than negative groups for both fingers and toes, and similar results were found for anti-CCP antibody. Compared with RF-/anti-CCP antibody-, no significant difference was observed for RF+/anti-CCP antibody- and RF-/anti-CCP antibody+. However, RF+/anti-CCP antibody+ showed the highest GS/PD score. [Conclusions] Both RF and anti-CCP antibodies positive patients had the severe ultrasound synovial findings. We have to pay attention for synovitis to avoid joint destruction in these patients.

## W5-2

**Value of musculoskeletal ultrasound in detecting early joint changes in patients with asymptomatic hemophilia arthropathy**

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Conflict of interest: None

[Objective] Early detection of hemophilic arthropathy (HA) is crucial, despite synovitis potentially being asymptomatic. This cross-sectional study aims to compare the clinical value of MSKUS and clinical joint assessments for detecting early joint damage in asymptomatic joints of PwH. [Methods] We analyzed PwH under 35 years of age with mild joint damage. Before MSKUS, we assessed clinical joint factors such as tenderness, swelling, Hemophilia Joint Health Score (HJHS), and radiographic factors (Petterson score). MSKUS followed HEAD-US guidelines for bilateral ankle, knee joints, and elbow joints. We defined synovitis as a synovial hypertrophy score ≧1. We compared clinical joint assessments for each joint with synovitis. [Results] Among 24 PwH (median age 13 years), 137 asymptomatic joints were enrolled. Synovitis frequency in each joint is as follows: Elbow (44 joints); 34%, Knee (45 joints); 33%, Foot (38 joints); 18%. Out of 38 joints with synovitis, 0% showed tenderness, 2.6% had swelling, 11% had HJHS scores ≧1, 11% had Petterson scores ≧1, and 0% were PD positive. [Conclusions] Synovitis was more prevalent in elbow and knee joints among asymptomatic joints. Our results highlight the clinical value of MSKUS in screening for asymptomatic synovitis in PwH.

## W5-3

**Joint examination and ultrasound findings in the wrist joints of patients with rheumatoid arthritis**

Takehisa Ogura[1], Norihide Hayashi[2], Chihiro Imaizumi[1], Yuto Takakura[1], Yasuto Minegishi[1], Reina Maezawa[1], Takaharu Katagiri[1], Hideto Kameda[1]
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Conflict of interest: None

[Objective] Joint examination is important in treating rheumatoid arthritis, but it is only sometimes consistent with imaging findings by ultrasonography (US). We investigated the findings on examination and US findings in the wrist joints of RA patients. [Methods] In 235 patients with RA, we investigated the factors that cause subclinical synovitis (SS) in joints with US arthritis without swelling or tenderness and clinical synovitis (CS) in joints with US arthritis with swelling and/or tenderness on examination. The factors that cause SS were investigated. [Results] Of 470 bilateral joints, 100 (21%) had SS, and 128 (27%) had CS. When divided into ulnar and median/radial regions, 18 (18%) and 13 (10%) of SS and CS patients had ulnar involvement, respectively (p=0.12), while 55 (55%) and 26 (20%) had median/radial involvement, respectively (p=<0.001). Factors contributing to the SS The odds ratio was 9.6 (p<0.001) in a generalized linear mixed model incorporating patient age, gender, duration of disease, BMI, and DAS28-CRP concerning the presence of lesions on the median and radial side only. [Conclusions] Detection of arthritis in the wrist joints of RA patients is difficult on examination when lesions are limited to the median and radial sides.

## W5-4

**Extensor tendon rupture of the wrist joint in rheumatoid patients and evaluation with modernthree-dimensional computed tomography reconstruction images**

Yosuke Takiguchi[1], Koichi Murata[1,2], Takayuki Fujii[1,2], Akira Onishi[2], Masao Tanaka[2], Hideo Onizawa[2], Kosaku Murakami[2], Akio Morinobu[3], Shuichi Matsuda[1]
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Conflict of interest: None

[Objective] The aim of this study was to identify factors associated with extensor tendon rupture in patients with rheumatoid arthritis based on the latest 3D-CT reconstructed images and radiographic changes. [Methods] Of the 89 wrist surgeries in which extensor tendons were identified intraoperatively at our hospital from 2006 to 2022, 68 cases were identified by CT and 61 cases were reconstructed by 3D-CT. In 61 cases, extensor tendon ruptures of the index, middle, ring, and little fingers were evaluated by 3D-CT (Vincent, Fujifilm) for poor extensor tendon delineation, tendon loosening, MP joint flexion, and radiographs for radial deformity, decreased carpal height, and ulnar subluxation. [Results] Multivariate analysis showed a significant association between tendon rupture and poor extensor tendon delineation and/or extensor tendon loosening in the 3D-CT of the middle, ring, and little fingers. The sensitivity and specificity were 75% and 87.8% for the middle finger, 73.3% and 93.5% for the ring finger, and 87.5% and 79.3% for the little finger. [Conclusions] Loosening of the extensor tendon in 3D-CT reconstruction images and poor visualization of the extensor tendon are useful for the diagnosis of rupture of the extensor tendon of the wrist in patients with rheumatoid arthritis.

## W5-5

**Diagnosis of Bone Marrow Edema in Simple X-ray image Using AI**

Kou Katayama[1], Yujiro Kon[2], Akira Sagawa[3], Akira Furusaki[3], Takeshi Suzuki[4], Yasuhide Kanayama[5], Makoto Onishi[6]
[1]Department of Othopedic Surgery, Katayama Orthopedic Rheumatology Clinic, Asahikawa, Japan, [2]Sapporo Rheumatology and Immunology Clinic, [3]Sagawa Rheumatology Clinic, [4]Department of Rheumatology, Mitsui Memorial Hospital, [5]Department of Orthpedic Surgery and Rheumatology, Toyota Kosei Hospital, [6]Department of Internal Medicine and Rheumatology, Center for Rheumatic Disease, Dohgo Spa Hospital Rheumatology

Conflict of interest: None

[Objective] Bone edema (BE) detected by MRI has been reported as a risk factor for joint destruction in the recommendations of the European League Against Rheumatism. BE has also gained attention as a risk factor for rapid joint destruction (RRP) by X-ray in the D2TRA criteria. On the other hand, simple imaging is a technique used to observe fractures, deformities, displacements, erosions, and shape changes. However, diseases within the bone, such as BE, could not be observed due to differences in contrast. Therefore, in collaboration with the Department of Information Engineering at Nagoya University, deep learning using AI was applied to X-ray images of groups with and without BE identified by MRI. We developed the application for detecting BE in the hand. [Methods and Results] In this study, using application, we report the results of, reduction of BE by Biologics,, early detection of BE in RRP cases, data reliability by multi-center registration (above 5 centers). [Conclusions] Newly developed BE detecting system may be useful for avoiding RRP.

## W5-6

**Evaluation of rheumatoid forefoot callus severity by 3D-VR**

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Conflict of interest: None

[Objective] Many patients with rheumatoid arthritis who underwent forefoot surgery had painful plantar callosities. We evaluated the morphology of the plantar callosities using 3D-volume rendering (3D-VR) and examined their relationship to the flexor tendons to determine if this is an indicator of the severity of the condition. [Methods] Twenty-one RA patients with 23 legs were included. All patients had painful calluses on the plantar surface, which led to surgery. The CT images taken as a preoperative exam were constructed using a 3D image analysis system, and the callosities, flexor tendons, and bony joints were visualized by changing the opacity. [Results] Twenty-seven calluses were visualized. 21 calluses on the second, third, and fourth toes were evaluated. Fourteen calluses without central defects and seven calluses with defects were observed. The flexor tendon was deviated from the plantar aspect of the metatarsal head in 17 toes. **71.4 (10/14)%** of the patients without a central defect of the corpus callosum had a deviation of the flexor tendon, while **all** patients with a defect had a deviation. [Conclusions] The flexor tendon was deviated in all cases of central deficit of the callosum in 3D-VR, and the central deficit of the plantar callosum is an indicator of a severe condition.

## W6-1

**Six cases with relapsing IgG4-related disease with rituximab therapy**

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Conflict of interest: None

[Background] IgG4-related disease (IgG4RD) is characterized by infiltration of IgG4-positive plasma cells, and tissue fibrosis resulting in organ damage throughout the body. Although steroid therapy is effective in the early stages of the disease, relapse after occurs following reduction or discontinuation of steroid therapy. We report six cases with relapsing IgG4RD treated with rituximab (RTX). The median age was 62 years (ranged from 43 to 65 years), median prednisolone (PSL) use was 5.5 mg/day (from 0 to 10 mg/day), median serum IgG4 levels was 403 mg/dL (from 269 mg/dL to 1270 mg/dL). Organ involvement was 4 submandibular gland, 3 lacrimal gland, 2 orbit, 2 lymph node, 2 lung, 1 sinus, 1 joint, 1 periaortic, 1 renal, and 1 prostate lesion. The reason for RTX therapy was difficulty in reducing steroid dose in 4 patients and active relapse in 2 patients. After the start of RTX therapy, 3 patients discontinued PSL, 2 successfully tapered dose of PSL, and 1 patient relapsed after completion of PSL but achieved remission with RTX alone. The median serum IgG4 level decreased to 112.9 mg/dL (from 45 mg/dL to 329 mg/dL). [Conclusion] RTX can be an effective treatment option for relapsing IgG4RD.

## W6-2

**IgG4-related Giant Coronary Aneurysm with Rapid Wall Thinning after Glucocorticoid Therapy: Case Report and Review of the Literature Focusing on Treatment Strategies and Complications**

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Conflict of interest: None

Coronary periarteritis is a dangerous manifestation of IgG4-related disease because it forms coronary artery aneurysms, which may cause sudden cardiac death. We report the case of a 78-year-old woman with IgG4-related coronary periarteritis and a coronary aneurysm which showed progressive enlargement despite maintenance therapy for type 1 autoimmune pancreatitis. Low-dose glucocorticoids suppressed the progression of periarterial lesions but led to rapid thinning of the aneurysmal wall and an increase in the size of mural thrombi, which poses a risk of myocardial infarction. Our systematic literature review including 98 cases of 86 articles was performed to examine its treatment strategies and complications. Among the cases in which the effect of immunosuppressive therapy could be followed radiologically, 33 of 37 (89.1%) cases showed improvement in wall thickening/periarterial soft tissue, while six of 13 (46.2%) showed worsening increase in the outer diameter of the coronary aneurysms. We suggest that immunosuppressive therapy for IgG4-related coronary periarteritis with coronary aneurysms should be conducted only after the therapeutic benefit has been determined to outweigh the risks.

## W6-3

**Efficacy of GC monotherapy in patients with IgG4-related disease**

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Conflict of interest: None

[Objective] We evaluated the efficacy of GC monotherapy in the initial treatment of IgG4-RD. [Methods] Patients with IgG4-RD diagnosed through May 2023 based on the 2020 revised comprehensive diagnostic criteria for IgG4-RD and undergoing treatment were included. Clinical indicators, the number of organs involved and laboratory findings were collected retrospectively. Treatment indicators included the initial dose of GC, the GC dose at three and six months, and relapse within 1 year of treatment were analyzed. Effect predictors was examined by comparing patients who did not improve or relapsed with those who did not relapse. [Results] Of the 95 patients with IgG4-RD, 59 were treated: 42 with GC alone and 17 with concomitant immunosuppressants at the start of GC or early at the time of GC tapering. Relapses occurred in 7 patients with GC monotherapy and no patient with immunosuppressants; the mean relapse time was 7.1±2.7 months after GC start, and the mean GC dose at relapse was 8.5±1.3 mg. Of GC monotherapy, no significant differences were observed between the relapsed or treatment-resistant group and the group that did not relapse. [Conclusions] We did not identify the effect predictors in GC monotherapy, but early concomitant use of immunosuppressive drugs might reduce relapse.

## W6-4

**Outcome of suspected cases of retroperitoneal fibrosis**

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Conflict of interest: None

[Objective] To clarify the clinical problems of retroperitoneal fibrosis (RPF), we investigated the outcomes of cases suspected of having RPF. [Methods] We retrospectively investigated cases in which RPF was suspected based on image diagnosis, and examined examinations, images, pathology, treatment, and outcomes from medical records. [Results] There were 35 suspected cases of RPF. High serum IgG4 levels (>135 mg/dl) were observed in 14 cases. There were 14 cases complicated by hydronephrosis. There were 16 cases of malignancy (including past ones). One case of cervical cancer had hydronephrosis, high IgG4 level, and suspected RPF. There were two cases with a history of asbestos exposure. Retroperitoneal biopsies were performed in 5 cases, and a definitive diagnosis was reached in 2 cases. There were 11 cases of IgG4RD that met the ACR classification criteria. Steroids were administered to 23 cases, and 11 cases of IgG4RD and 10 cases of difficult to diagnose, responded to steroids. One of the two steroid-refractory cases developed pancreatic cancer. There were 3 cases in which the retroperitoneal lesions disappeared during follow-up without treatment. [Conclusions] Cases of suspected RPF include IgG4RD, idiopathic, malignant, and secondary, and differential diagnosis is important.

## W6-5

**A case of malignancy that presented retroperitoneal fibrosis and periaortitis and was diagnosed from biopsy of periaortic femoral tissue**

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Conflict of interest: None

[Case] 73-year-old woman [History] She had a history of treatment for early gastric cancer and mesopharyngeal cancer, and was taking PSL 4 mg/day for Sjogren's syndrome and neuromyelitis optica. She was admitted due to vomiting, and the CT scan showed duodenal obstruction, bilateral ureteral obstruction. PET-CT showed accumulations around the abdominal aorta, and periaortitis was thought to be the cause of each obstruction. Malignancy was suspected, then the biopsy of tissue around the left femoral artery was performed on the 25th day. Intravenous infusion of PSL 40 mg was started on the 26th day. However, the biopsy showed invasion of the cancer, which was thought to be the cause of periaortitis-like presentation. High-dose PSL was discontinued, and gastric jejunal bypass was performed. but her general condition worsened and

she died on the 86th day. The pathological autopsy revealed cancer in the rectum. [Clinical Significance] There is no previous report showing that tissue biopsy around the femoral artery showed that the malignant tumor and presented a phenotype of periaortitis. The coexistence of duodenal obstruction and other autoimmune diseases in idiopathic retroperitoneal fibrosis is atypical, which suggested the importance of the biopsy in this case.

## W6-6

**A case of histologically diagnosed IgG4-related disease associated with myelodysplastic syndrome**

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Conflict of interest: None

We present the case of a 75-year-old man with diabetes. He was examined for neutropenia and anemia and diagnosed with myelodysplastic syndrome (MDS). While a CT scan showed aortic wall thickening and a left kidney mass, and an elevated IgG4 level of 144 mg/dl. So he was referred to our department. Cyclosporine was started for MDS but self-interrupted, followed by dyspnea. A CT scan showed worsening aortic wall thickening, increased masses in the left kidney and cervicothoracic spine, and bilateral pleural and pericardial effusions, which led to his hospitalization. Pleural biopsy revealed numerous IgG4-producing plasma cells, so IgG4-related disease (IgG4-RD) was diagnosed. After starting 30 mg prednisolone, his subjective symptoms improved, but he moved before determining effectiveness. Previous reports indicate that autoimmune disease complications in MDS range from 10-30%. Complications of IgG4-RD have been reported only infrequently. It has also been reported that autoimmune diseases associated with MDS often have high IgG4 levels, making tissue evaluation even more important in the diagnosis of IgG4-RD. We would like to report this case, a rare complication, and emphasize that histological diagnosis is more important for the diagnosis of this complication.

## W7-1

**Clinical characteristics and treatment information of TAFRO syndrome; Case series of seven patients**

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Conflict of interest: None

[Objective] TAFRO syndrome is a systemic inflammatory disease of unknown cause. This study aims to report the clinical characteristics of TAFRO syndrome treated at the Nara Medical University Hospital. [Methods] Seven cases treated at Nara Medical University Hospital between September 2015 and March 2023 were studied retrospectively. [Results] The median age was 51 years (43-78), 5 patients were female. Anterior mediastinal lesions were seen in 3 patients and adrenal involvement in 1 patient. Two patients had elevated liver enzymes. The time from onset to start of treatment was 29 days (17-32), and all patients survived. Therapy consisted of steroids (GC), cyclosporine (CyA), and tocilizumab (TCZ) in four patients, GC, TCZ, and rituximab (RTX) in one patient, and GC, CyA, TCZ, and RTX in two patients. TPO agonists were administered to 6 patients. From the start of treatment, it took 21 days (18-23) for CRP to become negative and 44 days (34-54) for platelet counts to exceed 50,000/μL. Complications during treatment included post-puncture bleeding in 2 patients, one of which met the diagnostic criteria for acquired hemophilia. The infectious complication was in 6 patients. [Conclusions] Early multidrug therapy and management of comorbidities and infections are important in treatment.

## W7-2

**Treatment strategies for TAFRO syndrome based on our clinical experience Obihiro-Kosei General Hospital Baba Daisuke, Ninagawa Keita, Sugawara Masanari, Shimizu Yuka**

Daisuke Baba
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Conflict of interest: None

A 76-year-old woman presented with edema, lymph nodes swelling, pleural effusion, thrombocytopenia, and renal dysfunction. The levels of CRP and IL-6 were elevated in serum and pleural fluid, and she was diagnosed TAFRO syndrome by lymph node biopsy. The disease activity remained high, despite of the induction therapy with high-dose steroids, tacrolimus, and tocilizumab, but, gradually began to be improved by adding plasma exchange (PEX). There are no clear treatment guidelines for TAFRO syndrome, and we analyzed prognostic factors for clinical outcome and treatment in 10 patients of our hospital (median age 69, 6 alive and 4 dead). The result showed that serum albumin levels (Alb, mg/dL) at the start of treatment were higher in the survival group than in the death group (2.6 [2.4-2.9] vs 1.9 [1.7-2.2], p=0.01). There were no significant differences in serum IL-6, CRP, serum creatinin, or platelets. And the result of receiver operating characteristic (ROC) curve of serum Alb for death (AUC=0.925, cut-off: 2.2 mg/dL, sensitivity: 100%, specificity: 80%) indicated that serum Alb may predict prognosis. In TAFRO syndrome, number of inflammatory cytokines and increased vascular permeability, and early induction of PEX with immunosuppressive therapy may reduce inflammatory cytokine.

## W7-3

**A case of rituximab response to TAFRO syndrome in a patient with rheumatoid arthritis on tocilizumab treatment**

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Conflict of interest: None

[Case] 56-year-old woman. She has been treated with tocilizumab (TCZ) for rheumatoid arthritis (RA) since X-10. In March X, she developed fever and edema, and consulted her previous doctor. Multicentric Castleman's disease was suspected on close examination, and she was transferred to our hospital in April after being refractory to prednisolone (PSL) and TCZ. (1) fluid retention, (2) thrombocytopenia, (3) unexplained fever and inflammatory reaction, (4) organ enlargement, (5) progressive renal dysfunction, bone marrow biopsy showed mild fibrosis, and cervical lymph node biopsy showed hypervascularization and plasma cell proliferation, so we diagnosed TAFRO syndrome. After a lack of response to high-dose steroid therapy, TCZ, and additional tacrolimus, they were replaced with rituximab. Gradually showed improvement in luminal hydrops, thrombocytopenia, and renal dysfunction. Four months after the onset of the disease, PSL was terminated, and she has not experienced any relapse. [Clinical Significance] There are few reports of autoimmune diseases complicated with TAFRO, especially RA. The pathogenesis of TAFRO is an excess of IL-6 and an increase in VEGF due to an increase in B cells and plasma cells, and removal of B cells at the onset during IL-6 inhibitory therapy may be useful. [COI] No

## W7-4

**A case of treatment-resistant TAFRO syndrome successfully treated with JAK inhibitor**

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Conflict of interest: None

**Case Study**: A 49-year-old male **Present Illness**: The patient was transported to previous hospital due to fever. Blood tests revealed thrombocytopenia, elevated hepatic enzymes, renal impairment, and increased CRP. CT imaging showed pleural and abdominal effusion and hepatosplenomegaly, but no lymphadenopathy. Despite antibiotics and steroid pulse therapy, no improvement was observed, leading to transfer to our department. **Course in Hospital**: Based on the symptoms and the findings,

TAFRO syndrome was suspected. We initiated prednisolone (PSL) 1 mg/kg and tocilizumab (TCZ) 8 mg/kg/week, followed by the administration of Rituximab (RTX). Despite this, clinical symptoms, white blood cell count, CRP and renal function did not improve. After starting ruxolitinib (RUX), the white blood cell count rapidly decreased, subsequently clinical symptoms and other findings gradually improved. **Discussion**: Treatment of refractory TAFRO syndrome hasn't been established. According to reports by Koga et al., abnormal activation of the PI3K/Akt/mTOR pathway is observed in TAFRO syndrome, and there are reports on the effectiveness of JAK inhibitors and mTOR inhibitors that target this pathway. We experienced a case of refractory TAFRO syndrome that was successfully treated with JAK inhibitors.

## W7-5

**Investigation of renal involvement in idiopathic multicentric Castleman's disease with plasma cell type on lymph node biopsy**

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Conflict of interest: None

[Objective] Idiopathic Multicentric Castleman Disease (iMCD) can be histologically divided into three types: hyaline vascular type, plasma cell type, and mixed type. The clinical features of iMCD are also variable. In this study, we examined renal histopathology of iMCD patients diagnosed as plasma cell type by lymph node biopsy to focus on cases of idiopathic plasmacytic lymphadenopathy (IPL) characterized by generalized lymphadenopathy and polyclonal hypergammaglobulinemia. We examined the renal histopathology of iMCD patients diagnosed as plasma cell type by lymph node biopsy to narrow the cases to those with IPL. [Methods] We examined the renal histopathology of 7 cases diagnosed as plasma cell type MCD by lymph node biopsy. [Results] Two of the seven cases were found to have AA amyloidosis. The other 5 cases showed focal inflammatory cell infiltration into the tubulointerstitium. Two of the five cases were IgG-positive by fluorescent antibody and subepithelial deposition by electron microscopy, consistent with membranous nephropathy. The two cases were IgA- and C3-positive and had deposits in mesangium, but both cases were mild. [Conclusions] This is the first report on the renal pathology of IPL, a uniform disease unit within iMCD, and the first to find commonalities among them.

## W7-6

**A histologically atypical case of idiopathic multicentric Castleman disease involving interstitial lung disease with autoantibody positivity**

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Conflict of interest: None

A 43-year-old woman was referred to this hospital because of the progressive interstitial lung disease with multiple bilateral ground-glass opacities (GGOs). Five years before the referral, elevated CRP and ESR were detected, and CT of the chest revealed multiple GGOs, which gradually progressed. Two months before the referral, cough and dyspnea with exertion developed, with anti-Scl-70 antibody level of 18.9 U/mL (CLEIA) detected. Generalized lymphadenopathy was present, and laboratory testing showed hypergammaglobulinemia, ANA at a titer of 1:40, and anti-DNA antibody level of 15.5 U/mL (RIA). The axillary lymph node biopsy specimen showed proliferation of mature plasma cells, which were stained IL-6 negative, with epithelioid cell granulomas. The patient was diagnosed with idiopathic multicentric Castleman disease (iMCD), and treated with tocilizumab and glucocorticoids, and had no relapse to this day. This case was clinically consistent with idiopathic plasmacytic lymphadenopathy (IPL) type of iMCD, with histologically atypical features. Non-specific autoantibodies are often detected in IPL, whereas iMCD-like histological findings are seen in autoimmune diseases. Comprehensive diagnosis and classification could help select the most appropriate treatment in iMCD.

## W8-1

**Identification of Transcription Factors Associated with Pathological Subsets of Rheumatoid Arthritis Synovial Fibroblasts**

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Conflict of interest: None

Objective: Synovial fibroblasts (SF) in Rheumatoid Arthritis (RA) comprise multiple subsets involved in the exacerbation or resolution of inflammation, as well as in the destruction or repair of bone and cartilage. This study aimed to identify transcription factors associated with pathological subsets by focusing on their expressions between these subsets. Methods: Microarray data from RASF subsets were compared to identify transcription factors differentially expressed among the subsets. Their expression were further validated using qPCR and Western blot. siRNA knockdown against GLIs and GLI1 inhibitor (GANT61) were employed to evaluate roles of GLIs by RNA-seq and qPCR. Results: In the pathological subset (THY1+CD34-), GLI3 was found to be highly expressed. Knockdown of GLI3 resulted in upregulation of GLI1, a target gene of GLIs, as well as pro-inflammatory cytokines such as IL6. Pathway analysis revealed that TNF and cytokine receptor signals were involved. The increased expression of inflammatory cytokines by GLI3 knockdown was suppressed by simultaneous knockdown of GLI1. In addition, GLI1 inhibitor GANT61 suppressed the TNF-induced expression of IL6. Conclusion: GLI3 functioned as a negative regulator of GLI1, which was involved in inflammation in pathological subsets of RASF.

## W8-2

**Investigation of the pathogenesis of rheumatoid arthritis based on the elucidation of the antigen-presenting mechanism of HLA class II molecules**

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Conflict of interest: Yes

[Objective] It has been shown that IgG heavy chains (IgGH) are presented on the cell surface by rheumatoid arthritis-susceptible HLA class II molecules and are specific targets for RF. We hypothesized that rheumatoid arthritis-susceptible HLA class II molecules might be associated with specific IgGH domains and that specific epitopes of the HLA class II molecule/IgGH complex might be involved in the response of T cells and B cells. Therefore, we analyzed the binding structure of IgGH to HLA class II molecules. [Methods] A combination of the four domains of IgGH, VH, CH1, CH2, and CH3, together with HLA-DR4, a susceptibility allele of rheumatoid arthritis, was expressed in HEK293T cells, and the IgGH presentation on the cell surface was analyzed by flow cytometry. In addition, the recognition sites of RFs for HLA class II molecules/IgGH complexes were analyzed. [Results] VH, CH1, and CH2 were presented by HLA-DR4, and especially with CH1. When HLA-DR4 and IgGH domains were expressed on the cell surface, RF recognized IgGH full-length (VH-CH1-CH2-CH3) or CH1-CH2-CH3, but not the IgGH region without CH3. [Conclusions] It was shown that IgGH containing the CH1 region is involved in presentation to HLA-DR and that RF recognizes IgGH regions with a contiguous structure of CH3.

## W8-3

**Elucidation of the point of action of antirheumatic drugs and the mechanism of treatment resistance by synovial single-cell analysis**

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Conflict of interest: None

[Objective] Despite the recent development of therapeutic agents, only about 40% of rheumatoid arthritis (RA) patients achieve clinical remission. This study aims to elucidate the action points of exiting antirheumatic drugs and the pathogenesis of treatment resistance. [Methods] Synovium was obtained from 51 RA patients and analyzed by flow cytometry and scRNA-seq, taken into an integrated analysis with clinical information. [Results] Multiple regression analysis of the drugs used at the time of sample collection and the cell balance in the synovium revealed that steroids tended to negatively control $CD4^+$ T cells, while methotrexate decreased $CD8^+$ T cells. Meanwhile, synovial fibroblasts (SF) persisted despite the use of any drugs, including biological agents, suggesting that they may contribute to the maintenance of inflammation. When we subdivided SF using scRNA-seq analysis, we found that *THY1*$^{low}$ sublining SF, which highly express chemokines and *IL6*, scarcely express genes that are suppressed by TNF or JAK inhibitors. Strikingly, patients with abundant *THY1*$^{low}$ sublining SF tended to have higher CDAI 3 months after starting IL6R or TNF inhibitors. [Conclusions] *THY1*$^{low}$ sublining SF could contribute to the acquisition of treatment resistance in Japanese RA patients.

## W8-4

**Involvement of oropharyngeal microbiota in the pathogenesis of late-onset rheumatoid arthritis**

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Conflict of interest: Yes

[Object] To clarify the relationship between the pathogenesis of late-onset rheumatoid arthritis (LORA) and the oropharyngeal microbiota, which has similarities with the pulmonary microflora. [Methods] Metagenomic analysis of oropharyngeal lavage fluid was performed in 47 patients with RA with no prior treatment and 47 healthy subjects, and the association between clinical presentation and bacterial species was analyzed by microbiome multivariable association with linear models ver. 2 (MaAsLin2) [Results] LORA (n=18) and younger-onset RA (YORA, n=29) did not differ in gender, anti-CCP antibody positivity, clinical disease activity index, and smoking history. The mean CRP and chronic lung disease (CLD) proportion were significantly higher in LORA than YORA. Fifteen bacterial species were increased in RA over healthy subjects, two of which were associated with LORA ($p<0.10$). Six species increased and nine decreased in LORA compared to YORA ($p<0.05$). Two of 10 species associated with increased CRP, one of seven species associated with CLD, and one of eight species associated with interstitial lung disease were increased in LORA. [Conclusion] The oropharyngeal bacterial flora of LORA and YORA are different and may be associated with high CRP levels and CLD in LORA.

## W8-5

**Inhibitory effect of JAK inhibitors on CEACAM1 expression on the surface of neutrophils**

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Conflict of interest: None

[Ovjective] Carcinoembryonic-antigen-related cell-adhesion molecule 1 (CEACAM1) is considered to be the important molecule for the regulation of autoimmunity. Our previous report demonstrated that CEACAM1 is predominantly expressed on neutrophils in peripheral blood of RA patients. However, the relationship between CEACAM1 expression and JAK/STAT pathway has not been reported. [Methods] We analyzed the inhibitory effects of three JAK inhibitors (JAKis) (tofacitinib, baricitinib, and filgotinib) on CEACAM1 expression. Peripheral blood neutrophils were obtained from healthy subjects. Isolated neutrophils were stimulated with inflammatory cytokines. The expression of CEACAM1 in peripheral blood neutrophils was analyzed by flow cytometry. STATs were assessed by Western blot. [Results] TNF-α stimulation upregulated CEACAM1 expression and induced phosphorylation of STAT1 and STAT3. Furthermore, CEACAM1 expression was upregulated in a concentration-dependent manner by GM-CSF stimulation and was suppressed by all JAKis. The inhibitory effect of baricitinib was greater than that of others. [Conclusions] The expression of CEACAM1 in neutrophils was dependent on inflammatory cytokines, and the inhibitory effect of baricitinib was closely related to the JAK1, 2/STAT3 pathway.

## W8-6

**Two cases thought to have developed polyarthritis after administration of Dupilumab**

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Conflict of interest: Yes

Dupilumab is an anti-human IL-4/13 receptor monoclonal antibody used for atopic dermatitis, bronchial asthma. We experienced two cases of polyarthritis after starting dupilumab. Case 1. A 59-year-old man had adult-onset bronchial asthma and atopic dermatitis. Dupilumab treatment was started due to lack of improvement despite topical steroids. Although the skin rash improved markedly, the patient developed polyarticular pain. Ultrasound showed no synovitis, and RF and anti-CCP antibodies were negative. Dupilumab was discontinued and joint symptoms improved. Case 2. A 49-year-old male with severe atopic dermatitis. There was no improvement with topical steroids, so dupilumab was started. The skin rash improved markedly, but the patient developed polyarthritis. Joint ultrasound revealed synovitis and RF157 and anti-CCP antibody levels were 130.9. Despite discontinuing dupilumab, joint pain persisted and the skin eruption tended to worsen. We started administering upadacitinib, and the condition improved. In case 1, cytokine imbalance was temporarily induced, which was assumed to improve upon discontinuation, but in case 2, it was thought to induced the onset of rheumatoid arthritis. This study is considered to demonstrate the problems associated with anti-cytokine therapy.

## W9-1

**Xerostomia-related symptoms in Sjogren's syndrome patients with unstimulated whole salivary flows >0.1 ml/min in EULAR recommendations**

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Conflict of interest: None

[Objective] The EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies do not indicate a treatment strategy for unstimulated whole salivary flows (UWSF) ≧0.1ml/min. The oral health-related quality of life (OHRQoL) of Sjögren's syndrome (SS) patients with UWSF ≧0.1ml/min was assessed. [Methods] In 45 SS patients, UWSF was measured by the spitting method and OHRQoL was assessed using the Oral Health Impact Profile-14 (OHIP-14). [Results] There was no significant difference in the percentage of patients who perceived xerostomia in the UWSF <0.1ml/min and ≧0.1ml/min groups (97% vs 82%, p=0.143), nor was the OHIP-14 score significantly different between the two groups (16.6 vs 13.6, p=0.227). Even the ≧0.1ml/min group scored significantly higher than the non-SS group (13.6 vs 7.1; p=0.029), and they had significantly higher scores for each of the OHIP-14 questions, "self-conscious," "diet unsatisfactory," "difficult to relax," and "life unsatisfying". [Conclusions] Even with UWSF ≧0.1ml/min, OHRQoL is poor. Since xerostomia signs are considered to appear when salivary flow rate decreases by 40-50%, the possibility of symptoms appearing due to decreased salivary flow rate should be considered even if salivary flow is maintained in a single measurement.

## W9-2

**Serological Examination Items in Diagnostic/Classification Criteria for Sjögren's Syndrome**

Yosuke Nagasawa[1], Kumiko Akiya[1], Masashi Uchikawa[1], Kiichi Sugito[1], Shinya Asatani[1], Masahiro Nishihara[1], Kaita Sugiyama[1], Natsumi Ikumi[2], Hirotake Inomata[1], Hitomi Haraoka[1], Noboru Kitamura[1], Masami Takei[1], Hideki Nakamura[1]
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Conflict of interest: None

[Objective] In addition to the results of lip biopsy, serological examination findings are important for the diagnosis of Sjögren's syndrome (SS), especially in patients with preserved amounts of saliva and tears. This study aimed to assess the serological examination items used in the diagnosis of SS. [Methods] 478 patients who visited Nihon University Itabashi Hospital from September 2010 to September 2023 and underwent lip biopsy and other examinations for the diagnosis of SS were included. Assuming that patients with positive lip biopsy results are true SS patients, we evaluated the sensitivity, specificity, and accuracy of the serological examination, referring to items included in the MHLW revised criteria (1999), the American and European revised criteria (2002), the ACR criteria (2012), the Guide for Diagnosis of Pediatric SS (2014), and the ACR/EULAR criteria (2016). [Results] The addition of antinuclear antibodies to anti-SS-A/Ro and anti-SS-B/La antibodies in the serological examination resulted in increased sensitivity and accuracy (sensitivity: 0.787 → 0.920, specificity: 0.466 → 0.304, and accuracy: 0.659 → 0.674). [Conclusions] More detailed consideration and discussiion regarding serological examination items in the diagnosis/classification criteria are needed.

## W9-3

**Association between anti-SS-A antibody positivity and smoking among healthy subjects in the Nagasaki Islands cohort**

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Conflict of interest: None

[Objective] To measure anti-SS-A antibodies in subjects undergoing health checkups and compare with clinical background. [Methods] Healthy subjects of Goto City, Nagasaki Prefecture (Approval No. 14051404) were asked about subjective symptoms as clinical background, as well as smoking and alcohol consumption as lifestyle habits, and anti-SS-A and anti-CCP antibodies were measured in serum. Fisher's exact test was used for univariate analysis, and nominal logistic fitting was used for multivariate analysis. [Results] Of the 1602 subjects, 65.4% were female and 68 (4.2%) were positive for anti-SS-A antibodies. The median antibody level was 221 U/m [quartiles 93.5 - 395.5]. In univariate analysis stratified by antibody positivity/negativity, women, ACPA positivity, smoking history, and weekly alcohol consumption were significantly higher in the positive group. In multivariate analysis, only gender was associated with antibody positivity. In univariate analysis of 1047 female samples, anti-CCP antibodies were significantly higher in the positive group. [Conclusions] The prevalence of anti-SS-A antibody positivity was 4.2% in healthy subjects. Since the sex ratio of SjS is larger than that of anti-SS-A, acquired factors may play a significant role in the pathogenesis of SjS.

## W9-4

**A Case of Sjögren Syndrome and Tubulointerstitial Nephritis Developing After Immune Checkpoint Inhibitor Administration**

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Conflict of interest: None

A 56-year-old female patient presented with complaints of dry mouth and dry eyes. She had previously been diagnosed with advanced lung squamous cell carcinoma and received chemotherapy, including immune checkpoint inhibitors. Although the cancer treatment was effective, she developed acute kidney indury, dry mouth, dry eyes, and swollen submandibular glands. Tests for specific antibodies related to Sjögren's syndrome (SjS) were negative, but other diagnostic assessments indicated SjS, with possible kidney involvement. Upon admission, the patient exhibited dry eyes and dry mouth. Laboratory results revealed kidney dysfunction, high CRP levels, and elevated immunoglobulin G (IgG) and IgG4 levels. Subsequent kidney biopsy confirmed severe tubulointerstitial nephritis. The patient was treated with prednisolone and showed some improvement in kidney function and a decrease in CRP levels. The clinical findings ultimately led to a diagnosis of SjS and associated kidney problems, possibly triggered by immune checkpoint inhibitors. The case remains intriguing due to the presence of negative autoantibodies and distinctive renal histopathological findings.

## W9-5

**A Study of Lymphoproliferative Diseases Associated with Sjögren's Syndrome in Our Hospital**

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Conflict of interest: None

[Objective] Sjögren's syndrome (SS) is a systemic autoimmune disease with extraglandular lesions such as lymphoproliferative disease (SS-LPD). Here, we report the clinical features of SS-LPD experienced in our hospital. [Methods] We reviewed 14 patients diagnosed with SS-LPD from 1990 to 2020. The difference between the LPD-relapsed group and the non-relapsed group was analyzed. [Results] All patients had sicca

symptoms. The median age at the onset of LPD was 64 years, and twelve patients had extra-nodal involvement. Four patients had MALT lymphoma and three had DLBCL. The others were AITL, low-grade B-cell lymphoma, LPL, plasmacytoma and unclassified. Three patients showed spontaneous remission and seven required chemotherapy. Five patients relapsed and two showed histological transformation. The LPD-relapsed group had significantly higher sIL-2R (849U/mL, p=0.0444), lower C4 (5 mg/dL, p=0.0135) compared to the others. Although the differences were not significant, the relapsed group tended to have higher serum IgG (2086 mg/dL), lower C3 (95 mg/dL) and lower white blood cell count (4400/μL). [Conclusions] We should be aware of the risk of extranodal lesions and relapse in SS-LPD. The patients with high serum IgG or hypocomplementemia should be followed closely for possible relapse.

## W9-6

**A case of TAFRO syndrome co-occurred with Sjögren's syndrome in HTLV-1 carrier**

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Conflict of interest: None

[Introduction] HTLV-1 is supposed to be associated with developing autoimmune disease such as Sjögren's syndrome. However, it has been unclear whether HTLV-1 is associated with the pathogenesis of TAFRO syndrome. [Case Report] 58-year-old woman was admitted to our hospital for examining her anasarca and generalized lymphadenopathy. Laboratory data showed that serum Cr 1.48 mg/dl, CRP 2.38 mg/dl, PLT 102,000/μL, Anti-SS-A antibody >=240 U/mL, ATLA positive, IL-6 24.2 pg/ml, VEGF 285 pg/ml. IL-6 and VEGF of pleural effusion were 2330 and 262 pg/mL, respectively. The biopsy of lymph node revealed that regressed germinal center and hypervascularization in the interfollicular area. Hyalinization of vessel wall and malignancy were not apparent. PCR of HTLV-1 was positive. The diagnosis was made of TAFRO syndrome in addition to Sjögren's syndrome and HTLV-1 carrier. Methel prednisolone 80 mg and tocilizumab 8 mg/kg per 2 weeks were started. Her body weight was improved from 59.4 kg to 41 kg and her pleural effusion was disappeared 8 weeks after the treatment. [Discussion] Past study revealed the expression of IL-6 of cells infected with HTLV-1 in human lymph node. This is the first time that our case showed the possibility that HTLV-1 might be associated with pathogenesis of TAFRO Syndrome.

## W10-1

**Clinical features of our patients with Behcet's disease with arthritis**

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Conflict of interest: None

[Objective] Arthritis with Behcet's disease (BD) is important in diagnosis and severity criteria. We clarify the clinical features in 260247 patients (pts) with BD. [Methods] We compared the clinical features in our pts, diagnosed according to the MHLW BD criteria (2003), with arthritis (n=119) or without arthritis (n=141). [Results] Uveitis were less (22.7 vs 41.1%, p<0.001), nodular erythema and intestinal ulcers were common (46.2 vs 30.1%, p=0.001/38.75 vs 26.2%, p=0.03) in pts with arthritis. In pts with arthritis, positivity of HLA-B51, HLA-26 and RF were 36.5, 22.5 and 14.1%, respectively, mean CRP was 1.7 mg/dl. The test values had no different in each group. TJC was 3.5 and SJC was 1.3 (Large joints were 53.1 and small joints were 46.9%). The HAQ score was 0.76, walking (0.90) and usual activities (1.05) were high. SJC had a correlation with score of walking and usual activities, respectively (p=0.0086/p=0.0213). Colchicine (76.6%), MTX (47.7%), anti-TNF-Ab (40.5%) and GCs (26.1%) were used. In 79 pts followed over a year, TJC (3.2→0.5) and SJC (1.4→0.1) were decreased. [Conclusions] In pts with arthritis, frequency of intestinal ulcers are common, and although the arthritis responds well to treatments, the affected joints often have major arthritis, which causes severe impairment in ADL.

## W10-2

**Comprehensive analysis including musculoskeletal ultrasound in joint symptoms of Behcet's disease**

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Conflict of interest: None

[Objective] To clarify the characteristics of joint symptoms in Behçet's disease (BD). [Methods] We examined 188 patients with BD for joint symptoms and evaluated inflammation using Doppler ultrasonography in patients with joint symptoms. [Results] The knee was the most common joint in which pain was present (37/188 [20%]), followed by the shoulder, elbow, hip, and wrist. The shoulder was the most frequently tender joint (19/188 [10%]), followed by the knee, talocrural joint, and elbow. Sixty-four patients (51 women, 13 men) underwent ultrasound. Synovitis was most common in PIP3 (3 cases), followed by the radiocarpal joint, metacarpal joint, distal radioulnar joint, PIP2, and talocrural joint (2 cases each). Enthesitis was most frequent in the triceps (6 cases), followed by the lateral epicondyle (5 cases). The latent class analysis identified two classes. One class had a higher frequency of pain and tenderness, a significantly higher proportion of women, and a history of methotrexate use, psychiatric disorders, and nausea. [Conclusion] A substantial proportion of BD patients have joint symptoms, while only a fraction have objective signs and findings of inflammation. There is a female-dominant group with widespread pain and tenderness.

## W10-3

**Association of high disease activity and serum IL-6 levels with major organ events in Behçet's disease**

Lisa Hirahara[1], Yohei Kirino[1], Yuki Iizuka[1], Yutaro Soejima[1], Ryusuke Yoshimi[1], Yuichiro Fujieda[2], Tatsuya Atsumi[2], Toshihiro Tono[3], Daisuke Kobayashi[4], Mitsuhiro Takeno[5], Hideaki Nakajima[1]
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Conflict of interest: None

[Objective] To investigate factors related with the onset and relapse of ocular, neurological, vascular and intestinal lesions, classified as major organ events of Behçet's Disease (BD). [Methods] Patients were enrolled from a prospective multicentre BD registry. Major organ events until 52 weeks after the survey was analyzed using the survival time analysis, stratified by Behçet's Disease Current Activity Form (BDCAF) score. Cluster analysis was performed using BDCAF score, serum cytokine levels, and treatment drugs to identify high-risk subtypes, as well as the cytokines associated with major organ events. [Results] A total of 260 consecutive patients were analyzed. Median BDCAF score was 2 [interquartile range: 1-3], indicating residual disease activity. Patients with BDCAF score 0 had a longer event-free survival than those with score 1 or higher. ($p=2.2 \times 10^{-4}$). Clustering results showed that patients with residual symptoms despite treatment with TNF inhibitors had higher serum inflammatory cytokine levels and experienced more major organ events. Among the cytokines, IL-6 was most associated with events. [Conclusions] Our results suggest that treatment strategies targeting overall disease activity and

monitoring serum IL-6 may be useful in preventing major organ events in BD.

## W10-4

**Characteristics of patients with elderly-onset Still's disease (EOSD) in our hospital**

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Conflict of interest: None

[Objective] Among the patients with adult-onset Still's disease (AOSD), elderly-onset cases (EOSD) are less common than younger-onset cases (YOSD), and previous studies suggested that EOSD has different characteristics compared to YOSD. The aim of study is to clarify the clinical characteristics of patients with EOSD. [Methods] Patients with AOSD who were treated in our department between 2001 and 2023 were included. EOSD was defined as age of onset ≧65, and YOSD as age of onset <65. We historically collected the clinical information and statistically analyzed the difference between these two groups. [Results] Six patients with EOSD (68.5±3.3 years-old) and 18 patients with YOSD (31.5±8.7 years-old) was enrolled in this study. Skin rash was significantly less common in EOSD group than YOSD group (11.8% vs 88.2%, p=0.038). However, there were no significant differences in other symptoms, inflammation markers and use of glucocorticoid and immunosuppressant. [Conclusions] This study revealed that patients with EOSD had significantly less skin rash than YOSD. Thus, even elderly patients with fever of unknown origin do not have typical features of AOSD, we have to consider AOSD as one of the differential diagnoses.

## W10-5

**Clinical features of patients treated with tocilizumab for adult-onset Still's disease**

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Conflict of interest: None

[Objective] To clarify the clinical features of patients treated with tocilizumab (TCZ) for adult-onset Still's disease (AOSD). [Methods] We examined patients with definite AOSD, who developed the disease between Jan 2006 and Aug 2023. We retrospectively compared 1) patient background and symptoms, 2) laboratory data, and 3) treatment and prognosis, between TCZ group and non-TCZ group. [Results] 54 patients (46.6±19.7 years old, 16 males/38 females) were examined (TCZ group: 17/non-TCZ group: 37 patients). 1) TCZ group had significantly younger age of onset (36.9 vs 51.1 years old), more typical rash (82.4 vs 45.9%) and hemophagocytic syndrome (HPS) (23.5 vs 2.7%) and higher severity scores. 2) In TCZ group, ferritin tended to be higher and IL-6 was significantly higher. 3) PSL dose was comparable between two groups, whereas concomitant immunosuppressants were significantly more frequent in TCZ group (64.7 vs 21.6%). Significantly more relapses were observed in TCZ group (47.1 vs 16.2%), whereas no relapses during TCZ treatment. One-year persistence rate for TCZ was 65%. [Conclusions] In TCZ group, age of onset was younger, typical rush and HPS were more frequent, severity scores and IL-6 were higher, concomitant immunosuppressants and relapses were more frequent than in non-TCZ group.

## W10-6

**Impact of Tocilizumab Use and Interval/Discontinuation on Relapse in Adult-Onset Still's Disease**

Yuki Oba, Shigekazu Kurihara, Daisuke Ikuma, Hiroki Mizuno, Akinari Sekine, Masayuki Yamanouchi, Eiko Hasegawa, Tatsuya Suwabe, Yoshifumi Ubara, Naoki Sawa
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Conflict of interest: None

[Objective] Tocilizumab (TCZ) is widely used as a useful treatment option for adult-onset Still's disease (AOSD) refractory to glucocorticoid. However, there are few reports focusing on the relationships between the interval/discontinuation of TCZ and relapse. We investigated the present use of TCZ in patients with AOSD to evaluate its impact on AOSD relapse. [Methods] Patients with AOSD treated from April 2002 to September 2023 were included. We retrospectively collected the clinical information. [Results] Thirty-six patients treated with steroids in our department were selected, and the mean severity score was significantly higher in the with-TCZ (n=19) than in the without-TCZ group (n=17) (1.0±0.24 vs. 3.0±0.28, p<0.01). However, there was no difference in the rate of first relapse (Fisher's exact test, p=0.736) or time to relapse (Log-rank test, p=0.73) between the with and without TCZ groups. Nine of 19 patients stopped TCZ, but there was no difference in recurrence rate (Fisher's exact test, p=0.630) or time to relapse between TCZ continuation and discontinuation (Log-rank test, p=0.64). [Conclusions] TCZ was used in AOSD with a high severity score. However, the recurrence rate and time to relapse were similar to those in patients with mild disease who received PSL alone.

## W11-1

**Characteristics of giant cell arteritis with ocular involvement**

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Conflict of interest: None

[Objective] Our aim was to understand the evolution of the position of these diagnostic modalities and the characteristics of cases with visual impairment. [Methods] The clinical characteristics of 83 cases diagnosed with GCA between 2013 and 2023 at our hospital, 49 cases in which vascular echocardiography was performed and 34 cases in which it was not performed, were compared. [Results] In visual impairment, 26.5% (13/49) had vascular echo compared with 32.4% (11/34) without, in blindness cases 4.1% (2/49) compared with 11.8% (4/34), and in cerebrovascular disease 6.1% (3/49) compared with 17.6% (6/34). When compared by presence/absence of visual impairment, it was more common in cranial type (p-value 0.004), less common in LV type (0.0143) and comparable in cranial+LV type. Visual impairment was more common in jaw claudication (p-value <0.05), temporal pain (0.006), temporal artery rage (0.021), cases with temporal artery clustering on PETCT (0.007), and more frequent concomitant cerebrovascular disease (0.019). [Conclusions] Risk factors for GCA with ocular involvement include cranial type alone, jaw claudication and temporal pain, and a high complication rate of cerebrovascular disease. Early assessment with PET-CT and vascular echocardiography is important to prevent blindness.

## W11-2

**Treatment Course of Tocilizumab for Giant Cell Arteritis at Our Hospital Including a Case of Long-Term Treatment with Tocilizumab**

Atsuhiro Yamamoto[1,2], Yuji Nozaki[2], Hirotaka Yamazawa[2], Kaori Ishimura[2], Hiroki Akazawa[2], Chisato Ashida[2], Daisuke Tomita[2], Tetsu Itami[2], Shinkai Ri[1,2], Toshihiko Shiga[2], Kazuya Kishimoto[2], Koji Kinoshita[2], Itaru Matsumura[2]
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Conflict of interest: None

[Objective] Tocilizumab (TCZ) is now covered by insurance for the treatment of giant cell arteritis (GCA), and has been used in many cases at our hospital, with some cases lasting up to 5 years and 3 months as of September 2023. We investigated the therapeutic efficacy of TCZ for GCA in our clinic. [Methods] As of September 2023, 11 patients in the TCZ group and 8 patients in the non-TCZ group were compared in terms of CRP, blood sedimentation rate, white blood cell count, and prednisolone (PSL) dosage, and for TCZ, the continuation status, dosage interval, and relapse were investigated. [Results] The mean follow-up period after the

first TCZ administration was 45.6 months. In comparison with the non-TCZ group, the PSL dose was significantly reduced in the TCZ group in all observation periods, and CRP and white blood cell counts were also reduced in almost all observation periods. The dose was discontinued in three patients, one each for thrombocytopenia and liver failure, and the other for good progress. The dosing interval was 1 week in 1 case, 2 weeks in 2 cases, 3 weeks in 1 case, and 4 weeks in 5 cases. Relapse occurred in 2 patients. [Conclusion]: The use of TCZ in the treatment of GCA may reduce PSL, prolong the dosing interval, and may even lead to drug-free treatment.

## W11-3

**The possibility of drug-free remission in Japanese giant cell arteritis patients receiving treatment with tocilizumab**

Hiroto Tomoda, Yuji Miyoshi, Naoto Yokogawa, Nanae Okimoto, Keisuke Hirobe, Yuki Terashima, Kei Karakida, Sayuri Mizumoto, Issei Takahashi, Tomoko Sano, Tomohiro Kato, Takaaki Ito, Akane Ito, Yoshitaka Ueda, Nanase Honda, Eisuke Takamasu, Kae Onishi, Masako Utsunomiya, Yoshiki Nagai, Kota Shimada
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Conflict of interest: None

[Objective] Tocilizumab (TCZ) has enabled us to quickly taper and discontinue prednisolone (PSL) in the treatment of giant cell arteritis (GCA). However, several foreign studies have reported that the rate of relapse after PSL and TCZ discontinuation is 42-52.7% in an observation period of 1-2 years. This study aims to evaluate the risk of GCA relapse in the Japanese population. [Methods] This study is a retrospective analysis of GCA patients treated with TCZ at our institution between January 2011 and September 2023. [Results] 39 GCA patients satisfied the above criteria. PSL was withdrawn while continuing TCZ in 9 patients, and only 1 (11.1%) patient experienced relapse. By contrast, TCZ was discontinued after withdrawing PSL in 8 patients, and 5 (62.5%) of these patients suffered relapse. Kaplan-Meier estimated relapse-free rate was 85.7% at 1 year after PSL discontinuation in the former group, and 38.9% at 1 year after TCZ discontinuation in the latter group ($p = 0.046$). 3 patients are currently maintaining drug-free remission after PSL and TCZ discontinuation (125, 302 and 455 days after TCZ discontinuation). [Conclusions] The relapse-free rate after PSL and TCZ discontinuation in the Japanese population did not differ greatly from previously conducted foreign studies.

## W11-4

**The Impact of Initial Prednisolone Dosage on Treatment Outcomes in Polymyalgia Rheumatica**

Yuji Miyoshi[1], Eisuke Takamasu[2], Nakako Mabuchi[2], Ryosuke Ito[2], Yoshiaki Kobayashi[2], Shunichiro Hanai[2], Kota Shimada[1], Daiki Nakagomi[2]
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Conflict of interest: None

Background: Limited data exist on the optimal initial prednisolone (PSL) dosage in Polymyalgia Rheumatica (PMR). Objective: To assess the impact of PSL starting dose on PMR treatment outcomes. Methods: A bi-center retrospective study included PMR patients based on EULAR/ACR 2012 criteria, monitored for 76 weeks post-treatment. Remission criteria were no musculoskeletal symptoms and CRP ≦0.3 mg/dL. Relapse meant requiring higher PSL or immunosuppressants post-remission. PSL-free remission was no relapse after stopping PSL. Results: Among 94 patients (average age 73.8 ± 8.5, 67.0% female), the average PSL start dose was 13.6 ± 2.8 mg/day, with 64 (68.1%) above 10 mg/day. Remission rates at 4, 12, and 24 weeks were 46.8%, 85.1%, and 93.6%. Thirty-nine (41.5%) relapsed, with 17 needing immunosuppressants. PSL-free remission occurred in 30 (31.9%). Multivariate analysis indicated an odds ratio (OR) of 2.84 for remission within four weeks with >10 mg/day PSL (p=.028), an OR of 0.26 for subsequent relapse (p=.007), and an OR of 1.46 for PSL-free remission (p=.49). Conclusion: Starting with >10 mg/day PSL in PMR correlated with quicker remission and fewer relapses but didn't influence PSL-free remission rates.

## W11-5

**Postpartum onset Takayasu's arteritis (TA) presenting with aortic dissection**

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Conflict of interest: None

Case: A 34-year-old healthy woman was performed cesarean section. After 2 weeks, she presented with chest pain and fever, followed by mild dysphagia and hoarseness. Laboratory findings showed CRP, 21.61 mg/dL and CT demonstrated thickening of the vessel wall of mainly ascending aorta. FDG-PET/CT revealed high FDG uptake in the same areas. We diagnosed with TA and steroid pulse therapy was started. However, five days after treatment, the patient developed worsening symptoms of hoarseness. A contrast-enhanced CT showed Stanford A type dissection, and emergency artificial vessel replacement was performed. The specimen from surgical resection of the ascending aorta suggested active TA associated with dissection. The PSL dosage was gradually tapered with TCZ. Then, her symptoms and laboratory findings improved. Discussion: Postpartum onset TA is rare. Recently, clinical significance of pregnancy-related aortic dissection is noted, and were associated with high mortality risk. TA is known as one of the important factor of pregnancy related aortic dissection. In the present case, the potential vascular fragility due to hormonal changes during pregnancy and further exacerbated by active TA caused by the release of immune tolerance postpartum, resulting in dissection.

## W11-6

**A case of Takayasu arteritis developing in a patient with ulcerative colitis and relapsing polychondritis**

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Conflict of interest: None

<Case presentation> A 19-year-old female, who had developed ulcerative colitis (UC) 5 months before and taking mesalazine, visited our hospital due to fever, hoarseness, and knee joint pain. She was diagnosed with relapsing polychondritis and glucocorticoid (GC) therapy showed a good response. However, the disease activity of UC got worse as the GC dose was tapered and golimumab was started 7 months after diagnosis of RP. A half year later, golimumab was switched to adalimumab due to lack of effectiveness. Serum CRP level started to elevate without any infectious signs 2 months after adalimumab started. Enhanced CT and PET-CT revealed large-vessel vasculitis including the aorta, pulmonary artery, superior mesenteric artery, renal artery, and so on. Takayasu arteritis was confirmed and the GC dose escalation yielded a rapid response. Because she experienced a relapse of UC and TAK after GC tapering, however, adalimumab was switched to upadacitinib 9 months after administration of adalimumab. Upadacitinib showed a good response to UC, TAK, and RP and resulted in GC dose reduction. <Clinical significance> This is the first case report of a patient with coexistence of UC, TAK, and RP. JAK inhibitors may be useful for TAK and RP.

## W12-1

**Efficacy of 12-month Sarilumab Treatment in Patients with Rheumatoid Arthritis in Daily Clinical Practice**

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Conflict of interest: Yes

[Objective] Treatment outcomes of SAR in RA patients were retrospectively investigated. [Methods] A total of 39 patients with RA treated with SAR from July 2019 to October 2022 were included. Baseline char-

acteristics, disease activity time-course, MTX and PSL concomitant rates, continuation rates of SAR, and reasons for SAR discontinuation were investigated. [Results] Mean age was 64.4 yo, females were 79.5%, and RA duration was 11.7 yrs. 16 patients (41.0%) were Bio or JAK-i naive. Mean SDAI was significantly decreased: 16.5 at 0m, 5.2 at 6m, and 4.6 at 12m. SDAI remission rate at 12m was 62.9%. Mean dose and concomitant rates of PSL were decreased from 3.1 mg/d (45.9%) at 0m to 0.8 mg/d (21.6%) at 12m, whereas the MTX were decreased from 5.1 mg/w (54.0%) at 0m to 2.6 mg/w (21.6%) at 12m. Continuation rates of SAR were 89.7% at 6m, and 71.8% at 12m. The 12-month continuation rate was 80.0%/63.2% for the MTX combination/non-MTX group, 68.7%/73.9% for BioJAK naive/switch, and 79.0%/65.0% for those under/over 65 years old, with no statistically significant difference. [Conclusions] SAR showed efficacy from an early stage, and it was possible to reduce the dose of PSL and MTX. The 12-month continuation rate was over 60% even in the BioJAK switch, without MTX and aged 65 years or older.

## W12-2

**Efficacy and safety of Sarilumab from FITRA data**

Satoshi Nakazaki[1], Kazunori Yamada[2,3], Ichiro Mizushima[4], Takashi Murayama[1], Hiroshi Fujinaga[5], Tetsuo Watanabe[5], Isao Matsushita[6,8], Toshiki Kido[6], Hiraku Motomura[7]

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Conflict of interest: None

[Objective] Data from FIT-RA, which is a multicenter collaboration in Hokuriku, were used to determine the efficacy and safety of Sarilumab (SAR) [Methods] Patients with RA enrolled in FITRA were treated with SAR at least once. Retention rates (RR) were examined using the Kaplan-Meier method. Efficacy was examined using the Wilcoxon method using CDAI. [Results] The total number of patients was 83, of which 78% were women and mean age was 66 years. After one and a half years, it was stable with a RR of 60%. Even in patients using two or more molecularly targeted drugs, the RR was 50% at 24 months. The RR was not significantly different by age, use of oral prednisolone, use of MTX, or prior use of tocilizumab (TCZ). CDAI, HAQ-DI, ESR, CRP, and MMP3 showed significant improvement. The types of adverse events for discontinuation were skin disease 4, injection reaction 3, gastrointestinal symptoms 3, malignant disease 2, and infection 1. [Conclusions] SAR was effective in arthritis in RA. And both cases who have used two or more molecularly targeted drugs and those who have used TCZ are considered to be effective for arthritis in RA. The reasons for discontinuation were more common skin diseases, and gastrointestinal symptoms, and less discontinuation due to infectious diseases.

## W12-3

**Investigation of the efficacy and safety of 52 weeks of sarilumab (SAR) administration to 41 patients with highly active rheumatoid arthritis at our clinic**

Heiseki Yu

Touei Internal Medicine Department of Rheumatology

Conflict of interest: None

[Objective] To investigate the clinical efficacy and safety of SAR in patients with highly active RA at our clinic. [Methods] 41 cases where SAR was introduced from July 2022 to September 2023 were included. M: F ratio 9:32 Age 63.5 years Disease duration 4.9 years Stage2.3 Class1.6 MTX17% PSL12% ACPA432.8U/mL RF343.5 IU/mL CDAI23.1 MMP364.4 ng/ml Bio-naive 22 cases Single-drug resistant 8 cases D2TRA 11 cases 11 patients with a history of malignant LPD will be evaluated up to 52 weeks. [Results] Continuation rate at 52w was 78% (Bio-naive 91%, 1-drug resistance 75%, D2TRA 55%), discontinuation 22% (7 cases of IR, 1 case each of drug eruption pneumonia), CDAI12W2.82 (P<0.005) 52W2.26 (P<0.001) significant improvement was observed. A significant decrease was observed in MMP12w 47.9 (P<0.003) and 52w37.5 (P<0.005). [Discussion] Significant improvement was seen in CDAI MMP3 in patients with highly active RA, and the 52w treatment continuation rate was as high as 78%, and the continuation rate was particularly high in bio-naive patients. Even in patients with a history of malignant tumor LPD, there was no recurrence in all cases, and even in patients who developed drug eruption pneumonia, the condition improved quickly after discontinuation, and no SAEs were observed, suggesting the safety of SAR.

## W12-4

**Evaluation of the efficacy and safety of the IL-6 inhibitor sarilumab in difficult-to-treat RA (D2T RA) and non-D2T RA in clinical practice**

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Conflict of interest: None

[Objective] We analyzed the efficacy and safety of the IL-6 inhibitor sarilumab in D2TRA/non-D2TRA. [Methods] The subjects were 235 patients who met the ACR/EULAR RA classification criteria and were treated with the IL-6 inhibitor sarilumab. 1) Continuation rate of IL-6 inhibitor sarilumab in D2TRA and non-D2TRA and cases of achieving LDA/REM of CDAI at 12 weeks. Characteristics, 2) Safety was evaluated. [Results] Among 235 patients treated with the IL-6 inhibitor sarilumab (32 men, 202 women, mean age at start of treatment 58.8+/-11.2 years), 178 patients were D2TRA, 70.3%, and 73 patients, 28.9% were non-D2TRA. D2TRA had a longer disease duration (15.2+/-6.5 vs. 10.1+/-7.6 years) and fewer late-onset RA (15.1% vs. 36.5%, p<0.001). The treatment continuation rate for D2TRA was 91.3% at 26 weeks and 82.7% at 52 weeks, and there was no difference in continuation rate between D2TRA and NonD2TRA (Log-rank, p=0.465). The LDA/REM achievement rate for CDAI at 12 weeks was 155 and 58 for D2TRA and Non-D2TRA, respectively, with no significant difference (p=0.181). The serious adverse event was 1 case of severe pneumonia in non-D2TRA and was age-dependent. [Conclusions] IL-6 inhibitor sarilumab contributes to improving the CDAI of D2T RA.

## W12-5

**Inhibition of bone destruction and efficacy of sarilumab for rheumatoid arthritis in clinical practice**

Takaaki Komiya[1], Yosuke Kunishita[2], Tomoyo Miki[1], Taketoshi Watanabe[1], Yuji Uzawa[1], Toshihisa Igarashi[1], Shohei Nagaoka[1]

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Conflict of interest: None

[Objective] To investigate the efficacy of sarilumab (SAR) in rheumatoid arthritis (RA) and its effect on bone destruction in clinical practice. [Methods] RA patients who visited our hospital and were started SAR administration between June 2018 and March 2023 were included. Patient background and clinical parameters were retrospectively collected from medical charts. Disease activity, modified Total Sharp Score (mTSS), and SAR continuation rates were evaluated at the start of SAR and 1 year later. Changes in disease activity were analyzed using a paired t-test, and the persistence rate was analyzed using the Kaplan-Meier method. [Results] Forty-four patients (mean age 64.7 ± 13.4 years, female 88.6%, mean disease duration 10.3 ± 10.2 years) were included in the study. DAS28-ESR and CDAI were 5.4 ± 1.0 and 21.5 ± 10.0, respectively, at the beginning of SAR, and significantly decreased to 1.7 ± 0.8 and 2.6 ± 2.5 at 1 year after (p <0.001). The continuation rate at 1 year after initiation was 80.2%. Seventeen patients discontinued SAR, of whom 9 had inadequate response and 3 had adverse events. The mean ΔmTSS at 1 year after initiation was 0.48 ± 0.83, with 85.0% of patients maintaining structural remission. [Conclusion] SAR showed good efficacy and inhibition of bone destruction.

## W12-6

**Analysis of parameters associated with early response to sarilumab**

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Conflict of interest: None

[Objective] To elucidate the parameters associated with early response to sarilumab (SAR). [Methods] 71 RA patients for whom SAR was introduced at the University of Tokyo between September 2017 and July 2023 were included. We collected baseline clinical information (e.g., age, sex, autoantibodies), and CDAI and blood data up to 6 months. Based on the speed of achieving CDAI remission (≦2.8), patients were classified as early responders (ER; within 1 month), general responders (GR; 2 to 6 months), and non-remission (NR). [Results] Age at introduction was 65.5 years (median), 77.8% female, CDAI 17.3 (median). There were no significant differences in patient background among the three groups (10 ER, 11 GR, and 50 NR), suggesting the difficulty of predicting efficacy using parameters available in daily clinical practice. One month following the introduction, the neutrophil count in the ER decreased by 44% from baseline, a significant difference compared to the NR ($P < 0.05$). [Conclusions] Humoral factors (e.g., IL-6, G-CSF) are involved in the migration of neutrophils from bone marrow to peripheral blood. Suppression of neutrophil counts by SAR suggests a relative IL-6 dependence of the inflammatory milieu. We will discuss the local pathology that leads to SAR responsiveness.

## W13-1

**Long term results and complication of semi linked total elbow arthroplasty for rheumatoid arthritis patients**

Taisei Kawamoto

Department of Orthopedic Surgery, Matsudo City General Hospital

Conflict of interest: None

[Objective] The goal of this report is inv investigate the prevalance loosening and faracture of total elbow arthroplasty for rheumatoid arthritis patients. [Methods] Between 2003 and 2012, thirty four elbows underwent total elbow arthroplasty in our hospital. and were reviewed retrospectively. At the time follow-up, Japanese Orthpedics Association Score was calculated. [Results] Average final follow-up period was 199.2 month. JOA score was 43.2 points before operation, was improved86.5 points after operation one year, final JOA score was 65.1 points. Range of motion, extension was -32.4 degree before operetion to -23.0 degree at final follow-up. Flexion was 113.8 degree before operetion to 123.7 degree at final follow-up. The prevalance loosening was four cases in humerus and seven cases in ulnar. Humerus fracture were three cases, ulnar fracture were four cases. Survival rate was 80.1% iat final follow-up. [Conclusions] Long term Survival rate of semi-linked type Fine TEA was comparatively similarly to taraditional TEA.

## W13-2

**Impact of accumulated disease activity over 10 years following wrist surgery in rheumatoid arthritis patients in the biologic era on the postoperative outcome**

Ryo Okabayashi[1,2,3], Hajime Ishikawa[2], Asami Abe[2], Hiroshi Otani[2], Kiyoshi Nakazono[2], Motohiro Suzuki[3,4], Yukihiro Matsuyama[3], Akira Murasawa[2]

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the influence of the accumulation of disease activity of rheumatoid arthritis (RA) over 10 years period after wrist surgery on the outcomes 10 years after surgery in the biologic era. [Methods] The study included 60 wrists in 55 RA patients (9 male and 46 female), who underwent wrist surgery at our hospital from 2006 to 2009. DAS28-ESR was measured every 3-4 months, and the cumulative mean value of disease activity for 10 years after surgery (Integrated Disease Activity: IDA) was calculated. The wrists were divided into two groups: Remission to Low disease activity group (IDA < 3.2, RL group) and Moderate to High disease activity group (IDA ≧3.2, MH group). [Results] There were 13 wrists in the RL group and 47 wrists in the MH group, and IDA was 2.51 in the RL group and 3.53 in the MH group. There were no significant differences in grip strength and the range of wrist extension/ flexion and forearm rotation between the two groups. However, there was a significant difference in carpal collapse on X-rays. [Conclusions] Accumulation of disease activity over 10 years after wrist surgery appeared to affect postoperative carpal collapse, but it might have little effect on clinical outcomes such as grip strength and range of motion.

## W13-3

**The case report of one-stage surgery of MCP joint arthroplasty, wrist arthroplasty and extensor tendinoplasty due to rheumatoid arthritis**

Chinatsu Ichikawa[1], Keiichiro Nishida[2,3], Noriyuki Shimizu[1], Shuichi Naniwa[1], Yoshifumi Hotta[1], Ryuichi Nakahara[2,4], Yoshihisa Nasu[2,4], Toshifumi Ozaki[3]

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Conflict of interest: None

[Cases] We have reviewed 9 cases involving 10 hands (39 artificial joints and 17 fingers with extensor tendon ruptures) that underwent one-stage surgery of the wrist, extensor tendinoplasty, and MCP joint arthroplasty. The patients' ages ranged from 53 to 87 years, and the mean duration of RA is 30.5 years (7.6~42.5 years). The mean ROM of MCP joint extension significantly increased from -65.5 to -29.5 degrees, while the mean flexion range significantly decreased from 88.6 to 73.2 degrees. Hand20 scores improved 6 of 7 cases. Worsening case is 1, waited 17 months for operation from tendon ruptured. The average operative time was 220.3 minutes (129~354 minutes). No complications such as infection or extensor tendon re-rupture were observed. [Discussion] To achieve appropriate soft tissue balance in MCP arthroplasty, normal excursion of tendons is required. Conversely, the reconstruction of the extensor tendon needs to reference the ROM of the MCP joint. Therefore, when both conditions coexist, surgery should be performed in one stage. In this case series, patients have achieved improvement in their finger extension. Upper limb function generally improved. But if waited time for operation was long, suggested that improving rate trend.

## W13-4

**Short-term postoperative result of MCP joint replacement surgery - A comparative study of INTEGRA versus SBi silicone finger prosthesis**

Shuichi Naniwa[1], Chinatsu Ichikawa[1], Noriyuki Shimizu[1], Ryuichi Nakahara[2,3], Yoshihisa Nasu[2,3], Toshihumi Ozaki[1], Keiichiro Nishida[3]

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Conflict of interest: None

[Objective] This study aims to compare the short-term postoperative outcomes of two different prostheses, AVANTA and INTEGRA silicone implants, used to correct MCP joint deformities. [Methods] 34 consecutive cases were included in this study. The cases were divided into groups: those with AVANTA (Group A, consisted of 59 fingers from 17 patients) and those with INTEGRA (Group I, consisited of 48 fingers from 17 patients). ROM of the MCP joint, grip strength, pinch strength, HAQ, Hand20 and DASH score were compared before and one year after surgery, and implant fractures were checked at the last observation. [Results] The mean preoperative extension and flexion angles (in degrees) for

Group A/I were -43.4/-37.9 and 78.3/78.0, respectively. The mean postoperative extension and flexion angles were -13.4/-17.8 and 59.8/68.5, respectively. The pre- and postoperative pinch strengths (in kg) were 1.85/1.61 and 1.71/2.55, respectively. Significant differences were observed in the change in flexion angle and pinch strength postoperatively. There was no significant difference in grip strengths and clinical scores. No implant fractures were observed during the mean observation period of 23.4 months in Group I. [Conclusions] Better flexion and pinch strength were observed in the INTEGRA group.

## W13-5

**Balance reconstruction for the rheumatoid boutonnière deformity of the fingers**

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Conflict of interest: None

[Objective] To investigate the outcome of the modified Ohshio's method, a corrective surgery of the boutonnière deformity of the fingers in patients with rheumatoid arthritis. [Methods] Forty-one boutonnière deformities of the fingers in 31 patients with rheumatoid arthritis underwent surgical correction. The active range of motion (ROM) at the proximal interphalangeal (PIP) joint, a visual analogue scale (VAS), the pulp-palm distance (PPD), the grip and pinch power were investigated. [Results] Preoperative pain at the PIP joint reduced or disappeared. The active extension at the PIP joint improved and the arc of motion was generally well preserved in Nalebuff's stage I and II. In stage III, extension deficit of 30 to 40 degrees remained particularly at the PIP joint with moderate to severe destruction. The grip and pinch power tended to decrease, and the mean PPD worsened, but improvements in daily activities were noted as the deformity was corrected. [Conclusions] As one of the balance restoration procedures for the boutonnière deformity of the rheumatoid fingers, the modified Ohshio's method was useful particularly in stage II or less.

## W13-6

**Patient satisfaction with the Swanson metacarpoohalangeal joint arthroplasty for the rheumatoid hand**

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Conflict of interest: None

[Purpose] To investigate the factors that influence satisfaction with the operated hand in patients who underwent the Swanson MP joint arthroplasty. [Methods] Eighty-three hands in 69 rheumatoid arthritis patients (M/F: 5/64) who underwent surgery at our hospital from 2016 to 2019 underwent clinical evaluation and postoperative satisfaction survey 3 years after surgery were conducted. The mean age at the operation was 65 years old. The patient's satisfaction level (pain, appearance, mobility, power, usability, overall) was evaluated using VAS (0: worst, 100: best). [Results] Postoperative overall satisfaction of 51 or higher was considered to be the high satisfaction (HS) group (n=63), and below 50 is considered to be the low satisfaction (LS) group (n=20). In the HS group, all items of satisfaction improved, However, in the LS group, only appearance improved. In the LS group, the preoperative J-HAQ, the MP joint ulnar deviation angle in the index finger, and the prehensile pattern score were significantly worse than in the HS group. [Conclusion] It is preferable to perform surgery before systemic physical dysfunction and loss of prehensile pattern due to hand deformity become extremely severe.

## W14-1

**Seasonal and Regional Impact on Relapse in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis: A Retrospective Analysis from J-CANVAS, a Japanese Multicenter-Cohort Study**

Hiroki Kobayashi[1], Yusuke Yoshida[1], Takashi Kida[2], Nobuyuki Yajima[2], Satoshi Omura[2], Daiki Nakagomi[2], Yoshiyuki Abe[2], Masatoshi Kadoya[2], Naoho Takizawa[2], Atsushi Nomura[2], Yuji Kukida[2], Yasuhiko Yamano[2], Takuya Yanagida[2], Koji Endo[2], Kiyoshi Matsui[2], Tohru Takeuchi[2], Kunihiro Ichinose[2], Masaru Kato[2], Ryo Yanai[2], Yusuke Matsuo[2], Yasuhiro Shimojima[2], Ryo Nishioka[2], Ryota Okazaki[2], Mayuko Moriyama[2], Ayuko Takatani[2], Yoshia Miyawaki[2], Toshiko Ito-Ihara[2], Takashi Kawaguchi[2], Yutaka Kawahito[2], Shintaro Hirata[1,2]
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Conflict of interest: None

Objective: To clarify seasonal and residential effects on relapse of ANCA-associated vasculitis (AAV). Methods: Patients registered in the J-CANVAS study and relapsed AAV between January 2017 and December 2019 were enrolled in this study. The seasonal differences in AAV relapse were analyzed using Pearson chi-square test, with an expected probability of 25% for each season. Results: A total of 101 patients were enrolled. Of them, 43, 39, and 19 patients were classified as having microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA), respectively. The seasonality of relapse in whole AAV significantly deviated (21.8%, 41.6%, 17.8%, and 18.8%, in spring, summer, autumn, and winter, respectively; p=0.0017), indicating that AAV relapse was frequently observed in summer. In patients with GPA, marked seasonality was observed (30.8%, 46.2%, 10.3%, and 12.8%; p=0.0042), while not in MPA and EGPA. Among patients with PR3-ANCA, the seasonal difference was significant (33.3%, 44.4%, 3.7%, and 18.5%; p=0.0171). The relapse of whole AAV was not associated with rural residence. Conclusion: The relapse of AAV was influenced by seasonal variations and was frequently observed in summer.

## W14-2

**Bilateral spermatic cord findings of CT reflects testicular arteritis in polyarteritis nodosa**

Eisuke Takamasu[1], Hiroto Tomoda[1], Nanae Okimoto[1], Keisuke Hirobe[1], Yuki Terashima[1], Kei Karakida[1], Sayuri Mizumoto[1], Issei Takahashi[1], Tomoko Sano[1], Tomohiro Kato[1], Takaaki Ito[1], Akane Ito[1], Yoshitaka Ueda[1], Nanase Honda[1], Shuko Mishima[2], Kae Onishi[1], Satoshi Watanuki[2], Yuji Miyoshi[1], Masako Utsunomiya[1], Yoshiki Nagai[1], Naoto Yokogawa[1], Kota Shimada[1]
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Conflict of interest: None

[Objective] In polyarteritis nodosa (PAN), testicular artery involvement (TA) is a relatively specific diagnostic finding. However, identifying TA through non-invasive methods other than angiography or biopsy is challenging. [Methods] We conducted the following study, focusing on male cases diagnosed with PAN and systemic vasculitis. Step 1; To establish CT findings of TA in PAN (PAN-TA sign: PTS), we compared the CT findings between cases where testicular artery involvement was confirmed by pathological tissue examination or angiography and cases without such confirmation. Step 2; We statistically examined whether the PTS findings were specific to PAN throughout the spectrum of systemic vasculitis. [Results] The study included 16 cases of PAN, 76 cases of other systemic vasculitis, and 20 cases of BD. TA was confirmed in 7 cases (43.8%) of PAN, and the defining features of PTS included "increased fat tissue density throughout the spermatic cord", "bilateral findings present", and "Circular swelling with a maximum transverse diameter of both spermatic cords >20 mm." The sensitivity of PAN-TA with the same findings, including other systemic vasculitis such as BD, was 85.7%, and the specificity was 99.0%. [Conclusions] The PTS is a highly significant finding in the diagnosis of TA and PAN.

## W14-3

**Lymphopenia is a risk factor for severe infections in older patients with microscopic polyangiitis: a retrospective cohort study in Japan**

Makoto Yamaguchi, Keisuke Kamiya, Akimasa Asai, Fumiya Kitamura, Hirokazu Sugiyama, Hironobu Nobata, Shogo Banno, Yasuhiko Ito, Takuji Ishimoto

Aichi Medical University

Conflict of interest: None

**Objectives:** Previous studies have identified the predictors of severe infections in antineutrophil cytoplasmic antibody-associated vasculitis. However, lymphopenia has not been fully evaluated as a predictor of subsequent severe infections in patients with microscopic polyangiitis (MPA). **Methods:** This single-centre retrospective cohort study included 130 consecutive patients with newly diagnosed with MPA from Aichi Medical University Hospital, Japan, who received immunosuppressive therapy between March 2004 and December 2020. **Results:** During the follow-up period (median: 38 months; interquartile range: 15-63 months), 56 severe infectious episodes occurred in 51 patients (39.2%). Time-dependent multivariate CPH analyses identified older age (adjusted hazard ratio [HR] = 1.74, 95% confidence interval [CI]: 1.13-2.67, per 10 years), methylprednisolone pulse therapy (adjusted HR = 2.04, 95% CI: 1.03-4.02), moderate lymphopenia (vs. normal, adjusted HR = 7.17, 95% CI: 3.10-16.6), and severe lymphopenia (vs. normal, adjusted HR = 36.1, 95% CI: 11.8-110.9) as significant predictors of severe infection. **Conclusion:** These results suggest the importance of sustained infection surveillance, particularly in older patients who develop lymphopenia during strong immunosuppressive therapy.

## W14-4

**Analysis of the Cytokine Profile Associated with Untreated Eosinophilic Granulomatosis with Polyangiitis**

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Division of Rheumatology and Clinical Immunology, Jichi Medical University, Tochigi, Japan

Conflict of interest: None

[Objective] To explore the pathology of EGPA based on the serum cytokine profile. [Methods] We quantified the levels of 28 cytokines in the serum of 10 untreated EGPA patients. Untreated patients with SLE or PsA were served as controls. Differences in cytokine profiles based on symptoms were also investigated. [Results] Compared to SLE, EGPA showed higher levels of IL-1Ra, IL-6, -7, -12, and -15, PDGF, RANTES, and VEGF and lower levels of BAFF and IP-10. Compared to PsA, EGPA exhibited higher levels of IFN-γ, IL-1β, -1Ra, -6, -8, and -13, MCP-1, MIP-1α, RANTES, and BAFF while IL-9 levels were lower. IL-13 levels were higher in MPO-ANCA-positive patients. In patients with rhinosinusitis and/or pneumonia, PDGF-BB levels were elevated and correlated with IL-1Ra levels. Patients with muscle symptoms had significantly elevated levels of TNF-α, IL-8, and MCP-1. IL-5 and IP-10 levels were significantly elevated in patients with purpura and those with cardiac lesions, respectively. [Conclusions] Serum IL-5 levels were not always elevated in EGPA. This study suggests that the production of Th1, Th2, and Th17-type cytokines can coexist in EGPA. Due to substantial variations in humoral factors with EGPA symptoms, cytokine profiling appears to be useful in understanding the pathology of EGPA.

## W14-5

**Predictors of relapse in patients with eosinophilic granulomatosis with polyangiitis (EGPA): multicenter study in Japan: the REVEAL cohort study**

Ayana Okazaki[1], Yuichi Masuda[1], Shogo Matsuda[1], Takao Kiboshi[1], Takayasu Suzuka[1], Yumiko Wada[1], Takeshi Shoda[1], Takuya Kotani[1], Ryosuke Tsuge[2], Mikihito Shoji[2], Tomoki Taniguchi[2], Atsushi Manabe[2], Mayu Shiomi[3], Ryu Watanabe[4], Motomu Hashimoto[4], Wataru Yamamoto[5], Tohru Takeuchi[1]
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Conflict of interest: None

[Objective] To explore predictors for relapse in EGPA patients. [Methods] We enrolled 107 patients with EGPA in the cohort. Diagnosis was based on ACR/EULAR 2022 criteria, and data on pretreatment conditions, treatments, and outcomes were collected retrospectively. [Results] Median values are presented. Age 59 years, 53.2% female, eosinophil count 5100/μL, CRP 1.8 mg/dL, IgG 1567/μL, FFS was 1 point and four types of EUVAS disease severity were as follows: Localized 1.0%, Early systemic 25.2%, Generalized 58.9%, Severe 15.0%. Post-treatment, there were 58 cases of relapse (54.2%) and 49 cases of non-relapse (45.8%). Relapse group was more likely to be Early systemic, had lower pre-treatment CRP and IgG (P=0.02 and 0.002), and lower BVAS score. There was no significant difference in the rate of immunosuppressive drugs, but the relapse group was lower corticosteroid doses at remission induction therapy. More patients in the non-relapse group received mepolizumab (MEP) within 6 months of induction of remission (P=0.001). [Conclusion] Relapse group had a lower inflammatory response prior to induction of remission and a higher proportion of the Early systemic. A possible risk factor for relapse was low-dose steroid. It was suggested early introduction of MEP may reduce the relapse rate.

## W14-6

**Clinical features of ANCA-associated vasculitis with large vessel vasculitis**

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Division of Rheumatology and Allergy, Osaka General Medical Center, Osaka, Japan

Conflict of interest: None

[Objective] To assess clinical features of large vessel vasculitis (LVV) in patients with ANCA- associated vasculitis (AAV). [Methods] We assessed patients with LVV, GPA and MPA who visited our division between January 2018 and September 2023. [Results] LVV was identified in five (3.8%) patients among those with GPA (n=29) and MPA (n=102). Three, one, and one patient had aortitis, temporal arteritis (TA), and periaortitis, respectively. All patients had positive myeloperoxidase-antineutrophil cytoplasmic antibodies (MPO-ANCA); four had MPA and one had GPA. The mean age at AAV diagnosis was 79 years, and three patients were male. Four patients were diagnosed with LVV at the time of vasculitis diagnosis. One patient was diagnosed with GCA at onset, however, upon relapse five years after glucocorticoid (GC) withdrawal, the diagnosis was revised to MPA with TA owing to elevated MPO-ANCA levels and temporal artery wall thickening on MRI. Three patients had histopathologically confirmed AAV in lesions other than the large vessels. Treatment regimens included GC for all patients, RTX for two, CY for three, and avacopan for one patient. [Conclusions] LVV was identified in 4% of AAV cases, with variations in the affected sites. Therefore, AAV should be considered in cases of LVV.

## W15-1

**Treat-to-Target in RA Clinical Practice: Global and Japanese Evidence of Practice Gaps**

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Conflict of interest: Yes

Objective A global survey assessed the barriers and facilitators of T2T implementation in RA. Methods From Jun-Sep 2022, a quantitative survey targeted rheumatologists in 35 countries. The survey consisted of 9 questions, across 6 key areas of T2T in RA: knowledge, skill, confidence, agreement, contextual/systemic barriers, and behaviors. Data from Japan are presented here. Results Of 903 respondents, 88 were from Japan. In Japan, 94% had 11+yrs experience in rheumatology practice and 90% reported that they frequently-consistently apply T2T. The largest gaps in

knowledge and skills were related to assessing pts' health literacy. Globally, the main barrier to documenting disease activity was poor pt adherence; in Japan, it was unsuitable medical records. Encouraging pts to use disease activity monitoring tools and using telehealth were the least frequent behaviors. Besides pt educational resources, other tools listed in the survey were infrequently used in Japan. Conclusion Even among experienced rheumatologists with extensive self-reported T2T implementation, barriers still exist and are slightly different from the global ones. Recommended focus areas in Japan include optimization of medical documentation, using additional T2T tools as well as encouraging pt disease activity monitoring.

## W15-2

**Effect on renal prognosis of achieving early remission in rheumatoid arthritis patients treated with b/tsDMARDs -The ANSWER cohort study-**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients are reported to have a higher incidence of chronic kidney disease than non-RA patients. In this study, we examined the effect of early response to treatment with b/tsDMARDs on long-term renal prognosis. [Methods] From the ANSWER Cohort database, we selected 1042 patients who had received the same b/tsDMARDs for at least 2 years since 2009. Patients were divided into two groups: CDAI remission group and CDAI moderate/high disease activity group at 3 months of treatment, and eGFR change (ΔeGFR) between baseline and 24 months was evaluated. Secondary endpoints included multivariate logistic regression analysis of factors contributing to worsening renal function (defined as >25% decrease in eGFR at 24 months from baseline). [Results] In 174 patients in each group after adjustment for background, ΔeGFR was lower in the moderate/high disease activity group compared with the remission group (moderate/high disease activity group vs. remission group: -9 vs. -5 mL/min/1.73m$^2$, p=0.0097). Baseline CRP levels were identified as a contributing factor for worsening renal function at 24 months (OR: 1.15, 95% CI 1.01-1.31, p=0.033). [Conclusions] Our results suggest that early remission with b/tsDMARDs is important for improving long-term renal prognosis.

## W15-3

**The influence of Joint Cartilage on Functional Remission (HAQ remission) in Patients with Rheumatoid Arthritis (RA)**

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Conflict of interest: None

[Objective] The HAQ of RA patients has been reported to be affected by JSN by radiographic examination but has not been examined with the direct assessment of cartilage damage. We investigated the factors affecting HAQ remission using US. [Methods] In 101 RA patients, the HAQ-DI, JSN score, and the presence of a subluxation by X-ray of the finger joints and cartilage by the US were evaluated by a semiquantitative method. HAQ-DI≦0.5 was defined as HAQ remission, and logistic regression analysis was performed incorporating age, gender, disease duration, DAS28-CRP, BMI, and use of biological agents as explanatory variables for HAQ remission. [Results] Age, duration, and DAS28-CRP were a median of 64 years, 5.8 years, and 1.71, respectively; the median HAQ-DI was 0.12, and 78 patients (77%) achieved remission. In the model including JSN and US scores, JSN score had no significant effect on HAQ remission with an odds ratio of 0.98 (p=0.50) and US score with an odds ratio of 1.02 (p=0.78), respectively. However, when US score and presence of subluxation were incorporated, the odds ratio for US score was 1.11 (p=0.22), while the odds ratio for subluxation was 0.19 (p=0.048). [Conclusions] This study suggests that subluxation of joints, rather than cartilage damage, may affect HAQ remission.

## W15-4

**Development of a rheumatoid arthritis medical support system using a custom app and changes before and after its us**

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Conflict of interest: None

[Purpose] Rheumatoid arthritis (RA) is a disease that requires continuous treatment centered on drug therapy and requires a variety of evaluations. We developed an RA clinical support system for these purposes and examined changes before and after use. [Methods] The subjects were 140 patients with stable RA. There were 44 men and 96 women, ages 26 to 90 years. The system was developed using FileMaker Pro19 (Claris). The 1,384 consecutive visits were divided into 629 before and 655 after, VAS, and patient length of stay were compared. Multiple regression analysis was performed using length of stay as the objective variable and VAS, presence or absence of intravenous fluids, prior blood sampling, combined consultation with other departments, as the dependent variables. SPSS was used for statistical analysis. [Results] There was no change in VAS before and after operation (P=0.21), and the factors that influenced length of stay were pre-blood sampling, presence or absence of intravenous fluids, concurrent consultation with other departments, and VAS (all P<0001). [Conclusion] Although it did not lead to patient benefits, it was possible to implement one's own examination style into the application, and it greatly contributed to improving the efficiency of medical treatment.

## W15-5

**Over-time change in Health Assessment Questionnaire in patients with rheumatoid arthritis: from ANSWER cohort**

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Conflict of interest: None

[Objective] More patients with rheumatoid arthritis (RA) have

achieved clinical remission, as treatment developed. We investigated whether functional remission has been also increasing over-time. [Methods] We longitudinally investigated age, treatment, laboratory data, disease activity, physical function (HAQ and 8 components) among RA patients registered to ANSWER cohort from 2012 to 2021. Over-time change in HAQ was investigated. In addition, factors cross-sectionally associated with HAQ were analyzed. [Results] Among 5909 patients (21354 in cumulative), HAQ was improved from 0.77 to 0.58 and functional remission has increased from 52.4% to 63.9% during 10 years. Functional remission has increased in patients in clinical remission (74.6% to 82.8%), but functional remission has not increased (30.3% to 38.7%). Furthermore, age (OR=1.02), BIO/JAKi use (OR=1.41), glucocorticoid use (OR=2.16), DAS28ESR (OR=2.43) were independent risk factors in non-functional remission in multivariate logistic regression. [Conclusion] HAQ has been improved and functional remission has increased during 10 years. This tendency was especially seen in clinical remission. Older age, high disease activity, and glucocorticoid use were independent risk factors in non-functional remission.

## W15-6

**Central sensitivity syndrome affects the disease activity index and satisfaction with treatment in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] In this cross-sectional study, we evaluated the effects of central sensitivity syndrome (CSS) in patients with rheumatoid arthritis (RA) on the assessment of clinical disease activity and satisfaction with treatment. [Methods] Participants were 240 consecutive patients with RA who were receiving long-term follow-up. All patients were evaluated for clinical disease activity and satisfaction with treatment. CSS was evaluated with the Central Sensitization Inventory (CSI). [Results] The mean CSI score was 18.1±14.3 (range, 0-86). Of the 240 patients, 20 (8.3%) had CSI scores of ≧ 40 and thus had CSS. CSI score was significantly associated with tender joint counts and with patient global assessment (PtGA), pain visual analogue scale, Health Assessment Questionnaire Disability Index (HAQ-DI), clinical disease activity index scores, and patient satisfaction with treatment. Multivariable analysis revealed that CSI score, PtGA and HAQ-DI scores were associated with patient satisfaction. [Conclusions] In patients with RA, CSS may affect the disease activity index and reduce patients' satisfaction with treatment.

## W16-1

**Accuracy of FRAX Assessment for the determination of severe osteoporosis**

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Conflict of interest: None

[Objective] To evaluate the accuracy of FRAX in determining severe osteoporosis (T-score less than -2.5 SD with at least one fragility fracture, lumbar T-score less than -3.3 SD with at least two vertebral fractures, or grade 3 vertebral fractures using SQ grade). [Methods] The study involved 1364 patients (mean age 76.9 years, 1016 women), including 47 rheumatoid arthritis patients, and the evaluation of severe osteoporosis and FRAX were obtained. The accuracy of major osteoporotic fracture risk and hip fracture risk in FRAX were evaluated and compared using ROC curves for the determination of severe osteoporosis. [Results] The sensitivity and specificity of FRAX were 0.763 and 0.723 for major osteoporotic fracture risk and 0.780 and 0.720 for hip fracture risk when the cutoff values were 21.0% and 7.1%, respectively. The area under the curve did not differ between major osteoporotic fracture risk (0.823) and hip fracture risk (0.815) (p=0.15). [Conclusions] The FRAX results were moderately accurate when aligned with the criteria for severe osteoporosis. Even if patients did not meet the criteria, pharmacological interventions equivalent to those for severe osteoporosis should be considered in patients with a major fracture risk of 21.0% or hip fracture risk of 7.1% or greater.

## W16-2

**Fracture risk using FRAX® in patients with rheumatoid arthritis: 10-year longitudinal study using the IORRA cohort**

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Conflict of interest: None

[Objective] This study aimed to compare the predicted fracture risk using FRAX® with actual fractures in Japanese patients with rheumatoid arthritis (RA). [Methods] The subjects were 547 patients with RA (mean 58.3 years, 88.8% female) who participated in the fracture risk survey of the 17th IORRA patient survey in 2008 and continued to participate in the IORRA cohort study for 10 years. The 10-year probabilities of hip and a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture) were calculated using FRAX® without BMD. The ratio of the observed number to the expected number of FRAX® (O/E ratio) was calculated using patient self-reported fractures, and equality was determined when the 95% confidence interval (CI) of the O/E ratio covered 1. [Results] Over the 10 years, 148 patients (27.1%) reported fractures including 12 hip (2.2%) and 42 major osteoporotic (7.7%) fractures. The 10-year probabilities of hip and a major osteoporotic fracture were an average of 2.6% and 9.7%. The O/E ratios for hip and major osteoporotic fractures were 0.85 (95% CI 0.49-1.30) and 0.79 (95% CI 0.60-1.003) indicating that the two were equivalent. [Conclusions] FRAX® appears to be a valid method for predicting hip and major osteoporotic fractures in Japanese patients with RA.

## W16-3

**AI-assisted diagnostic system for osteoporosis using the A-P chest X-ray images**

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Conflict of interest: Yes

[Objective] We evaluated the accuracy of BMD estimates for the femur and L-spine when calculated from A-P chest X-ray images alone on our AI-assisted diagnostic system for osteoporosis. [Methods] The subjects were patients who underwent both A-P chest X-ray and BMD of the femur (Group F: 11,265 cases) or L-spine (Group L: 9,283 cases) using a DXA. A-P chest X-ray images were correlated with the measured BMD of the femur and L-spine and as the femur and lumbar dataset, respectively. Each dataset was randomly divided into 5 groups. The 4 groups of datasets were input as the training data. After the training, the only X-ray images in the one untrained dataset group were input as the test dataset. Five-fold cross validation was performed to evaluate the accuracy of the estimated BMD. [Results] The absolute error between the measured and estimated

values and the correlation coefficient was 7.4%/0.83 for Group F and 8.3%/0.82 for Group L. The AUC to discriminate YAM <80% and YAM≦70% was 0.89/0.89 for Group F and 0.90/0.89 for Group L, indicating high accuracy. [Conclusions] The practical application of this system, which outputs highly accurate BMD estimates of the femur and L-spine from only one image, is expected to lead patients to early treatment and prevent fragility fractures.

## W16-4

**Vertebral Strength in Rheumatoid Arthritis Patients Assessed by Biomechanical CT**

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Conflict of interest: None

[Objective] We assessed vertebral bone strength in Japanese RA patients using finite element analysis, highlighting alendronate's effects (Arthritis Rheum, 2008). Recently Japanese female reference value for osteoporotic bone strength of 4000N has been established (E-JOS Vertebral Study, ASBMR 2023). This study evaluates RA patient vertebral strength with this reference. [Methods] The RA group had 29 females, average age 61.6, RA duration 9.8 years, no bo, bs, ts-DMRAD use, 28 took csDMARD, 20 used oral steroids, 3 had fragility fractures, and average DAS28-CRP was 2.53. The general group had 20 patients, average age 62.5. Bone strength of L1, trabecular strength (Trab), and cortical shell strength (Cort) were calculated using Biomechanical CT (VirtuOst®, O.N. Diagnostics, CA). [Results] RA group: vertebral BMD 0.715 g/cm2 (T-score -2.64 SD), strength 3920 N, Trab 1656 N, Cort 2264 N. General group: BMD 0.787 g/cm2 (T-score -1.90 SD, Z-score -0.11 SD), strength 4320 N, Trab 2171N, Cort 2147N. [Conclusions] RA patients, mean age 61.6, had vertebral strength roughly 10% less than the general population, signifying osteoporosis. Trab was notably lower in RA patients, while Cort remained comparable.

## W16-5

**Low Hounsfield Unit Values on Computed Tomography Predicts Vertebral Fracture in Patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) have disease-specific risk factors for osteoporosis, in addition to those that affect the general population and identification of osteoporosis is of critical importance. The Hounsfield units (HU) measured using computed tomography (CT) have gained considerable attention for detecting osteoporosis. This study aimed to investigate whether opportunistic CT can predict vertebral fracture in RA patients. [Methods] A total of 233 patients with RA who underwent CT imaging, including chest were included in the study. The HU values of the anterior 1/3 of the vertebral bodies based on sagittal plane at T11-L2 after reconstruction were measured. The incidence of vertebral fractures with respect to the HU value was investigated. [Results] Vertebral fractures were identified in 32 patients during the mean follow-up period of 3.8 years. In patients who had vertebral fractures within 2 years of CT imaging, the HU values of vertebral bodies (T11-L2) were lower than those in patients who did not experience vertebral fractures. [Conclusions] HU measurement of the anterior 1/3 of vertebral body predicts the risk of vertebral fracture in RA patients.

## W16-6

**Investigation of osteoporosis in patients with Parkinson's disease**

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Conflict of interest: None

[Objective] The purpose of this study is to investigate and study the osteoporosis of PD patients in clinical practice. [Methods] Subjects were osteoporosis patients treated with bisphosphonates after vertebral body fracture since 2017. The PD group (N=31) and the control (Ct) group (N=62) were compared. Patient background, serum markers, BMD, and incidence of fragility fractures were evaluated retrospectively. [Results] Patient background (PD/Ct) was followed: Age (years) (79.4/79.9), female (%) (51.6/62.9), and BMI (18.0/20.3), with significantly fewer females in the PD group. Serum markers were Ca (mg/dl) (9.1/9.2), 25OHD (ng/ml) (13.8/14.1), and ALB (g/dl) (3.7/3.5), with no significant differences. BMD (DEXA, YAM) was lumbar spine (70.4/72.9) and total hip (50.6/62.0) at baseline, and lumbar spine (77.5/77.4) and total hip (48.1/60.4) at 1 year, with a significant decrease in total hip in the PD group. The incidence of fragility fracture was 8.2/100 person-years in the PD group and 5.1/100 person-years in the Ct group, with significantly higher incidence in the PD group. [Conclusions] Patients with PD had lower BMD of the proximal femur and a higher frequency of fragility fractures.

## W17-1

**Analysis of Periostin as a Biomarker of Rheumatoid Arthritis-associated Interstitial Lung Disease**

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Conflict of interest: Yes

[Background] We analyzed periostin as a biomarker for rheumatoid arthritis-related ILD (RA-ILD). [Method] Serum levels of monomeric and total periostin, KL-6, SP-D, and LDH were measured in 39 patients with RA and 137 healthy controls (HC) who participated in a multicenter prospective study. [Results] KL-6 accurately detected ILD in RA cases (AUC=0.939), and SP-D, monomeric and total periostin moderately (AUC=0.803, 0.767, 0.767). Both of periostin levels were negatively correlated with extent of normal lung area on HRCT, and positively correlated with extents of honeycombing, reticulation, lung fibrosis score (sum of honeycombing and reticulation), and traction bronchiectasis grade, but not inflammatory lesions. KL-6, SP-D, and LDH levels were not associated with the extent of fibrotic lesions on HRCT. Monomeric and total periostin levels were higher in RA-ILD with UIP pattern than in non-UIP pattern on HRCT, but there were no differences in KL-6, SP-D, and LDH levels. Immunohistochemical analysis of biopsy and autopsy lung tissue obtained from chronic and acute exacerbation stages of RA-ILD revealed that periostin was expressed only in active fibrotic lesions. [Conclusion] Periostin is a potential biomarker for the diagnosis and evaluation of fibrosis in patients with RA-ILD.

## W17-2

**Factors associated with high and low serum alkaline phosphatase levels in patients with rheumatoid arthritis: results from the IORRA cohort study**

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Conflict of interest: None

[Objective] This study aimed to investigate factors associated with serum alkaline phosphatase (ALP) levels in Japanese patients with rheumatoid arthritis (RA). [Methods] Serum ALP levels were evaluated in 2,315 patients with RA (mean 63.7 years, 87.5% female) who participated in the 44th IORRA cohort survey in 2022 using the IFCC method. High and low serum ALP levels were defined as >113 U/L and <38 U/L, respectively. Factors associated with high and low serum ALP levels were evaluated using multivariate logistic regression. [Results] The mean serum ALP levels were 77.6 U/L. High and low serum ALP levels were observed in 182 (7.9%) and 31 patients (1.3%). In multivariate analyses, high serum ALP levels were significantly associated with age (per 10 years, OR 1.21, 95% CI 1.05-1.40), BMI (OR 1.05, 95% CI 1.01-1.11), DAS28 (OR 1.41, 95% CI 1.20-1.65), and serum AST levels (OR 1.03, 95% CI 1.02-1.05), and low serum ALP levels were significantly correlated with age (per 10 years, OR 0.72, 95% CI 0.54-0.96) and DAS28 (OR 0.60, 95% CI 0.39-0.92). [Conclusions] In Japanese patients with RA, abnormal serum ALP levels were observed in 9.2%. High serum ALP levels appear to be associated with age, BMI, DAS28, and serum AST levels. Low serum ALP levels may be correlated with age and DAS28.

## W17-3

**Effect of HLA-B7 cross-reactive antigen in seronegative rheumatoid arthritis**

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Conflict of interest: Yes

[Objective] In rheumatoid arthritis (RA), anti-citrullinated peptide antibody (ACPA), an autoantibody against citrullinated peptide generated in the body, is thought to cause arthritis. On the other hand, seronegative RA is sometimes difficult to diagnose because of the lack of specific antibodies. Therefore, the background pathogenesis and genetic polymorphisms have not been thoroughly investigated. [Methods] We retrospectively studied 78 patients with seronegative RA who visited our clinic from June 2008 to September 2017. Patients whose Human Leukocyte Antigen (HLA)-A and B genotypes were measured were examined for change in diagnosis, eye lesions, stomatitis, pubic ulcers, skin lesions, arthritis, and treatment response. [Results] The mean observation period was 8.9 years (5.8-15.1 years). Forty-seven were female, and the mean age at the first visit was 49.5 years. HLA analysis showed that 76.9% of all patients were HLA-B7 cross-reactive antigen (B7CREG) positive. [Conclusions] HLA-B7CREG-positive cases are common in seronegative rheumatoid arthritis, and HLA-B7CREG-positive disease should be investigated in the future.

## W17-4

**Gram stain of the joint aspiration for the diagnosis of infection after total knee arthroplasty**

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Conflict of interest: None

[Objective] The purpose of this study in to evaluate the sensitivity and specificity of gram stain against aspirated joint fluid in the patients of infection after total knee arthroplasty. [Methods] We retrospectively reviewed the reports of synovial fluid samples retrieved from suspected infected joints at eight hospitals. A total of 179 samples of aspirated joint fluid from knee joints were evaluated in this study. [Results] Of the 80 gram stains performed on samples from infected patients, there were 60 true positives and 20 false negatives. In contrast, of the 99 stains performed on samples from aseptic knees, there were 99 true negatives and no false positives. The sensitivity and specificity for detecting periprosthetic knee infections were 75.0% and 100.0%, respectively. Further, we divided infected samples into the early aspiration group (within 14 days) and the late aspiration group (15 days or more) based on the duration between the onset of symptoms and aspiration. The sensitivity of the gram staining was 84.2% and 41.2% in the first and second groups, respectively. [Conclusions] In this study, gram staining of preoperatively aspirated joint fluid for the infected periprosthetic knee joint with short-lived symptoms showed high sensitivity.

## W17-5

**Late-onset rheumatoid arthritis has a marked decline in renal function over 3 years: the evidence from Niigata Orthopedic Surgery Rheumatoid Arthritis Database (NOSRAD)**

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Conflict of interest: None

[Objective] Age and renal function should be considered in the treatment of rheumatoid arthritis (RA). We investigated the trends at our hospital over a three-year period. [Methods] A total of 283 patients registered in the Niigata University Orthopedic Surgery Rheumatoid Arthritis Database were included in the study. The patients who could be followed over three years from July 2020 to June 2023 were divided into two groups: those <65 years old (young-onset RA; YORA) and those >65 years old (late-onset RA; LORA). Renal function and drug use were investigated. [Results] There were 212 YORA and 71 LORA. Renal function (eGFR) was 80.1 in 2020 and 65.5 in 2023 in YORA and 66.7 in 2020 and 56.4 in 2023 in LORA. 130 YORA and 26 LORA used Methotrexate (MTX) in 2020. 102 YORA and 24 LORA used MTX in 2023. 40 YORA and 20 LORA used prednisolone (PSL) in 2020. 50 YORA and 19 LORA used PSL in 2023. 96 YORA and 31 LORA used b-DMARDs in 2020. 88 YORA and 26 LORA used b-DMARDs in 2023. 3 YORA and 3 LORA used JAK inhibitors in 2020. 40 YORA and 12 LORA used JAK inhibitors in 2023. [Conclusions] Both groups showed declining renal function at 3 years. LORA had lower renal function than YORA; there was no difference in the usage of MTX or PSL. Usage of JAK inhibitors increased in both groups.

## W17-6

**Changes in Joint Destruction over 4 Years in Patients with Rheumatoid Arthritis in Remission-Comparison by MMP3 activity-**

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the impact of MMP-3 activity on joint destruction in patients with RA in remission. [Methods] We included 97 RA patients (mean age 66.2 years, mean disease 12.9 years) who attended our hospital from 2018 to 2010, and measured DAS28 and MMP-3 at the first, second, and fourth year. modified total sharp score (mTSS) was measured and ΔmTSS was obtained at the

first and fourth year. 4-year remission Of the patients in remission (82 patients), those whose MMP3 was (1) all positive (10 patients), (2) positive once or twice (17 patients), (3) all negative (55 patients), and those who were never in remission (15 patients) were considered. [Results] ΔmTSS was 3.6±5.6 points in the remission group and 31.9±29.1 points in the non-remission group, with the non-remission group significantly higher. In the comparison of MMP3 within the remission group, the group with all positive MMP3 scores was significantly higher than the other groups. [Conclusions] The study of joint destruction in patients with rheumatoid arthritis in remission by MMP3 activity showed that ΔmTSS was significantly higher in the group with high MMP3. If MMP3 is high even in patients who remain in remission, intensification of therapy should be undertaken.

## W18-1

**Patient Profiling for Glucocorticoid Withdrawal in Systemic Lupus Erythematosus and Subsequent Relapse Rates: Insights from a Retrospective Cohort Study in the LUNA Registry**

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Conflict of interest: None

[Objective] We studied the factors influencing glucocorticoid (GC) withdrawal in SLE patients and assessed whether GC withdrawal increases flares. [Methods] In the multicenter study using LUNA SLE registry, we followed patients for 2 years who met the following criteria: SLEDAI ≧ 4 at initial visit, disease duration ≧ 2 years, and history of ≧ 5 mg prednisolone (PSL) equivalent. The primary endpoint was GC withdrawal, and the factors influencing GC withdrawal were analyzed using Cox regression. We compared relapse rates between GC withdrawal and maintenance (PSL ≦ 5 mg) groups. [Results] 582 patients were included, and 31 of them achieved GC withdrawal. None of the following factors were significantly associated with GC withdrawal: age at diagnosis ≧ 50 years (HR 2.18 [0.89-5.38]), SLEDAI ≧ 12 at initial visit (HR 0.87 [0.41-1.84]), SLEDAI ≧ 12 at enrollment (HR 0.35 [0.05-2.59]), anti-dsDNA antibodies (HR 0.72 [0.3-1.7]), hypocomplementemia (HR 1.46 [0.7-3.07]), immunosuppressive drugs (HR 0.75 [0.35-1.6]), or HCQ (HR 0.63 [0.27-1.49]). There was no significant difference in relapse rates between GC withdrawal and maintenance groups (HR 1.54 [0.33-7.25]). [Conclusions] Patients diagnosed at age ≧ 50 years old were more likely to withdraw GC. GC withdrawal did not increase flares.

## W18-2

**Characteristics of patients with SLE who keep low disease activity and successful glucocorticoid withdrawal**

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Conflict of interest: None

[Objective] The aim of this study is to clarify the characteristics of patients with SLE who can keep Lupus Low Disease Activity State (LLDAS) and successful glucocorticoid (GC) withdrawal. [Methods] We retrospectively evaluated patients with SLE who kept LLDAS in our hospital. These patients have been categorized into two groups; those who stopped GC successfully (GC-off group) and those who have kept taking GC (GC-on group). We investigated the differences in patient characteristics between the two groups. [Results] Of 32 patients who have kept LLDAS, the GC-off group has 17 cases. We found no statistical differences between the two groups in age, disease duration, complications of lupus nephritis and neuropsychiatric lupus, and the use of hydroxychloroquine and biologics. Anti-dsDNA antibody positivity in the GC-off group was higher compared to the GC-on group (87.5% vs 50.0%, p=0.046). The PGA score of the GC-off group was lower compared to the GC-on group (0.11 vs 0.34, p=0.017) and the DORIS remission rate of the GC-off group was higher than that of the GC-on group (88.2% vs 33.3%, p=0.002). [Conclusions] Patients with SLE who have kept LLDAS and successful GC withdrawal have higher anti-dsDNA antibody positivity and clinical remission rates.

## W18-3

**Clinical features and treatment of late-onset systemic lupus erythematosus**

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Conflict of interest: None

[Objective] The patients with SLE in Japan have become older in recent years. We investigated the characteristics, treatment, and prognosis of late-onset SLE patients. [Methods] 305 SLE patients (45 men and 260 women) attending our hospital between 1984 and 2023 were included. Those onset at less than 50 years of age were classified as young-onset (group Y), 50 years or more as late-onset, those onset at 50 to 69 years (group L1), and 70 years or more (group L2). The numbers were 214, 58, and 33 cases, respectively. The relative risk ratios of each group were analyzed for each organ lesion. LLDAS attainment rates were also evaluated. [Results] The patient numbers onset before 2017 in each group were 167, 34, and 5 cases, and 47, 24, and 28 cases after 2018, showing an increase in the number of late-onset cases in recent years. NP-SLE incidence was 23, 13, and 9 cases in each group, respectively. The LLDAS attainment rate was 78, 69, and 33% in each group despite immunosuppressive therapy, and the L2 group had a poor prognosis. [Conclusions] Late-onset SLE has atypical clinical symptoms, such as the absence of a skin rash. Still, early intervention is needed in cases of cardiac failure and neurological symptoms. Further studies are also required on the treatment of older patients.

## W18-4

**Incidence of infection due to MMF in patients with SLE in maintenance therapy: A prospective cohort study from the LUNA registry**

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Conflict of interest: None

[Objective] We use the database of LUNA registry to compare the incidence of infection requiring hospitalization between MMF and other immunosuppressants in SLE patients on maintenance therapy. [Methods] Prospective cohort study was conducted. SLE patients on maintenance therapy were defined as those taking PSL≦15 mg. Exposure was defined as the MMF treatment group and comparison was defined as the other immunosuppressant (non MMF) treatment group. The primary outcome was incidence of infection requiring hospitalization. We conducted a multivariable analysis using time-dependent COX proportional hazards model adjusted for age, gender, PSL dosage, SDI, and SLEDAI. [Results] There were 964 SLE patients on maintenance therapy. 270 were in the MMF group and 8 of them were hospitalized due to infection. 694 were in the non MMF group and 35 of them were hospitalized due to infection. The hazard ratio for developing infections requiring hospitalization in the MMF group compared to non MMF group was 0.72 (95% CI 0.41-1.26, p=0.256), with no statistically significant difference between the two groups. [Conclusions] In SLE maintenance therapy, there may be no difference between MMF and other immunosuppressants in the risk of developing severe infections requiring hospitalization.

## W18-5

**Double filtration plasmapheresis reduces type I interferon-inducing activity of plasma from patients with systemic lupus erythematosus**

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Conflict of interest: Yes

[Objective] Type I interferon (IFN-I) plays a significant role in the pathogenesis of systemic lupus erythematosus (SLE). Double filtration plasmapheresis (DFPP) is a treatment option for SLE, but its effect on IFN-I remains unclear. Therefore, we conducted a study to investigate the effect of DFPP on IFN-I-inducing activity. [Methods] We collected plasma samples from patients with SLE (n=11) continuous undergoing DFPP at Juntendo Hospital and analyzed using a cell-based reporter system of quantifying IFN-I-inducing activity. We also assessed the STING pathway through reporter cells harboring knockouts of STING and Western blot, and measured double-stranded DNA (dsDNA) concentration using the Pico Green. [Results] IFN-I-inducing activity reduced after undergoing DFPP, with a more pronounced effect observed in patients with higher disease activity. This reduction was not observed in STING-knockout cells, and plasma dsDNA concentrations decreased following DFPP. Western blot analysis showed that phosphorylation of STING and IRF3 was suppressed after undergoing DFPP. [Conclusions] DFPP effectively suppresses IFN-I-producing activity via the STING pathway by eliminating dsDNA from the bloodstream. This is the first report to demonstrate IFN-I-inducing activity as a therapeutic effect of DFPP.

## W18-6

**Prescription status of systemic lupus erythematosus medications by prefecture according to the National Database**

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Conflict of interest: Yes

[Objective] Hydroxychloroquine (HCQ) is recommended for all cases of SLE. HCQ may still be under-prescribed in Japan owing to its late approval in 2015. We evaluated prescription status of SLE drugs by prefecture according to the National Database (NDB). [Methods] A patient with SLE was defined as having a disease with ICD10 code M321 or M329 between April 2019 to March 2020 for which corticosteroids, immunosuppressives, or biological agents were prescribed at least once during a given month. The prescription rate of HCQ, mycophenolate mofetil (MMF) and tacrolimus (TAC) were evaluated. [Results] In total, 74,277 patients met the definition of SLE. The HCQ prescription rate was low at 21.4%. Okinawa Prefecture had the highest and lowest rate of 35.0% and 10.7%, respectively. On the other hand, the prescription rate of MMF and Tac was 12.0% and 22.9% nationwide, and by prefecture the highest rate was 18.5% and 37.2% and the lowest rate was 6.6% and 15.2%, respectively. [Conclusions] The prescription rate of HCQ in Japan to be low, with the difference being even more pronounced among the prefectures. The prescription rate of other SLE medications also differed among the prefectures, indicating a lack of standardization of SLE treatment in Japan.

## W19-1

**Activation of peripheral monocytes via BAFF receptor/Nav1.7 channel pathways contributes to enhancement of B cell function in patients with primary Sjögren's syndrome**

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Conflict of interest: None

[Objective] We investigate the possible involvement of voltage-gated sodium channel 1.7 (Nav1.7) and BAFF signaling pathways in activation of monocytes, which consequently promote B cell activation in patients with primary Sjogren's syndrome (pSS). [Methods] The expression levels of Nav1.7 and BAFF receptor (BR3) in peripheral monocytes from patients with pSS (n=108) and healthy controls (HC; n=28) were analyzed by FACS. The expression level of Nav1.7 in BAFF-stimulated peripheral monocytes was analyzed by qPCR. PBMCs were stimulated with anti-IgM, anti-CD40, IL-21 and BAFF in the presence of a specific inhibitor against Nav1.7. The amount of IgG produced by the cells was measured by ELISA. [Results] The proportion of Nav1.7 and BR3 positive cells in monocytes were significantly elevated in pSS as compared to HC. The proportion of Nav1.7 positive cells was significantly correlated with that of BR3 positive cells in the monocytes. qPCR analysis revealed that BAFF enhanced the Nav1.7 expression in pSS monocytes. Moreover, elevated IgG production from PBMC by the stimuli including BAFF was suppressed by the Nav1.7 inhibitor in a dose dependent manner. [Conclusions] Our data suggest that the elevated expression of Nav1.7 and BR3 in monocytes are involved in activation of B cells in pSS.

## W19-2

**Elucidation of cellular senescence in rheumatoid arthritis-associated interstitial lung disease using a mouse model**

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Conflict of interest: None

[Objective] The pathogenesis of rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is unknown. We analyzed the involvement of cellular senescence (CSen) in the mechanism of RA-ILD, using SKG/Jcl mice. [Methods] We induced ILD in SKG/Jcl mice (SKG-ILD) by administration of zymosan. To evaluate CSen in SKG-ILD, immunohistochemistry (IHC) was used to detect the CSen markers, such as $p21^{WAF1/CIP1}$ (p21) and $p16^{INK4a}$. Due to determine the senescent cells, immunofluorescence (IF) and flow cytometric analysis (FCM) was performed. [Results] In IHC, CSen marker-positive cells were found in SKG-ILD and increased along with fibrosis progression. IF showed the majority of the p21-positive cells were leucocytes, but some vascular endothelial cells, epithelial cells, and the other interstitial cells were also p21-positive. FCM showed alveolar and interstitial microphages were the largest number of p21-positive cells among leucocytes. [Conclusions] In SKG-ILD, alveolar/interstitial macrophages mainly developed CSen and has been shown to be involved in the pathogenesis. CSen may also be associated with RA-ILD. Further research is needed into the roles of the senescent cells.

## W19-3

**Joint pain in inflammatory arthritis associated with anti-PD-L1 antibody treatment is exacerbated by synovial fibroblast-derived FGF through induction of neuronal apoptosis**

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Conflict of interest: None

[Objective] Immune checkpoint inhibitors such as anti-PD-L1 antibodies (αPD-L1 ab) have become innovative treatments for cancer, but also been linked to inflammatory / rheumatoid arthritis (RA), which are immune-related adverse events. In this study, we created inflammatory arthritis model mice administered with αPD-L1 ab to clarify the effects of αPD-L1 ab on arthritis, mainly on RA synovial fibroblasts (RA-FLS). [Methods] 250 μg of αPD-L1 ab was administered 4 times to arthritis-induced SKG mice, and arthritis score evaluation, calcaneal μCT analysis, von Frey test, and Rotarod test were performed. In vitro, we investigated the cell proliferation ability of RA-FLS by αPD-L1 ab. We also analyzed mature neurons apoptosis by humoral factors from RA-FLS. [Results] αPD-L1 ab treatment lowered the pain threshold in SKG mice without exacerbating arthritis, bone destruction or motor function. In RA-FLS, αPD-L1 ab stimulation enhanced cell proliferation and FGF-9 gene expression. Apoptosis of mature neurons was enhanced by rhFGF-9, and apoptosis was enhanced when mature neurons were stimulated with the culture supernatant of RA-FLS after αPD-L1 ab administration. [Conclusions] Anti-PD-L1 antibodies may exacerbate pain in arthritis by promoting apoptosis of neurons via FLS-derived FGF-9.

## W19-4

**Activation of TLR4 pathways is involved in the elevated expression of BAFF receptor, BR3, in peripheral CD14++CD16+monocytes of patients with primary Sjögren's syndrome**

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Conflict of interest: None

[Objective] We demonstrate the possible involvement of activation of TLR4 signaling in the enhanced expression of BR3 in peripheral monocytes of patients with primary Sjögren's syndrome (pSS). [Methods] The expression levels of TLR4 and BR3 in peripheral monocytes ($CD14^{++}CD16^{-}$; CM, $CD14^{++}CD16^{+}$; IM, $CD14^{+}CD16^{++}$; NCM) of pSS patients (n=71) and healthy controls (HC, n=21) were analyzed by FACS. FACS analysis was also employed to evaluate the phosphorylation of NF-kB p65 in LPS-stimulated pSS monocytes. PBMCs were stimulated with LPS or S100A9 for 3 days and the expression level of BR3 in the cells was analyzed by FACS. The serum level of S100A9 was measured by ELISA. [Results] The expression levels of TLR4 and BR3 were significantly higher in IM than those in CM and NCM in pSS. Notably, the TLR4 expression in IMwas positively and significantly correlated with that of BR3 in pSS patients ($p<0.001$). Phosphorylation of NF-kB p65 was enhanced in LPS-stimulated pSS monocytes. The serum level of S100A9 was significantly higher in pSS than HC ($p < 0.001$), and the proportion of $TLR4^{+}$ cells among IM was significantly correlated with the S100A9 level in pSS serum ($p<0.05$). [Conclusions] Our results suggest that TLR4 signaling pathways are involved in the elevated expression of BR3 in pSS monocytes.

## W19-5

**Clock gene Bmal1 regulates NF-kappaB transcription and contributes to the production of inflammatory mediators in RA-FLS**

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Conflict of interest: None

[Objective] We have reported that clock gene Bmal1 promotes production of inflammatory mediators. In this study, we examined how Bmal1 contributes to the production of inflammatory mediators in RA-FLS in terms of NF-κB, a representative transcription factor of RA. [Methods] After transfected Bmal1/siRNA, RA-FLSs were stimulated with or without TNF-α or IL-1β (20 ng/ml), and total protein was extracted to analyze the expression of both IκBα and phospho-/total p65 subunit of NF-κB by western blotting. RA-FLSs transfected with Bmal1/siRNA or Control/siRNA were subjected to immunoprecipitation with anti-p65 antibody followed by western blot with anti-BMAL1 antibody. Under conditions of Bmal1 overexpression, transcriptional activities of NF-κB were examined by luciferase assay. [Results] Phosphorylation of p65 (Ser536) in RA-FLS was decreased by suppression of Bmal1though TNF-α stimulation, while degradation of IκBα was not affected by either TNF-α or IL-1β stimulation. In RA-FLS, BMAL1 was bound to p65 and overexpression of Bmal1 promoted transcriptional activities of NF-κB under TNF-α stimulation. [Conclusions] These results suggest that Bmal1 may increase the transcriptional activity of NF-κB and exacerbate inflammation in RA.

## W19-6

**DLL4 induces expression of DLL4 and Langerin on monocytes and activates T cells**

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Conflict of interest: None

[Objective] Investigating the relationship between Notch ligands and dendritic cells (DCs). [Methods] Monocytes were analyzed by FACS whether DLL4 and Langerin express by stimulation with Notch ligands (DLL1, DLL3, DLL4, JAG1 and JAG2), GM-CSF, TGF-β1 and IL-4. T cells were analyzed by FACS whether T cells activate by co-culture with monocytes stimulated by DLL4, GM-CSF and TGF-β1. The monocytes were compared with the DCs derived from monocytes (Mo-DCs) and macrophages (Mφs). [Results] DLL4, GM-CSF and TGF-β1 induced DLL4 and Langerin on monocytes, while IL-4 suppressed expression of

DLL4 and Langerin. Furthermore, monocytes stimulated by DLL4, GM-CSF and TGF-β1 significantly activated T cells more than Mφs. However, there was no significant difference in T cell activation between expression of DLL4 and Langerin. [Conclusions] Our results indicate IL-4 suppressed expression of DLL4 on Mo-DCs, although the reason why Mo-DCs do not express DLL4 remains unclear to date. In addition, because there was no significant difference in T cell activation between expression of DLL4 and Langerin, another molecule might be involved in T cell activation.

## W20-1

**Progression of Hallux Valgus Angle with Rheumatoid Arthritis is associated with worsening Disease Activity in Hardy Classification 5 and Below**

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Conflict of interest: None

[Objective] The factors of the change of hallux valgus in patients with rheumatoid arthritis are unknown. The purpose of this study was to examine longitudinally the progression of hallux valgus in patients with rheumatoid arthritis and the factors associated with it. [Methods] Patients with foot X-rays (non-weight bearing) in 2015 (baseline) and 2021 were included. Hallux valgus angle (HVA), M1-M2 angle, M1-M5 angle, 1st TMT joint angle, Calcaneal pitch angle (CP angle), and Meary's angle (MP angle) were measured. Factors related to the change in HVA per year (HVA/y) >1° were investigated. [Results] A total of 316 patients and 616 legs were included. The mean HVA/y was 0.29±0.63° (-2.17-3.81). Univariate analysis showed that HVA/y >1° was associated with moderate or higher disease activity from 2015 to 2021, ACPA positivity, M1-5 angle, left/right, and gender, while HVA (baseline), biologic use, and RF positivity were not significantly correlated. In multivariate analysis, moderate or higher disease activity, ACPA positivity, M1-M5 angle, left and right, and gender were significant factors. [Conclusions] Disease activity, positive ACPA, wide feet, right side, and female gender are significant risk factors for progression of bunion with rheumatoid arthritis of Hardy's classification 5 or below.

## W20-2

**Examination of Factors Associated with Osteoporotic Fractures in Patients with Rheumatoid Arthritis Using the NinJa2020 Database**

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Conflict of interest: None

[Objective] To investigate the factors associated with osteoporotic fractures in rheumatoid arthritis (RA) patients using the NinJa2020 database. [Methods] From the 15,553 RA cases registered in the 2020 NinJa, we examined 153 RA cases hospitalized due to osteoporotic fractures. This group was compared to a matched group of 153 non-fracture RA cases based on age and gender. Patient backgrounds (age, gender, BMI, RA disease duration, DAS28-CRP, SDAI, HAQ-DI, EQ-5D, PSL dosage, MTX usage, RF, ACPA) were compared. A logistic regression analysis was performed based on the presence or absence of fractures. [Results] The fracture group constituted 0.98% (153/15553 cases) of the total. In univariate analysis, RA disease duration, DAS28-CRP, SDAI, HAQ-DI, EQ-5D, and PSL dosage were significantly associated ($p<0.001$). Furthermore, multivariate logistic regression analysis revealed that HAQ-DI (OR 1.84, 95% confidence interval (CI) 1.36-2.49, $p<0.001$) and PSL dosage (OR 1.15, CI 1.02-1.30, $p=0.025$) were factors related to fractures. [Conclusion] This study showed that HAQ-DI and PSL dosage were associated factors for osteoporotic fractures in RA patients.

## W20-3

**Blockade of proinflammatory cytokines with biologics increases the major psoas muscle cross-sections in chronic inflammatory disease patients**

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Conflict of interest: None

[Objective] To evaluate whether blockade of proinflammatory cytokines influence on muscle mass in chronic inflammatory disease patients [Methods] The data were obtained from bio-naïve patients from 2012 to 2023, and assessed before and after the treatment. CT images in the major psoas muscle cross-sections were obtained using HRCT. Body mass index (BMI) and skeletal Muscle mass index (SMI) were measured using dual energy X-ray absorptiometry. [Results] At baseline, 15.9% of patients (35/157) were male, and 75.2% and 11.5% were PsA. Sixty and 97 patients were treated with TNF and IL-6 inhibitors respectively. DAS28-ESR and CRP were significantly decreased. BMI at 1 year was significantly increased compared with those at baseline. The major psoas muscle cross-sections also increased (16.48±5.4 $cm^2$ at baseline, 17.04±5.6 $cm^2$ [$p=0.004$] at 1 year, 17.55±6.0 $cm^2$ [$p=0.018$] at 2 year, 16.56±5.1 $cm^2$ [$p=0.0006$] at 3 year). However, there were no significant difference in SMI. [Conclusions] Blockade of proinflammatory cytokines increased BMI and major psoas muscle mass. The treatment improved disease activity, and increasing physical activities elevated the major psoas muscle mass. Whereas, SMI did not change because SMI is calculated using the sum of the arm and leg skeletal muscle mass.

## W20-4

**A cross-sectional study of the association between anxiety state and various factors in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] In RA patients, the anxiety rate is 1.2 times higher than healthy controls and weakly correlated with disease activity. The present study investigated the relationship between anxiety state and disease activity, ADL, and depression. [Methods] A total of 155 RA patients attending Showa University Hospital and Northern Yokohama Hospital as outpatients who agreed to participate in this cross-sectional study were included. The patient's background included age, gender, PSL use, the SDAI, the HAQ, the CES-D, and PHQ-9. The STAI was used to evaluate anxiety status with cutoff scores of 41 for men, 42 for women for state anxiety, 44 for men, and 45 for women for trait anxiety. [Results] State anxiety and trait anxiety were 39.0±11.0 (points) and 39.5±11.6 (points), and 64 and 51 of the patients were above the cutoff level, respectively. Concerning the CES-D, state anxiety was correlated with a correlation coefficient of 0.57 and trait anxiety with 0.65; about the PHQ-9, state anxiety was associated with a correlation coefficient of 0.54 and trait anxiety with 0.60. [Conclusions] The high rate of anxiety in RA patients was associated with disease activity, patient VAS, and depression, suggesting that controlling disease activity may be necessary from a bio-psycho-social perspective.

## W20-5

**Changes in arterial stiffness monitored using the cardio-ankle vascular index in patients with rheumatic disease receiving initial glucocorticoid therapy**

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Conflict of interest: None

[Objective] The purpose of this study was to elucidate the effect of glucocorticoid (GC) therapy on arterial stiffness in rheumatic diseases by evaluating the cardio-ankle vascular index (CAVI). [Methods] We conducted an observational study to address GC therapy's effect on arterial stiffness using the cardio-ankle vascular index (CAVI) in patients with rheumatic diseases. Twenty-eight patients with rheumatic disease received initial GC therapy with prednisolone 20-60 mg/d. CAVI was examined at baseline and 3 and 6 months after GC therapy. Changes in CAVI and inflammatory markers were evaluated. [Results] GC therapy increased the mean CAVI after 3 months but decreased it to pretreatment levels after 6 months. The mean CAVI substantially decreased with GC treatment in patients < 65 years but increased in patients ≧ 65 years. Changes in CAVI during the 6 months GC treatment negatively correlated with the lymphocyte-to-monocyte ratio (LMR) at baseline. Multivariate analysis of factors related to changes in CAVI highlighted young age and LMR at baseline. [Conclusions] GC temporarily exacerbates but eventually improves arterial stiffness in rheumatic diseases. Particularly in young patients, GC may improve arterial stiffness by reducing inflammation.

## W20-6

**The Prognosis of Borderline Pulmonary Hypertension Associated with Connective Tissue Diseases**

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Conflict of interest: Yes

[Objective] The definition of pulmonary hypertension (PH) was changed from a mean pulmonary arterial pressure (mPAP) greater than 25 mmHg to 20 mmHg. We aimed to clarify the prognosis of borderline PH associated with connective tissue disease (PH with CTD). [Methods] Among patients who underwent right heart catheterization (RHC) at the Kitasato University Hospital from 2019 to 2022, we enrolled patients with mPAP between 20 mmHg and 25 mmHg. Events were defined as death or PH manifestation and we examined retrospectively. [Results] 13 patients with borderline PH with CTD were extracted. They included 1 male, 7 SSc patients, and 3 MCTD patients. The mean age at RHC was 71.2 years, and the mean observation period was 15.7 months. The mean mPAP was 22.9±1.8 mmHg and the mean pulmonary artery wedge pressure was 9.5±3.8 mmHg. Interstitial lung disease (ILD) was present in 7 patients (54%), none of whom were treated with PAH-specific drugs. 3 patients had poor prognosis (including 2 patients with malignancy) and 1 patient developed PH. The incidence rate (100 person-years) of PH manifestation was 5.07. [Conclusions] In borderline PH with CTD, the risk of PH manifestation is not high. And then, the introduction of PAH-specific drugs should be considered with caution.

## W21-1

**A case of Muckle-Wells syndrome with hypertrophic meningitis in which a novel NLRP3 gene variant was identified**

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Conflict of interest: None

A 50-year-old man have had cold urticaria since childhood. He suffered bilateral hearing loss at the age of 23 and began using bilateral hearing aids at the age of 35. He had repeated migraines since he was young. At the age of 49, his headache worsened, he performed a head MRI. Hypertrophic pachymeningitis (HP) was observed, and he was referred to the neurosurgery department of our hospital. He was transferred to our department for the purpose of examining the primary disease. He had hearing loss from the age of 23, a family history of hearing loss (mother, uncle, brother), cold-stimulated urticaria, daily headache suspected of chronic aseptic meningitis, and joint symptoms, so he suspected an autoinflammatory disease. We found a new heterozygous variant in the *NLRP3* gene, and diagnosed Muckle-Wells syndrome (MWS). As treatment, steroids (prednisolone: PSL 40 mg) were started, gradually tapered, and headache tended to improve slightly, but HP did not improve on head MRI one month after steroid start. Currently, IL-1 inhibitors (canakinumab 150 mg) are administered every two months. Cryopyrin-associated periodic syndrome, including MWS, may present with aseptic meningitis, but there are no reports of HP as in this case, and it seems to be a valuable case.

## W21-2

**Analysis of the physiology of TNF inhibitor in Pyrin-associated autoinflammation with dermatosis**

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Conflict of interest: None

[Objective] Pyrin-associated autoinflammation with dermatosis (PAAND) is an autoinflammatory disease characterized by persistent systemic inflammation and neutrophilic dermatitis by the specific *MEFV* gain-of-function variant. Previous reports showed that steroids, IL-1β inhibitors, or TNF inhibitors were effective for PAAND, although the physiology of TNF inhibitors has not been determined. [Methods] We show a 2-year-old boy with PAAND complicated with inflammatory bowel disease (IBD) treated with infliximab, prednisolone, and colchicine. He attained remission and now continues only infliximab. We examined his serum and skin biopsy specimen. [Results] In serum cytokines analysis, elevated IL-6 and IL-18 levels were confirmed, whereas TNFα level was within the normal range. TUNEL staining and immunohistochemistry of the skin biopsy specimen showed significant cell death and TNFα-positive cells in the dermis and IL-18-positive cells in the epidermis. [Conclusions] Recent IBD or idiopathic inflammatory myopathy studies demonstrated the association between cell death, especially necroptosis, and inflammation. Our study indicated this association could apply to PAAND. Since TNFα is closely related to necroptosis, TNF inhibitors could suppress cell death and inflammation in the lesions.

## W21-3

**Clinical characteristics of juvenile-onset systemic sclerosis according to autoantibody status**

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Conflict of interest: None

[Objective] To evaluate the clinical characteristics of juveile-onset systemic sclerosis (jSSc) according to autoantibody status in Japan. [Methods] Based on the data from a national survey conducted in 2021 of patients with jSSc who developed under the age of 18 years with a history of medical visits from 2016 to 2020, we evaluate the clinical features according to autoantibody. [Results] Among 130 cases, 78 (62.4%) were anti-topoisomerase I (ATA) positive, 15 (12.9%) were anti-centromere antibody (ACA) positive, and 23 (19.2%) were anti-U1RNP antibody positive. ATA-positive cases were predominantly diffuse subtype (73.1%), while ACA-positive cases were predominantly limited subtype (60%). Interstitial lung disease (ILD) was more common in ATA-positive patients (57.7% vs. 13.3%), and puffy fingers were more common in ACA-positive patients (5.1% vs. 33.3%). There was no difference in the frequency of vascular, pulmonary hypertension, or esophageal imvolevement, but arthritis was more frequent in anti-U1RNP antibody-positive cases. [Con-

clusions] The ATA-positive rate was particularly high in Japanese jSSc. The higher rate of diffuse subtype and ILD in ATA-positive cases and the higher rate of females and limited subtype in ACA-positive cases were similar to adult patients in Japan.

## W21-4

**Juvenile Idiopathic Arthritis in a Girl with anti-ganglionic acetylcholine receptor antibody (Anti-gAChR antibody)-Positive Autoimmune Autonomic Ganglionopathy**

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Conflict of interest: None

A 16 year-old girl had been suffered from fever, anorexia, dyspepsia, diarrhea/constipation, malaise, weight loss, eya pain, thirst since age 13 and was diagnosed with "Functional hyperthermia, dysautonomia, and eating disorders." She complaint lower back pain and knee swelling at age 14. She was diagnosed as juvenile idiopathic arthritis and was administered 1 mg/kg of PSL. Polyarthralgia appeared during tapering and she was referred to our department. The remission was achieved with MTX and adalimumab (ADA), but bacterial infections repeated since age 15. The antibiotics prophylaxis was ineffective and MTX was discontinued. After that, fever, high levels of CRP and cytokine markers appeared. Systemic glucocorticoids and cyclosporine were administered, and ADA switched to tocilizumab, and the inflammation was improved. Around that time, she began to show personality changes, altered consciousness, hypertension, asthma, eye pain, bladder-rectal disorder, and paralysis of the left lower limb. The oligoclonal bands in the cerebrospinal fluid were positive and immunoglobulin was administered. She was positive for anti-gAChR antibody beta4 and was diagnosed with autoimmune autonomic gangliopathy. Childhood onset cases are rare and I will report with a review of the literature.

## W21-5

**The effectiveness of abatacept in treating refractory juvenile dermatomyositis**

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Conflict of interest: None

[Background] Abatacept (ABA) is effective in some cases of refractory juvenile dermatomyositis (JDM). [Objective] To investigate the usefulness of ABA in cases of refractory JDM. [Methods] The subjects in this study were seven patients with JDM who had started ABA therapy. We retrospectively examined their medical records for clinical characteristics, course, concomitant medications, and side effects. [Results] The median time from disease onset to starting ABA treatment was 52 months. The types of myositis-specific autoantibodies were anti-NXP2 antibody in four cases, anti-MDA5 antibody in two cases, and anti-TIF1γ antibody in one case. All patients were on immunosuppressants prior to ABA initiation: prednisolone (PSL) in all; mycophenolate mofetil in six, methotrexate in six, cyclosporine in two, tacrolimus in one, and azathioprine in one patient. The reasons for starting ABA were disease worsening in three, refractory calcification in three, and worsening of interstitial pneumonia in one patient. With ABA, the symptoms improved, and the dose of PSL could be reduced in five of the seven patients, excluding two patients who had just started ABA. No serious infections or new autoimmune diseases developed after initiating ABA. [Conclusions] ABA may be effective in treating refractory JDM.

## W21-6

**Subcutaneous Methotrexate therapy for Pediatric Rheumatic Diseases: Case Series**

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Conflict of interest: None

Subcutaneous methotrexate (SC MTX) is an alternative choice for intolerance of oral MTX due to nausea in adults. However, there are few reports to use SC MTX in patient with pediatric rheumatic diseases. Case 1: A 8-year-old boy with juvenile idiopathic arthritis (JIA). He received oral MTX, however switched to SC due to nausea seven months later. After switching, nausea and relapse of JIA were not observed. Case 2: A 21-year-old woman with JIA and uveitis. She received oral MTX, however switched to tacrolimus due to nausea and started Golimumab for relapse of JIA. At the age of 20, she started SC MTX for relapse of JIA. SC MTX was effective, however discontinued due to nausea 4 months later. Case 3: A 6-year-old boy with idiopathic uveitis (IU). He received oral MTX, however had a relapse of IU. It was difficult to increase the dose of oral MTX due to nausea and switched to SC. SC MTX was effective. A blister followed by pigmentation was observed at the injection site after self-injection at home. Case 4: A 11-year-old girl with IU. She received oral MTX, however switched to tacrolimus due to nausea. She had a relapse of IU one year later and started SC MTX. After switching, nausea and relapse of IU were not observed. SC MTX might be effective as an alternative treatment in children.

## W22-1

**Efficacy and Safety of Upadacitinib Through One Year in Patients with Active Ankylosing Spondylitis and an Inadequate Response to Biologic DMARD Therapy: Results from a Phase 3 Study with Japanese Subjects Sub-analysis**

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Conflict of interest: Yes

Objectives: To assess the 1-year efficacy and safety of Upadacitinib (UPA) 15 mg once daily (QD) in patients (pts) with active ankylosing spondylitis (AS) who have inadequate response or intolerance to biologic disease-modifying antirheumatic drugs (bDMARD-IR) in SELECT-AXIS 2. Methods: In the SELECT-AXIS 2 AS bDMARD-IR study, pts who completed the 14-week (wk) placebo (PBO)-controlled period were eligible to enter long-term extension and receive open-label UPA 15 mg QD for up to 90 wks. Results: A total of 420 pts including 12 Japanese pts were randomized and received study drug. Response rates increased rapidly after initiation of UPA and were maintained up to wk 52. ASAS40 response rate at wk 52 for the PBO to UPA and continuous UPA groups were 64.6% and 65.9% (non-responder imputation with multiple imputation analysis) respectively. Safety was assessed in 414 pts (534.4 pt-years [PY] of exposure) who received ≧1 dose of UPA. Efficacy and safety of Japanese pts were generally consistent with overall pts. 19 events of herpes zoster were observed in overall population, of which 3 events were seen in Japanese pts. Conclusions: UPA showed sustained efficacy up to wk 52. UPA was generally well tolerated, with no new safety signals identified.

## W22-2

**Placebo-Controlled Efficacy and Safety of Upadacitinib Through One Year in Patients with Non-Radiographic Axial Spondyloarthritis: The Results of Overall Population and Japanese Subjects Sub-analysis**

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Conflict of interest: Yes

Objective: To assess the efficacy and safety of upadacitinib (UPA) vs

placebo (PBO) through 1 year in patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA). Methods: The SELECT-AXIS 2 nr-axSpA study included a 52-wk randomized, double-blind, PBO-controlled period. Enrolled adults had a clinical diagnosis of active nr-axSpA fulfilling the ASAS classification criteria, inflammation based on MRI sacroiliitis and/or elevated CRP. Results: Of the 314 pts including 11 Japanese pts randomized, 259 (82.7%) completed wk 52 on study drug. More pts achieved an ASAS40 response with UPA vs PBO up to wk 52 (62.8% vs 42.7% at wk 52, non-responder imputation with multiple imputation analysis). Consistent improvements were also seen with UPA vs PBO across other efficacy measures through wk 52. A similar proportion of pts in each treatment group had a treatment-emergent adverse event (TEAE) (UPA 68.6%, PBO 65.6%). Infections were the most common TEAE; the rates of serious infections and herpes zoster were higher with UPA vs PBO (1.3% vs 0.6% and 3.2% vs 0.6% respectively). Efficacy and safety of Japanese pts were generally consistent with overall pts. Conclusion: UPA showed consistent efficacy vs PBO through 1 year. No new safety risks were identified with longer-term UPA exposure.

## W22-3

**Placebo-Controlled Efficacy and Safety of Upadacitinib Through One Year in Patients with Non-Radiographic Axial Spondyloarthritis: Post-hoc Analysis of Sub-group Similar to the Diagnostic Guidance in Japan**

Mitsumasa Kishimoto[1], Hideto Kameda[2], Filip Van den Bosch[3], Xenofon Baraliakos[4], Kimitoshi Ikeda[5], Yuki Furusawa[5], Yihan Li[6], Anna Shmagel[6]
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Conflict of interest: Yes

Objective: To assess the efficacy and safety of upadacitinib (UPA) in patients (pts) sub-group that is similar to the Japan non-radiographic axial spondyloarthritis (nr-axSpA) diagnostic guidance in the SELECT-AXIS 2 nr-axSpA study. Methods: The SELECT-AXIS 2 nr-axSpA study included pts with active inflammation (consistent with axSpA on MRI sacroiliitis or hsCRP > ULN at screening). A post-hoc analysis was performed by stratifying overall population into those who met the Japan diagnostic guidance-like criteria (Age of onset < 40, exclusion of psoriasis and inflammatory bowel disease). Results: Of the 314 pts randomized, 213 pts met the Japan nr-axSpA diagnostic guidance-like criteria. In this sub-group, more pts achieved an ASAS40 response with UPA vs placebo (PBO) at wk 52 (65.8% vs 35.7%, non-responder imputation with multiple imputation analysis), and consistent improvements with overall population were also seen across other efficacy measures. Rates of treatment-emergent adverse events were similar between treatment groups (UPA 64.0%, PBO 73.5%) and consistent with overall population. Conclusion: As seen in the overall population, UPA showed consistent efficacy and similar safety profile vs PBO in sub-group met the Japan nr-axSpA diagnostic guidance-like criteria.

## W22-4

**Comparison of time to achieve minimal disease activity for ixekizumab versus adalimumab in patients with psoriatic arthritis: post-hoc analysis of Phase 3 SPIRIT-H2H study**

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Conflict of interest: Yes

**Objectives** To evaluate the time to achieve minimal disease activity (MDA) in patients with psoriatic arthritis (PsA) treated with ixekizumab (IXE) or adalimumab (ADA). **Methods** bDMARD-naïve patients with PsA were enrolled in the SPIRIT-H2H study and randomized to receive either IXE or ADA treatment. Median times to reach first and sustained MDA response and its individual components were estimated by treatment group over the 52-week (W) observation period, using Kaplan-Meier analyses. Sustained response was defined as meeting response criterion at two consecutive visits. **Results** With IXE (N=283) and ADA (N=283), 68.8% and 63.7% of patients achieved a first MDA during the 52W period, respectively. The proportion of patients achieving MDA at W52 was 47.3% for IXE and 41.0% for ADA. Median time to first MDA response tended to be reached earlier with IXE than with ADA (16.2Ws vs 24.4Ws, p=0.100). A sustained MDA response was achieved by 54.6% for IXE and 47.0% for ADA. Median time to sustained MDA response was 32.1W for IXE and could not be estimated for ADA (p=0.0421). The same trends were identified for all components of MDA. **Conclusion** The results of study suggest that, in patients with PsA, time to first and sustained MDA response is likely to be shorter with IXE than ADA.

## W22-5

**Investigation of MTX administration in the clinical practice of psoriatic arthritis**

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Conflict of interest: Yes

[Objective] PsA has a varied clinical presentation, is often already treated with therapy for the preceding psoriatic skin lesions, and often has multiple comorbidities. Therefore, it difficult to use MTX in accordance with treatment recommendations. We discuss the administration of MTX in the clinical practice of PsA. [Methods] We analyzed 282 PsA in our department's spondyloarthritis registry (TOSPAR) for use of MTX administration. [Results] Currently MTX administered to 37% of the past combined. Current MTX administration is 18%, of which 64% are in combination with molecular-targeted therapies. In the MTX started group, as the first-line therapy, continued for 12 months, DAPSA decreased significantly compared to the NSAIDs group (p=0.03). However, MTX administration was not a factor in achieving DAPSA remission on multivariate analysis. MTX in combination with a molecular-targeted therapy improved DAPSA similarly to that of a single molecular-targeted therapy, and this effect did not differ between molecular-targeted agents. [Conclusions] Since MTX administration in clinical practice for PsA is rarely sufficiently effective as a first-line therapy and is not effective in combination with molecular-targeted therapies, it is necessary to consider the method of MTX administration.

## W22-6

**Can methotrexate (MTX) induce liver dysfunction in patients with psoriatic arthritis (PsA) ?**

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Conflict of interest: None

[Objective] To clarify whether MTX can induce liver dysfunction in patients PsA. [Methods] PsA patients who visited our hospital between 2012-2019 and fulfilled the CASPAR criteria were included. The patients

were stratified into MTX group and biologics (non-MTX) group. Clinical information was retrospectively collected. AST, ALT and a liver-fibrosis biomarker (Fib-4 index) were measured at baseline (0M) and 36-month after the treatment. Patients with liver dysfunction at 0M were excluded. [Results] Fifty-three cases (MTX 24, non-MTX 29) were included. In MTX group, mean age and disease duration were 47 and 4 years. Of these, 75% were male, 21% on glucocorticoid (GC), 63% on NSAIDs. 21% had dyslipidemia (DL), and 29% had fatty liver (FL). In non-MTX group, mean age and disease duration were 50 and 2 years. Of these, 45% were male, 10% on GC, 35% on NSAIDs. 34% had DL, and 17% had FL. Significant differences were observed in sex, duration, and NSAIDs use. In MTX group, Fib-4 Index, AST were significantly elevated after the treatment, but no difference was observed in non-MTX group. Higher age and proportion of usage of GC were observed in Fib-4-elevating cases. [Conclusions] MTX can induce liver dysfunction even in the patients with PsA, especially with elderly and GC-treated cases.

## W23-1

**In adalimumab treatment, Remission induction and treatment continuation at 472 weeks in 230 patients**

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Conflict of interest: Yes

[Objective] Clinical usefulness and treatment continuation following 368 weeks of adalimumab (ADA) in rheumatoid arthritis (RA) patients were investigated. [Methods] Subjects were 186 analyzable patients introduced to ADA at the author's institution from May 2009 to Oct. 2014. Mean age was 54.3 years, mean duration of illness 6.5 years. 189 received MTX ≧10 mg/week (≧10 group) and 34 MTX<10 mg/week (<10 group). The course of DAS28 (ESR), HAQ and remission rate were analyzed. [Results] Overall DAS28 (ESR) remission rate showed clinical remission in 51% of patients from 12 weeks, and achieved 68% from 52 weeks, after that this condition continued. Overall HAQ remission rate at 472 weeks was 83%; treatment continuation rate was 50.9%., and those of≧10 group was 50.0%. [Conclusions] ADA plus an adequate dose of MTX with early escalation in early-stage RA and Bio Naïve patients is the best approach to maximally exploit the ADA potential.

## W23-2

**Outcomes in Patients Using Etanercept Biosimilar for Rheumatoid Arthritis**

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Conflict of interest: None

[Purpose] Etanercept biosimilar (ETN-BS) can be introduced at about 70% of the price of etanercept and is an effective option for patients who have difficulty using biological agents for economic reasons. We reviewed the outcomes of rheumatoid arthritis (RA) patients treated with ETN-BS in our department. [Methods] From July 2019 to September 2023, we selected 23 patients who could be followed at our hospital for at least 1 year, excluding changes from prior formulations. Patient background, overall disease activity index (DAS28-CRP, SDAI), laboratory data and reasons for continuing or discontinuing treatment were investigated. [Results] The mean age of the 23 patients was 54.7 years and the mean disease duration was 7.8 years. The mean pre-treatment DAS-CRP and SDAI were 3.40 and 13, respectively, but improved from the start of treatment: 2.39 and 7.34 after 1 month of treatment, 2.13 and 5.5 after 3 months, and 2.02 and 4.96 after 12 months. There were 5 discontinuations, 3 of which were due to inadequate response, but there were no adverse events. [Conclusion] We reviewed cases in which ETN-BS was used from the start of treatment in our department. Improvement in disease activity was observed in the first month of treatment, and clinical results up to 12 months were excellent.

## W23-3

**Long-term retention of tocilizumab (TCZ) treatment in patients with rheumatoid arthritis (RA)**

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Conflict of interest: None

[Objective] To investigate the long-term clinical results of TCZ in RA patients. [Methods] After initiating TCZ for 206 RA patients between May 2008 and March 2023, 41 cases have consistently received TCZ for over 5 years as of July 31, 2013. We investigated the clinical results of long-term usage of TCZ at the final assessment on July 31, 2023, in these cases. [Results] 29 cases were considered. 28 cases (96.6%) continued TCZ, with an average duration of 13.8 years. Disease activity at the 5-year/the final assessment was as follows: DASCRP; 1.8 ± 0.64 / 1.5 ± 0.3, CDAI; 5.6 ± 2.8 / 3.2 ± 2.2, and mHAQ; 0.4 ± 0.6 / 0.5 ± 0.5. Complications requiring treatment interruption were observed in 1 case, with a periprosthetic joint infection of the knee, and 1 case with urinary infection. After controlling the infections, TCZ could be resumed, and no other complications requiring treatment interruption were reported. MTX use was observed at the 5-year/the final assessment; 9 cases/1 case, and PSL; 2/0. [Conclusions] Patients for whom TCZ could be continued for over 5 years could receive continuous TCZ for more than 10 years. Not only low disease activity but also physical function could be maintained for over 10 years, and it was indicated that there was no longer a need for MTX or PSL.

## W23-4

**Ultrasonographic evaluation of Sarilumab and Tocilizumab therapy in patients with rheumatoid arthritis**

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Conflict of interest: Yes

[Objectives] To evaluate the clinical efficacy of Salilumab (SAR) and Tocilizumab (TCZ) therapy in patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used SAR and TCZ treated 21 and 51 RA patients more than 12 weeks. We evaluated the improvement of gray scale (GS) and power doppler (PD) score from baseline to week 24. [Results] In the patients receiving SAR (n=21) and TCZ (n = 51), the mean age was 65.7 vs 64.8 years old (p=0.965), disease duration was 6.7 vs 8.3 years (p=0.838), the mean MTX dose was 8.2 vs 10.2 mg/w (p=0.178), the rate of ACPA positive was 81% vs 88% (p=0.417), DAS28-ESR was 5.40 vs 5.50 (p=0.692), GS score was 22.4 vs 23.4 (p=0.701) and PD score was 17.3 vs 15.8 (p=0.624). The respective changes in GS and PD score after 4 weeks were as follows: GS: -2.9 vs -2.7 (p=0.845) and PD: -5.0 vs -3.0 (p=0.261). The respective changes in GS and PD score after 12 weeks were as follows: GS: -7.3 vs -7.1 (p=0.682) and PD: -9.3 vs -6.8 (p=0.406). The respective changes in GS and PD score after 24 weeks were as follows: GS: -11.4 vs -12.3 (p=0.431) and PD: -11.0 vs -10.3 (p=0.618). [Conclusion] The present study provides the improvement in ultrasonographic findings between SAR and TCZ was almost similar.

## W23-5

**Effects of sarilumab on pain in patients with rheumatoid arthritis at our hospital**

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Conflict of interest: Yes

[Objective] To evaluate the effect of sarilumab (SAR) on pain in patients with rheumatoid arthritis (RA) at our hospital. [Methods] Of 69 RA patients who received SAR between June 2018 and July 2023, 62 patients (12 males and 50 females) who were able to continue treatment for at least 3 months were included. Unacceptable pain (UP) (defined as pain VAS >40 mm) and disproportionate articular pain (DP) (defined as TJC28-SJC28≧7) were used to assess pain. The percentages of UP and DP were

examined at the start, 2 weeks, 1, 2, 3, 6 months, and 1 year. [Results] UP was observed in 41 patients (66%); UP rate decreased from 66% at start to 50% at 2 weeks, 40% at 1 month, 29% at 2 months, 23% at 3 months, 24% at 6 months, and 27% at 1 year; DP was observed in 28 patients (45%); DP rate decreased from 45% at start to 35% at 2 weeks, 31% at 1 month, and 21% at 2 months, The DP rate decreased from 45% at the start to 35% at 2 weeks, 31% at 1 month, 21% at 2 months, 16% at 3 months, 13% at 6 months, and 13% at 1 year. [Conclusions] SAR improved pain assessment early in treatment and the improvement was sustained.

## W23-6

**The HLA-DRB1 shared epitope in combination with anti-citrullinated peptide antibody is strongly associated with a better response to abatacept in patients with rheumatoid arthritis**

Wataru Hirose[1], Masayoshi Harigai[2], Koichi Amano[3], Masahiro Nakashima[4], Kenji Itoh[5], Toshihiko Hidaka[6], Kazutoshi Aoki[7], Hayato Nagasawa[8], Yukiko Komano[9], Toshihiro Nanki[10]

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Conflict of interest: None

[Objective] The aim of study was to investigate relationship between anti-citrullinated peptide antibody (ACPA) and HLA-DRB1 shared epitope (SE) alleles to effectiveness of abatacept (ABT) in patients with rheumatoid arthritis (RA). [Methods] Data from 183 RA patients who received ABT in the TOF-ABT study, a multicenter, longitudinal observational study, were used for the analysis. The 183 patients consisted of ACPA+SE+ (n=112), ACPA+SE- (n=45), ACPA-SE+ (n=11) and ACPA-SE- (n=15). [Results] ACPA+SE+ showed the highest proportion of DSA28-ESR remission among the 4 groups at week 52. Among ACPA+, proportion of patients achieving good EULAR response at week 52 significantly increased as copy number of SE alleles became higher. A logistic regression model after adjusting for factors at baseline revealed OR for achieving DAS28-ESR remission with ACPA+SE+ group as a reference (OR=1); OR=0.286; $p$=0.010 for ACPA + SE-; OR=0.099, $p$=0.024 for ACPA-SE+; OR=0.053, $p$=0.039 for ACPA-SE-. [Conclusions] Double positivity for ACPA and SE was found to be significantly associated with achieving DAS28-ESR remission in RA receiving ABT. In contrast, one-third of ACPA+ without SE alleles responded less effectively to ABT. Identifying SE in combination with ACPA may predict a better response to ABT.

## W24-1

**Epidemiological features of polymyalgia rheumatica in Japan**

Hiroshi Furukawa[1,2], Shinichi Nogi[3], Shomi Oka[1,2], Takashi Higuchi[1], Takanori Azuma[4], Takao Sugiyama[5], Fuminori Hirano[6], Misuzu Fujimori[7], Yoshiro Horai[8], Akitomo Okada[8], Atsushi Ihata[9], Masao Katayama[10], Shigeru Yoshizawa[11], Toshihiro Matsui[2,3], Kiyoshi Migita[8,12], Shigeto Tohma[1,2]

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Conflict of interest: None

*Objective:* Polymyalgia rheumatica (PMR) is a chronic inflammatory disease characterized by arthralgia and myalgia of the shoulder and hip girdles. PMR affects people over 50 years of age and is frequently complicated with giant cell arteritis in Europeans, but not in Japanese. The incidence rate of PMR was 13-113 per 100000 people aged 50 years and older and the prevalence was 600-800 per 100000 people aged 50 years and older in European populations. However, epidemiological features of PMR were not sufficiently described in Japanese populations. We investigated the epidemiological features of PMR in Japan. *Methods:* The incidence rate and the prevalence of PMR were estimated from the incidence ratio and the prevalence ratio between rheumatoid arthritis (RA) and PMR. *Results:* Since the incidence ratio between RA and PMR was 0.37, the incidence rate of PMR was estimated to be 24 per 100000 people aged 50 years and older in Japanese populations. Since the prevalence ratio between RA and PMR was 0.07, the prevalence of PMR was estimated to be 90 per 100000 people aged 50 years and older in Japanese populations. *Conclusion:* Further larger scale studies including other hospitals should be conducted to confirm the results of the study.

## W24-2

**Investigation of Factors Contributing to the Discrepancy between Joint Findings and Composite Measures in Patients with Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] This study explores contributing factors in rheumatoid arthritis (RA) patients with persistent disease activity despite the paucity of joint findings. [Methods] NinJa2021 dataset was analyzed, including 7011 RA patients with zero TJC and SJC across 68 joints. They were divided into remission (5266 patients) and non-remission (1745 patients) groups by CDAI. Univariate analysis covered age, disease duration, gender, BMI, Stage, Class, CRP, ESR, ACPA, RF, mHAQ, EQ5D, HADS-A, HADS-D, GC use, NSAIDs use, MTX use, Bio use, and JAK inhibitor use. Significant factors underwent multivariate analysis. [Results] Univariate analysis revealed significant differences, except BMI, ACPA, Bio use, and JAK inhibitor use. In the subset of 3078 patients without deficiencies in these factors, multivariate analysis highlighted disparities in EQ5D, HADS-A, CRP, and GC use. Notably, CDAI remission was most strongly associated with EQ5D (OR1.64; 95%CI 1.52-1.78). [Conclusions] This study indicated that compromised QOL and anxiety, along with elevated inflammatory response and GC use, were factors hindering remission even without tender and swollen joints. In the practice of Treat to Target, it is desirable to consider these factors that cannot be assessed by the composite measures.

## W24-3

**Characterization of patients with RA not using b/stDMARDs despite insufficient disease activity control: an analysis on FRANK registry**

Hisakata Yamada[1], Ryosuke Tsurui[1], Masakazu Kondo[2], Junichi Fukushi[3], Tomoya Miyamura[4], Tomomi Tsuru[5], Toshihide Shuto[6], Seiji Yoshizawa[7], Yasushi Inoue[8], Masanobu Ohishi[9], Akira Maeyama[10], Kenta Kamo[11], Hiroaki Niiro[12], Yasuharu Nakashima[1]

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Conflict of interest: None

[Objective] One of the remaining issues in the treatment of RA is the presence of patients who are not well controlled even by using b/tsDMARDs. EULAR has proposed the definition of such difficult to treat (D2T) RA patients. However, in clinical settings, there are patients who are not using b/tsDMARDs despite insufficient disease activity control, and we analyzed in this study the frequency and the characteristics of those patients. [Methods] We analyzed 3243 RA patients registered in the FRANK registry. The patients are divided into three groups: using b/tsDMARDs, not using b/tsDMARDs due to remission or low disease activity, and not using b/tsDMARDs despite insufficient control. The latter is further divided into 6 groups by the reason for not using. [Results] About 10% of patients are not using b/tsDMARDs despite insufficient control. Many patients not using b/tsDMARDs due to aging or comorbidity are using PSL and in lower ADL/QOL state but are almost satisfied with the current treatment. Patients with economic reasons are young and frequently use PSL and MTX. The frequency of patients at work is highest in this group. [Conclusions] The frequency and characteristics of RA patients not using b/tsDMARDs despite insufficient disease control are clarified.

## W24-4

**Prediction of rheumatoid arthritis development from the results of Nagasaki Island Study (NaIS)**

Mami Tamai[1], Fumiaki Nonaka[1,2], Yoshika Tsuji[1], Shin-ya Kawashiri[1,3], Serina Koto[1], Kazuhiko Arima[4], Kiyoshi Aoyagi[4], Atsushi Kawakami[1]
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Conflict of interest: None

Objective. To identify the onset of rheumatoid arthritis (RA) at early-stage. Methods. The subjects were 123 patients who underwent secondary rheumatoid arthritis screening from 2014 to 2023, and the observation period was 2-105 months. The diagnosis of RA was based on the 2010 RA classification criteria. The diagnosis of RA was based on the 2010 RA classification criteria, and the clinically suspect arthralgia (CSA) score at the time of initial diagnosis was used to evaluate the predictive value of RA progression. Results. RA progression was observed in 16 (14%) patients at a median of 6 months after initial diagnosis. 16 (31%) of 51 ACPA-positive patients progressed to RA at a median of 13 months, with a median CSA score of 0. Sixty percent of patients with a score >3 and 15% of patients with a score <3 developed RA, i.e., sensitivity 30%, specificity 95%, and accuracy 83%. The positive predictive value was 60%, the negative predictive value was 85%, and the accuracy was 83%. Conclusions. RA progression was observed in 14% of patients. The CSA score had low sensivity but high specificity, because of the subjects in this study were healthy population with rarely symptomatic.

## W24-5

**Increased risk of autoimmune diseases associated with COVID-19: A retrospective cohort study using a nationwide electronic medical record database in Japan**

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Department of Research & Analytics, Real World Data, Co., Ltd., Kyoto, Japan

Conflict of interest: None

[Objective] This study aimed to investigate the risk of developing autoimmune diseases (AIDs) associated with COVID-19 in Japan. [Methods] This retrospective cohort study used an electronic medical record database in Japan. The COVID-19 group comprised patients diagnosed with COVID-19, whereas the non-COVID-19 group was randomly extracted from the database. The outcomes included 16 AIDs, including RA and SSc, as well as a composite of them (any AIDs). The RRs of AIDs were examined using SMRW and the Cox proportional hazards model. Subgroup analyses based on epidemic variants were performed. Short- and long-term risks were investigated using piecewise constant hazard models. [Results] A total of 90,855 COVID-19 and 459,827 non-COVID-19 patients were included between Jan 16, 2020, and Dec 31, 2022. The RR of any AIDs was 2.32 (95% CI, 2.08-2.60). All the investigated outcomes showed a significant risk. Several AIDs exhibited a risk associated with COVID-19 across the terms, and the long-term risk was notable for SSc and IgG4RD. The variant-specific risk varied across outcomes. [Conclusions] COVID-19 was associated with an increased risk of developing AIDs. This study provides insights into the association between viral infections and autoimmunity.

## W24-6

**Clinical factors associated with ultrasound remission at 1 year after the initiation of rheumatoid arthritis treatment**

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Hokkaido Medical Center for Rheumatic Diseases

Conflict of interest: None

[Objective] To regulate the radiographic progression of rheumatoid arthritis (RA), it is required to achieve the imaging remission at an early stage of disease onset. We investigated the clinical factors associated with ultrasound (US) remission at 1 year after start of treatment. [Methods] We consecutively recruited RA patients who were started treatment with csDMARDs between January 2018 and August 2022 at our hospital. Disease activity indices, US findings at the diagnosis and at 1 year after the treatment, and treatment details were analyzed retrospectively. [Results] 265 patients were included (mean age 60.7 years, rheumatoid factor positive 204 (77%), anti-CCP antibody positive 199 (75%)). The disease activity indexes at the diagnosis were SDAI 21.6 and CDAI 19.8. Multivariable analysis identified three factors which were associated with US remission (PD=0, GS=0); (1) older age (OR 0.970, 95% CI 0.935-0.980, p<0.001), (2) use of bDMARDs/tsDMARDs within 1 year (OR 2. 808, 95% CI 1.072-4.088, p=0.031), and (3) presence of “active erosion” at the first visit (OR 0.244, 95% CI 0.072-0.685, p=0.012). [Conclusions] To achieve US remission, the use of bDMARDs/tsDMARDs should be considered when intra-erosive blood flow is present at the initial RA diagnosis.

## W25-1

**The utility of diffusion-weighted whole-body imaging with background body signal suppression in the diagnosis and the assessment of disease activity in large-vessel vasculitis**

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Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: Yes

[Objects] Diffusion-weighted whole-body imaging (DWIBS) is a systemic imaging technique also called MRI-PET that is used to evaluate the progression of malignant tumors. In this study, we conducted to compare the usefulness of DWIBS in the diagnosis of large vessel vasculitis (LVV). [Methods] A total of 26 patients (22 women and 4 men, mean age 70 years) with giant cell arteritis (GCA: 14 cases) and Takayasu arteritis (TA: 12 cases) performed DWIBS and 18F-FDG-PET/CT. The correlation between DWIBS and FDG-PET/CT grade and correlation between CRP, ESR, platelet count and imaging were examined by logistic regression. [Results] DWIBS mean grade correlated significantly with FDG-PET/CT mean grade (R=0.72, ***P<0.0001) and CRP level (R=0.53, ***P<0.0001). Of the six patients diagnosed with clinically active vasculitis, four were diagnosed by DWIBS and five by FDG-PET/CT (sensitivity: 66.6% vs. 83.0%). Of the patients diagnosed in clinical remission, 75.0% and 91.6% were diagnosed with inactive vasculitis by imaging (negative predictive value). [Conclusion] The results of this study indicate that DWIBS is a

useful imaging test for the evaluation of LVV disease activity in the future, as it provides an evaluation comparable to that of FDG-PET/CT in LVV.

## W25-2

**Detective accuracy of temporal arteries in the imaging modalities of giant cell arteries (GCA)**

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Conflict of interest: None

[Objective] The importance of non-invasive diagnostic imaging tools in giant cell arteritis (GCA) is increasing. We aimed to evaluate the diagnostic accuracy of imaging in GCA. [Methods] We retrospectively analyzed 24 GCA patients, who were diagnosed from June 2017 to October 2023 and fulfilled with the 2022 ACR/EULAR classification criteria. Clinical features including temporal artery ultrasound (TAUS), head contrast MRI and PET/CT were collected. [Results] Prevalance of isolated cranial, isolated extracranal and cranial with extracranial GCA was 12.5%, 8.3% and 79.2% respectively. In 22 cases with PET/CT, 27.3% showed uptake in temporal arteries, and 77.3% showed uptake in large vessels. Also, 66.7% of TAUS in 21 cases, and 47.8% of head contrast MRI in 23 cases were consistent with GCA. In 15 cases of pathologically-proven temporal artery vasculitis in TAB, sensitivity of TAUS, head contrast MRI and PET/CT was 64.3%, 50.0% and 35.3% respectively. The combination of imaging increased the sensitivity and the sensitivity of TAUS with MRI, TAUS with PET/CT and MRI with PET/CT was 83.3%, 84.6% and 61.5% respectively. [Conclusion] Our study indicated that the sensitivity of imaging studies increased the sensitivity to detect temporal artery vasculitis in GCA patients.

## W25-3

**Validity of the OMERACT ultrasonography score for giant cell arteritis in the diagnosis of 93 Japanese patients**

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Conflict of interest: None

[Objective] To assess the validity of the Outcome Measures in Rheumatology (OMERACT) ultrasonography (US) score for giant cell arteritis (GCA) in the diagnosis of cranial GCA. [Methods] Patients undergoing temporal artery (TA) US for suspected GCA at one center between 2009 and 2023 were identified and the OMERACT GCA US score (OGUS) was calculated. OGUS was compared between patients with and without GCA. The OGUS was defined as the [sum of intima-media thickness measured in bilateral axillary arteries, common trunks, frontal and parietal branches of the superficial TAs] divided by the number of segments available, and an OGUS > 1 was deemed abnormal. [Results] US was performed on 93 suspected GCA patients and found 14 GCA and 36 non-GCA. With TA biopsy, the abnormal OGUS-GCA group (n=28) and the abnormal OGUS-non-GCA group (n=15) were classified. They had similar background characteristics. Platelet count was higher in the abnormal OGUS-GCA group ($p = 0.02$). OGUS was 1.41 in the abnormal OGUS-GCA group and 1.26 in the other ($p = 0.03$). In the ROC curve, the AUC was 0.72 and the optimal cutoff value for the OGUS was 1.36 (1-specificity: 0.13, sensitivity: 0.63). The sensitivity of OGUS was 0.83. [Conclusions] The OGUS was valid and sensitive in diagnosing cranial GCA.

## W25-4

**Temporal artery biopsy is not recommended for fever of unknown origin without large vessel vasculitis on CT**

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Department of Internal Medicine, Tokyo Metropolitan Tama-Nambu Chiiki Hospital

Conflict of interest: None

[Objective] Temporal artery biopsy (TAB) is considered for elderly patients in fever of unknown origin (FUO), because giant cell arteritis (GCA) has no specific serum marker and GCA with only systemic symptoms exists. Papers showing usefulness of TAB for FUO were published in 1990s, therefore we discuss the significance of TAB in nowadays. [Methods] TAB, performed at our hospital from April 2019 to September 2023 were collected retrospectively. TAB for FUO was defined as fever or elevated CRP without new onset headache, jaw claudication or limb claudication, and TAB positivity was based on the pathologist's judgment. [Results] There were 24 cases of TAB, 8 cases of TAB for FUO. 6 of the 8 cases had no LVV on CT. 6 cases were all over 65 years old and 5 cases were male. 6 cases were TAB negative and did not clinically diagnosed as GCA during the follow-up period. Final diagnosis was rheumatic disease in 2 cases, hematologic malignancy in 3 cases, and unknown in 1 case. [Conclusions] In elderly, GCA in FUO is about 17%, TAB was recommended based on its frequency, 4.5% of GCA is diagnosed by TAB. This was before the widespread use of FDG-PET, and TAB may not be performed if LVV is proven by CT. TAB for FUO in absence of LVV on imaging has become less significant.

## W25-5

**Marker identification of multinucleated giant cells based on transcriptome analysis of temporal artery biopsy from patients with giant cell arteritis**

Makoto Sugihara[1,2,4], Eisuke Takamasu[2], Naofumi Chinen[3], Masahiro Iida[1,2], Sayaka Koizumi[1], Shoko Kimura[1], Naoto Yokogawa[2], Kota Shimada[2]
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Conflict of interest: Yes

[Objective] To identify markers of multinucleated giant cells (MNGC) in inflammatory vessels of GCA and to elucidate their function in the pathogenesis. [Methods] We collected temporal artery biopsy specimens (TAB) from 3 hospitals. Based on transcriptome analysis, we performed pathway analysis and immunohistological examination. [Results] Sixteen TAB were collected: 10 with GCA and 6 with non-GCA. Principal component analysis classified these into 2 clusters: the inflammatory profile (GCA group) and the non-inflammatory profile. Transcriptome analysis revealed high expression of osteoclast-related genes such as ACP5, ATP-6V0D2, MMP-9, and macrophage-related genes in the GCA group. Pathway analysis showed that the osteoclast differentiation pathway was highly upregulated in the GCA group and the macrophage-related phagocytosis pathway. The immunohistological study showed that MNGCs infiltrating were $CD206^{+}$, a marker of M2 macrophages, suggesting that they might be derived from tissue remodeling macrophages. We also identified TREM2 expression on MNGCs, suggesting these cells had enhanced phagocytosis ability, and the expression APC5 and ATP6V0D2 was confirmed. [Conclusion] MNGCs infiltrated GCA vessels may function highly with phagocytic ability and similarly to osteoclast.

## W25-6

**A case of giant cell arteritis occurring during treatment of ulcerative colitis with ustekinumab**

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Conflict of interest: None

A 62-year-old man with ulcerative colitis (UC) had a fever and was admitted to our hospital. He was diagnosed with UC 5 years ago and was in remission with prednisolone (PSL) and GCAP therapy 3 years ago. However, because of recurrent flare, tacrolimus and azathioprine were

added 2 years ago. Still the disease control was poor, ustekinumab was introduced 1 year ago, which was successful. After admission, CT showed thickening of the vessel wall from the ascending to the arch aorta, suggesting large vessel vasculitis. Ultrasonography showed no thickening of the temporal artery. Colonoscopy revealed scattered ulcers in the sigmoid colon. We diagnosed the patient with giant cell arteritis with large vessel arteritis (LV-GCA), which was associated with UC relapse, and treated with PSL 40 mg/day. Both UC and LV-GCA improved. After that, infliximab was added and PSL was gradually decreased and discontinued. GCA associated with inflammatory bowel disease (IBD), including UC, has been reported in some cases and some reports suggest that IBD patients are at high risk of GCA. However, there have been few reports of GCA in patients receiving biological agents, and this case is particularly significant because it is a rare case of LV-GCA in a patient receiving an IL12/23 inhibitor for UC.

## W26-1

**Experience with Mepolizumab for eosinophilic granulomatosis with polyangiitis**

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Conflict of interest: Yes

[Objective] To investigate the clinical course of patients treated with mepolizumab (MEP) for eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] We extracted the medical records of patients diagnosed with EGPA at our department between April 2010 and July 2023 and those who were introduced to MEP during the course of the disease, and investigated the reasons for starting MEP, continuation rate, glucocorticoid use, and other factors. [Results] During the observation period, MEP was used in 15 (7 males and 8 females) of 24 (62.5%) EGPA patients. Median age at induction of MEP was 59.0 (34-79) years old. MEP was started at the time of relapse in 5 patients, maintenance therapy in 4 patients, and induction of remission in 6 patients. Six complications (5 infections) were observed in 4 patients during treatment; however, none of which led to MEP discontinuation. All patients continued MEP without relapse, and the median duration was 31.2 months (1.1-56.1 months). The median prednisolone dosage was 17.3 mg (4-40 mg) at the start of MEP and 4 mg (1-25 mg) at the last observation. [Conclusions] In our case, the continuation rate of MEP was good in all phases, and PSL reduction was achieved in all patients.

## W26-2

**Treatment details of 60 cases of eosinophilic granulomatosis with polyangiitis (EGPA) at our hospital**

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Conflict of interest: None

[Objective] We consider treatments that can achieve long-term remission of EGPA and reduction of glucocorticoid (GC) doses. [Methods] We retrospectively reserched 60 patients with EGPA who were treated at our hospital from 2004 to 2023. [Results] Glomerulonephritis was more common in ANCA-positive cases (25 cases) compared to negative cases. were more common than ANCA-negative cases (35 cases) (44% vs. 20% $p = 0.045$). There were 21 cases and 43 cases of severe cases that met at least one item in FFS (1996) and FFS (2009), respectively. The average GC dose at the induction therapy was PSL 51.4 mg/day, and IVCY or POCY was administered in 30 patients. Immunosuppressant (IS) were used in 29 cases during the maintenance treatment period, but the relapse rate did not decrease. Relapse rate decreased when switching to IS after IVCY ($p = 0.03$). The GC dosage during the maintenance therapy was PSL 2.92 mg, which was decreased from PSL 4.52 mg in 2018 ($p = 0.0007$). The combination rate of IS and Mepolizumab was increased. Mepolizumab was mainly used for relapsed and refractory cases, GC reduction effects were observed (PSL 6.81 mg vs PSL 3.28 mg). [Conclusions] Combining IVCY with IS reduce the relapse rate of EGPA, and Mepolizumab in refractory cases may reduce the dose of maintenance GC.

## W26-3

**The Potential of Avacopan for Tapering Glucocorticoid in Treatment of ANCA-related Vasculitis**

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Conflict of interest: None

[Objective] To investigate the capability of avacopan to taper glucocorticoid earlier than conventional therapy in real-world practice. [Methods] This was a retrospective observation study where patients with ANCA-related vasculitis (AAV) treated in our hospital were eligible since 2019. Age, diagnosis, clinical symptoms, BVAS scores at onset and the last appearance, ANCA titer at onset, treatment, and adverse events were reviewed in their medical charts. [Results] A total of 34 patients with AAV treated in our hospital for over 6 months (18 females, 16 males, the average age: 71.3, 25 MPA, 9 GPA) were eligible for this study. Pulmonary lesions were observed in 70.6% and nephritis in 61.8%. At the onset, CRP was 11.3±8.9 mg/dl, and the BVAS score was 15.4±7.1. Avacopan was used in 44%. Comparing patients using avacopan concomitantly with those without the drug, lower frequency of renal lesions and concomitant use of rituximab and azathioprine in the patients with avacopan. Glucocorticoid doses at three and six months were significantly lower in the patients with avacopan than those without the drug. One case presented liver injury was thought to be caused by avacopan. [Conclusions] The real-world data suggested the potential of avacopan for tapering glucocorticoid in AAV treatment.

## W26-4

**A case of avacopan-induced liver injury and LpX-dependent hypercholesterolemia during treatment of granulomatosis with polyangiitis**

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Conflict of interest: None

[Case] A 51-year-old woman had hearing loss on right side seven months ago, and bone destruction of the right temporal bone five months ago. C-ANCA was 158 U/mL. She was diagnosed with granulomatosis with polyangiitis. Remission was achieved by prednisolone, rituximab, and avacopan. On the 29th day after administrating avacopan, small erythema appeared and avacopan was discontinued. Liver damage was observed with AST 111 U/mL, ALT 477 U/mL, and T-Bil 3.7 mg/dL, and the patient was hospitalized. Liver function improved with ursodeoxycholic acid, but worsened again and T-Bil increased to 15 mg/dL. Liver biopsy suggested drug-induced liver damage. The LDL-cholesterol (LDL-C) increased around 1400 mg/dL. This was suggested to be pseudohyper-LDL-cholesterolemia due to an increase of Lipoprotein X (LpX), a lipid protein with a similar density to LDL-C. The patient had symptoms such as a headache that suggested hyperviscosity syndrome, and plasma exchange was performed, and the symptoms disappeared. [Discussion] Although avacopan reduces the total steroid dose and increases the therapeutic effect, we need to be careful about severe liver damage and atypical dyslipidemia. A similar case has also been reported from Japan, and we found that LpX is involved as a cause of lipid abnormality.

## W26-5

**The Differences in Efficacy and Safety Due to Rituximab Doses in Induction Therapy for ANCA-Associated Vasculitis: A Single-Center Retrospective Study**

Naohisa Tsuchida, Keita Ninagawa, Yuka Shimizu
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Conflict of interest: None

[Background] As remission induction therapy for ANCA-associated vasculitis (AAV), rituximab (RTX) is "usually administered once a week for a total of 4 doses at a single dose of 375 mg/m$^2$ intravenously in adults" in Japan. However, it is unclear how many doses of RTX are appropriate. [Objective] To clarify the differences in efficacy and safety due to RTX doses in induction therapy for AAV. [Methods] This retrospective observational study enrolled patients with AAV who received induction therapy with 2 or 4 times of RTX in our hospital from June 2013 to July 2023. Clinical outcomes at 6 months after induction therapy were analyzed statistically. [Results] Forty-one patients (33 recieved 2 times and 8 received 4 times) were included. Age at entry of therapy was significantly higher in 2 times group (median 76 vs. 66 y.o.), and prednisolone dosage (30 vs. 45 mg/day) and eGFR (38.37 vs. 80.12 mL/min/1.73 m$^2$) were higher in 4 times group. Logistic regression analysis using propensity scores showed no significant difference in the rates of remission, relapse, mortality, dialysis induction, and adverse events at 6 months. [Conclusion] In induction therapy for AAV, there is no significant difference in outcome between 2 and 4 times of RTX. The times of RTX could be reduced from 4 times.

## W26-6

**Efficacy of Mepolizumab for ANCA positive vs. negative EGPA: a 96-week single-center, retrospective study**

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Conflict of interest: Yes

[Objective] Mepolizumab (MPZ) is effective in EGPA, but the efficacy with and without ANCA is not well understood. [Methods] Patient background at the MPZ administration and eosinophis, CRP, IgE, and PSL doses at 4 to 96 weeks, BVAS and VDI at 48, 96 weeks by ANCA negative and positive treated with MPZ more than 96 weeks as of October 2023 were investigated. The differences between the baseline and each time point, between the two groups were examined. [Results] 9 positive and 14 negative cases were applicable. At the baseline, the ANCA-negative group had higher VDI and the positive group had more renal involvement, but there was no difference in their treatment. The ANCA titers, eosinophils and PSL doses in both groups maintained a significant decrease after 4 weeks compared to the baseline. BVAS was already 0 (0-2) lower in the positive group at the baseline and only the negative group showing significant improvement thereafter. VDI improved significantly in both groups. The only difference between the two groups was a significant decrease in eosinophils in the ANCA-positive group at 96 weeks, with no difference between ANCA-negative and -positive cases in other parameters. [Conclusions] It was suggested that MPZ is equally effective for EGPA regardless of the presence of ANCA.

## W27-1

**Do High RF Levels Impact Response to the TNF Inhibitors Certolizumab Pegol (CZP) and Adalimumab (ADA) in Patients with RA? A Post Hoc Analysis of the Phase 4 EXXELERATE Trial (NCT01500278)**

Yoshiya Tanaka[1], Motomu Hashimoto[2], Josef S Smolen[3], Peter C Taylor[4], Carlos Cara[5], Bernard Lauwerys[6], Ricardo M Xavier[7], Alejandro Balsa[8], Jeffrey R Curtis[9], Ted R Mikuls[10], Michael Weinblatt[11], Tsutomu Takeuchi[12,13]
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Conflict of interest: Yes

[Objective] We assessed efficacy outcomes of CZP, a PEGylated Fc-free TNFi, versus ADA (Fc-containing TNFi) in pts with RA and high RF levels. [Methods] Pts were randomized 1:1 to CZP 200 mg every 2 wks (Q2W) plus methotrexate (MTX), or ADA 40 mg Q2W plus MTX. We report mean disease activity score (DAS) 28-CRP score at Wk104. Results were stratified by RF (≦Q3: ≦204 IU/mL; >Q3: >204 IU/mL) and ACPA (≦Q3: ≦761.4 IU/mL; >Q3: >761.4 IU/mL) level and reported as observed case. [Results] Baseline data by RF quartile were available for 453 CZP-randomized pts and 454 ADA-randomized pts. For pts in RF ≦Q3, mean DAS28-CRP scores were similar between CZP- and ADA-treated pts at Wk104 (mean [SD]: 2.5 [1.2] vs 2.5 [1.1]). However, for pts in RF=Q4, mean DAS28-CRP scores were nominally lower in CZP- vs ADA-treated pts (Wk104: 2.5 [1.2] vs 2.9 [1.2]). Across ACPA levels, mean DAS28-CRP scores were similar between CZP- and ADA-treated pts at Wk104 (≦Q3 mean [SD]: 2.5 [1.2] vs 2.6 [1.2]; Q4: 2.5 [1.1] vs 2.5 [1.1]). [Conclusions] CZP-treated pts with RA and high RF levels had similar clinical responses to pts without high RF levels, a pattern not seen in ADA-treated pts; treatment response was not correlated with ACPA levels. This may have implications for treatment choice in pts with RA and high RF levels.

## W27-2

**Clinical characteristics of patients with polymyalgia rheumatica stratified by cumulative glucocorticoid dose: A cohort study using routinely collected health data**

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Conflict of interest: Yes

[Objective] This study aims to profile characteristics of PMR patients stratified by cumulative GC (cGC) dose. [Methods] In this cohort study, we used a nationwide electronic medical records database. The study included PMR patients initiating GC in 2010-2019 (GC initiation=D0). Subgroups (Q1-4) were defined based on the quartile point of cGC dose during D0-90. We assessed baseline characteristics and outcomes over 52 weeks including longitudinal GC dose and CRP levels, GC-free achievement, and increase in GC dose. [Results] A total of 373 patients were identified. The median initial GC dose in Q1 was 10 mg/day and reduced to 1 mg/day at week 52 with relatively rapid tapering. Q4 started at 20 mg/day, reducing to 6 mg/day at week 52, with gradual tapering. Q1 included many patients aged ≧90 years and with several comorbidities. Longitudinal CRP analysis showed higher levels in Q1 and slower improvement in Q4. GC-free was more common in Q1, while GC dose increases were prevalent in Q4. [Conclusions] The study indicated that Q1 involves at least two types of PMR; PMR responsive to low-dose GC, and PMR who are not prescribed an adequate dose of GC. GC-resistant PMR was observed in Q4. Unmet medical needs in PMR are reconfirmed, necessitating further treatment strategy development.

## W27-3

**Prospective observational study of sarilumab in routine care of patients (pts) with rheumatoid arthritis (RA): An interim analysis of enrolled patient characteristics and disease activity**

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Conflict of interest: Yes

**Aims:** PROFILE-J a prospective observational study of sarilumab (SAR) therapy to assess pt characteristics, effectiveness, quality of life, and tolerability. **Methods:** Pts with RA prescribed SAR therapy were enrolled from Jul 2019 to Oct 2023. This interim analysis uses data up to Jun 2023, including background and baseline characteristics grouped by initial therapy (mono-/combination [combi] therapy). **Results:** Among 2009 pts, 97% (n=1941) started with SAR 200 mg; 33% (n=671) received SAR mono and 67% (n=1338) received SAR combi. Pts receiving mono- and combi- therapy had mean age of 68.6 and 65.5 years, respectively; 68% (n=457) and 60% (n=807) of pts were ≧65 years and mean disease duration was 43.9 and 48.7 months in each group, respectively. Prior treatments included: 69% (n=1385) of pts were bio-naïve, 23% (n=460) received TNF inhibitors, 16% (n=325) received other bDMARDs and 4% (n=89) JAK inhibitors. Concomitant drugs included glucocorticoids (33%, n=657) and methotrexate (40%, n=810). At baseline, mean (standard deviation) CDAI: mono 22.5 (13.0); combi 20.9 (11.8); HAQ-DI: mono 1.05 (0.82); combi 0.95 (0.76). **Conclusion**: Most pts receiving SAR in PROFILE-J were older, bio-naïve, with at least moderate disease activities. Further analysis will be conducted in these subgroups.

## W27-4

**Long-term efficacy and safety of ozoralizumab (a Novel anti-TNF-alpha multivalent NANOBODY® compound) in rheumatoid arthritis patients**

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Conflict of interest: Yes

[Objective] To evaluate the efficacy and safety of ozoralizumab (OZR), a novel anti-TNFα multivalent NANOBODY® compound, the results of long-term treatment. [Methods] Efficacy and safety of OZR treatment including after transition to a long-term extension study (HOSHIZORA trial), were evaluated in the patients who enrolled the phase II/III study (OHZORA trial; n=381) with methotrexate (MTX) or the phase III study (NATSUZORA trial; n=140) without MTX. [Results] The completion rates for the HOSHIZORA trial (treated with OZR over 156 weeks) were 58.2% for patients randomized to the OZR group in the OHZORA trial concomitant with MTX and 41.4% for patients from the NATSUZORA trial without MTX. The proportions of SDAI remission achievement (non-responder imputation) in patients who were randomly allocated OZR 30 mg at initial allocation (n=246) were 28.5% and 26.0% at week 52 and 104, respectively, and 24.4% maintained through week 156. There were no specific safety concerns in all patients treated with OZR until completion of the HOSHIZORA trial (n=513). [Conclusions] Long-term treatment with OZR demonstrated efficacy and was well tolerated.

## W27-5

**Long-Term Safety and Efficacy of Upadacitinib or Adalimumab in Patients with Rheumatoid Arthritis: 5-Year Data From the SELECT-COMPARE Study (Encore)**

Yoshiya Tanaka[1], Roy Fleischmann[2], Jerzy Swierkot[3], Sara K Penn[4], Patrick Durez[5], Louis Bessette[6], Xianwei Bu[4], Nasser Khan[4], Yihan Li[4], Charles Peterfy[7], Eduardo Mysler[8]
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Conflict of interest: Yes

[Objective] To assess the safety and efficacy of UPA vs ADA through 5 yrs in the SELECT-COMPARE LTE. [Methods] Pts receiving background methotrexate were randomized 2:2:1 to UPA 15 mg QD, PBO, or ADA 40 mg EOW. Rescue was mandated for lack of response, or failure to achieve CDAI LDA at wk 26. All remaining PBO pts switched to UPA at wk 26. Pts who completed the 48-wk double-blind period could continue to receive open-label UPA or ADA in the LTE for up to 10 yrs total. Data up to 5yrs are reported. [Results] Through 5 yrs, 1417 pts were exposed to UPA and 579 to ADA. UPA was generally well tolerated. Rates of most AEs of special interest with UPA were similar vs ADA, except for numerically higher rates of herpes zoster, CPK elevation, lymphopenia, and hepatic disorder with UPA. Greater proportions of pts achieved CDAI LDA and remission, and disease activity scores, with UPA vs ADA. Through 192 wks, similar proportions of pts treated with UPA vs ADA had no radiographic progression. [Conclusions] The safety profile of UPA over 5 yrs was consistent with the results previously reported. UPA consistently continued to show numerically better clinical responses than ADA at 5 yrs. Radiographic progression remained similarly low through 192 wks with UPA and ADA.

## W27-6

**Upadacitinib (UPA) as Monotherapy in Japanese Patients with Rheumatoid Arthritis and Prior Inadequate Response to Methotrexate: Sub-Analysis Results at 5 years (260 Weeks) From the Global Phase 3 SELECT-MONOTHERAPY Study**

Yoshiya Tanaka[1], Josef S Smolen[2], Paul Emery[3], William Rigby[4], Juan I Vargas[5], Nemanja Damjanov[6], Manish Jain[7], Koji Kato[8], Kyle Carter[8], Nasser Khan[8], Kazuho Kawase[9], Stanley B Cohen[10]
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Conflict of interest: Yes

**Objective** UPA monotherapy was shown to be safe and effective in RA patients (pts) with a prior inadequate response to MTX through 260 weeks (5yrs). This analysis aims to assess the efficacy and safety of UPA monotherapy in the subgroups of Japanese pts in SELECT-MONOTHERAPY up to 5yrs **Methods** Pts on stable dose of MTX were randomized to either continue MTX (cMTX) or switch to UPA 15 (UPA15) or 30 (UPA30) mg monotherapy for 14 weeks. At entry of LTE, cMTX pts were switched to UPA15 or 30 in a blinded manner; other pts continued UPA15 or 30. UPA30 pts were switched to UPA15 prior to marketing approval in Japan.

Efficacy (as observed) and safety results in Japanese pts through 5yrs were assessed. **Results** Out of 65 Japanese pts, 26 (40.0%) discontinued study drug by 5yrs, primarily due to AEs (24.6%), consent withdrawal (4.6%) or lack of efficacy (4.6%). Of the remaining 41pts, 36 and 22pts achieved CDAI low disease activity and clinical remission at 5yrs. The event rate of serious TEAEs (E/100PYS) in UPA15, 30 and switch to UPA15 were 10.2, 26.8, 15.5, HZ; 7.8, 19.4, 6.6, malignancies excluding NMSC; 1.6, 1.5, 2.2, respectively. No MACE and 1 VTE was reported. **Conclusions** UPA monotherapy is effective in Japanese RA pts through 5yrs. No new safety signals were identified with longer-term exposure to UPA.

## W28-1

**Impact of parenting on patient reported outcome in patients with systemic lupus erythematosus: A cross-sectional study from lupus registry of nationwide institution (LUNA) cohort**

Dai Kishida[1,2], Ryota Takamatsu[1,2], Takanori Ichikawa[1,2], Yasuhiro Shimojima[1,2], Nobuyuki Yajima[2], Ken-ei Sada[2], Yoshia Miyawaki[2], Ryusuke Yoshimi[2], Shigeru Ohno[2], Kunihiro Ichinose[2], Shuzo Sato[2], Hiroshi Kajiyama[2], Michio Fujiwara[2], Takashi Kida[2], Yusuke Matsuo[2], Keisuke Nishimura[2], Yoshiki Sekijima[1]

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Conflict of interest: None

[Objective] Although pregnancy and delivery outcomes for patients with SLE have improved, the condition of patients with childcare has not received much attention. We aim to examine the impact of parenting on disease-specific quality of life (QOL) in a large cohort. [Methods] Cross-sectional data from 185 female patients with SLE who were parenting children aged 0-18 years were analyzed. The exposure was parenting young children (0-5 years), and the outcome was QOL score of lupus patient-reported outcomes (LupusPRO). The association between age group of children and QOL were analyzed using univariate analysis and multiple regression analysis with age of patients and number of children as covariates. [Results] In univariate analysis, patients with young children had higher QOL scores in domains of cognition (85.9 vs 78.2, p=0.035) and desires-goals (81.9 vs 70.9, p=0.0065) than those without young children. Multiple regression analysis revealed that parenting young children was associated with higher scores of desires-goals (coefficient 11.1, 95%CI 1.5-20.8, p=0.023). [Conclusions] In parenting patients with SLE, the presence of young children did not worsen patient's QOL, but rather was associated with higher desire-goals scores.

## W28-2

**Predictive validity of the Lupus Patient-Reported Outcome tool (Lupus PRO) for the SLICC/ACR damage index: LUNA Registry Cross-Sectional Study**

Yoko Nose[1], Akira Onishi[2], Keisuke Nishimura[1], Yuzuru Yamamoto[1], Hirotaka Yamada[1], Sho Sendo[1], Yo Ueda[1], Ken-ei Sada[3,4], Kunihiro Ichinose[5,6], Ryusuke Yoshimi[7,8], Shigeru Ohno[9], Nobuyuki Yajima[10,11,12], Hiroshi Kajiyama[13], Shuzo Sato[14], Yasuhiro Shimojima[15], Michio Fujiwara[16], Takashi Kida[17], Yoshia Miyawaki[4], Yusuke Matsuo[18,19], Jun Saegusa[1]

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Conflict of interest: None

Purpose: Patient-reported outcomes (PROs) are associated with prognosis and commonly used as a component of disease activity measurements in connective tissue diseases. We aimed to examine prognostic validity of disease-specific quality of life (QOL) assessments in systemic lupus erythematosus (SLE). Methods: Patients enrolled in the multicenter SLE registry (LUNA) with ≧2 LupusPRO measurements were included. We assessed the association between the LupusPRO scores at baseline and longitudinal SLICC/ACR damage index (SDI) scores using a mixed effects model adjusted for prognostic factors. Results: Among 1295 patients with SLE (female: 89%, mean age: 47 years), patients with higher health-related (HR) QOL of the LupusPRO had a significantly lower SDI (-0.005, 95% confidence interval: -0.007 to 0.004, p<0.001). HR-QOL was associated with both corticosteroid-dependent and -independent SDI scores. The association was prominent in patients with the physician's global assessment score <1 and with lupus low disease activity state. Non-HR-QOL was not significantly associated with SDI scores. Conclusions: Higher HR-QOL of Lupus PRO was associated with lower SDI scores. Incorporating PRO in remission criteria and disease activity score in SLE may be warranted.

## W28-3

**Impact of quality of life on overall work productivity impairment (OWPI) and activity impairment (AI) in patients with systemic lupus erythematosus (SLE) from PEONY: The multicenter, prospective, cross-sectional study**

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Conflict of interest: Yes

[Objective] To clarify the residual burden in lupus low disease activity state (LLDAS) and investigate the association of quality of life (QoL) with OWPI and AI in Japanese SLE patients. [Methods] We collected data from SLE outpatients at 8 sites, including physician assessments of disease activity and patient-reported outcomes (PRO: LupusPRO, WPAI-Lupus, etc.). We compared LLDAS and non-LLDAS using analysis of covariance with WPAI-Lupus as the response variable to assess residual burden. We examined the association between LupusPRO domains and WPAI-Lupus using multivariate analysis. [Results] In the analysis set, there were 205 patients, 93.2% were female, the mean age at diagnosis was 38.6±15.0 years, the mean duration of morbidity was 167.2±125.2 months, and LLDAS was 164 patients. AI and OWPI (least-squares mean) was 29.2% and 36.4% (p=0.22) in LLDAS and 23.7% and 29.2% (p=0.46) in non-LLDAS, respectively. In LLDAS, AI and OWPI were significantly affected by LupusPRO domains: Pain Vitality, Physical Health, and SLE symptoms

and Pain Vitality, Desires-Goals, and Body Image, respectively. [Conclusions] WPAI-Lupus uncovered residual burden in LLDAS. LupusPRO domains impacting WPAI-Lupus are QoL-related symptoms unable to be identified by disease activity, indicating the importance of PRO.

## W28-4

**Association between Disease-Specific Health-Related Quality of Life Assessed with the Japanese version of LupusQoL and LLDAS in Patients with SLE**

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Conflict of interest: None

[Objectives] We have translated and validated the Japanese version of LupusQoL©, SLE disease-specific HRQoL questionnaires. We investigated the association between disease-specific HRQoL assessed with the LupusQoL-JP and LLDAS in patients with SLE. [Methods] A cross-sectional study of Japanese SLE patients was conducted. The patients who completed the LupusQoL-JP were eligible. Association between the domain scores in the LupusQoL-JP and other demographic and SLE disease-related data including LLDAS were analyzed. [Results] A total of 133 patients participated. The majority of LupusQoL-JP domains, namely physical health, pain, emotional health, body image, and fatigue, but not planning, intimate relationships, or burden to others were able to discriminate between LLDAS and non-LLDAS groups ($p < 0.05$). Scores in most domains of the LupusQoL-JP were rarely correlated with the SLEDAI-2K, SDI, disease durations, and PSL dosages. In contrast, the LupusQoL-JP and the SF-36 correlated well regarding comparable domains. [Conclusion] SLE patients in LLDAS were associated with better disease-specific HRQoL assessed with the LupusQoL-JP. LupusQoL-JP was independent from SLEDAI-2K and SDI, whereas the LupusQoL-JP demonstrated good concurrent validity with the comparable domains of the SF-36.

## W28-5

**Lupus Impact Tracker and BILAG relate presenteeism of working patients of SLE**

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Conflict of interest: None

[Objective] To elucidate the work productivity and associated factors of its impairment among patients with systemic lupus erythematosus (SLE). [Methods] We enrolled 317 patients with SLE. We evaluated work productivity impairment based on WPAI questionnaire. We collected their background, medications, disease activity, SLICC-DI, and patient-reported outcome (LIT), then analyzed cross-sectionally. [Results] The median of age and disease duration were 50 and 17 years, respectively. 178 (56%) were workers in which 41 (22%) had absenteeism and 65 (37%) had presenteeism. Univariable analysis revealed that patient VAS, LIT, PGA, BILAG, and SLICC-DI were associated with work productivity impairment, which was more remarkable in presenteeism than absenteeism. Multivariable analysis revealed that LIT and BILAG independently associated with absenteeism and presenteeism. ROC analysis showed that the cut-off value for LIT to identify presenteeism was 15 (AUC 86%, sensitivity 73%, specificity 83%), and the patients with LIT 15 or higher had a significantly higher frequency of presenteeism than those without it (88% vs. 12%, $p<0.0001$). [Conclusions] Among SLE patients, LIT and BILAG were associated with presenteeism, suggesting that these measures may represent the work productivity impairment.

## W28-6

**The association of anti-phospholipid antibodies (aPL) and quality of life (QOL) of systemic lupus erythematosus (SLE) without antiphospholipid syndrome (APS): a cross-sectional study of the LUNA registry**

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Conflict of interest: None

[Objective] There are no reports on the relationship between cell damage caused by aPL and QOL of SLE patients. We analyzed the association between relapse of aPL and QOL of SLE without APS. [Methods] The patients without APS registered in the multicenter SLE registry "LUNA" were divided into aPL-positive group (one or more of lupus-anticoagulant, anti-cardiolipin β2GPI antibody, and anti-cardiolipin IgG antibody were positive) and negative group (all the three items were negative). The Japanese version of LupusPRO's "Pain/Vitality" domain score at the time of LUNA registration was used as the outcome. We adjusted for age, sex, disease duration, smoking, current prednisolone dosage, hydroxychlorquine administration, number of immunosuppressants, past plasma exchange, SLEDAI, and SDI, and analyzed using a general linear model. [Results] There were 362 patients included in this study. Median age was 46 years [34-57], and 87% were female. There were 138 patients in the aPL positive group and 224 in the negative group. In univariate analysis, there was no significant difference (p=0.592). Multivariate analysis identified no association between either group and QOL. [Conclusions] This study suggested that injuries caused by aPL were unlikely to have an impact on the QOL of SLE patients.

## W29-1

**Evaluation of the efficacy and safety of the JAK1 selective inhibitor upadacitinib in difficult-to-treat RA (D2T RA) and non-D2T RA in real-world clinical practice**

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Conflict of interest: None

[Objective] We analyzed the efficacy and safety of the JAK1 selective inhibitor upadacitinib in D2TRA/NonD2TRA. [Methods] The subjects were 131 patients who met the ACR/EULAR RA classification criteria and received upadacitinib. Disease activity evaluation was evaluated by CDAI, Continuation rate of upadacitinib in D2TRA and NonD2TRA and characteristics of cases achieving LDA/REM of CDAI at 12 weeks, Safety was evaluated. [Results] Among 131 patients treated with the JAK1 selective inhibitor upadacitinib (13 men, 118 women, mean age at initiation of treatment 66.8+/-11.7 years), 57 patients received D2TRA, 43.5%, and 74 pa-

tients received non-D2TRA, 56.5%. There were no significant differences between D2TRA and NonD2TRA in clinical characteristics such as disease duration, late-onset RA, anti-CCP antibodies, and MTX concomitant use rate. The treatment continuation rate for D2TRA was 89.4% at 26 weeks and 75.4% at 52 weeks, and there was no difference in continuation rate between D2TRA and NonD2TRA (Log-rank, p=0.663). The LDA/REM achievement rate of CDAI at 12 weeks was 69 cases, 93.2% and 54 cases, 94.7% for D2TRA and Non-D2TRA, respectively, with no significant difference (p=0.880). [Conclusions] JAK1 selective inhibitor upadacitinib contributed to improving CDAI.

## W29-2

**The clinical efficacy of inhibitors of interleukin-6 receptor and Janus kinase in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate the clinical efficacy of inhibitors of interleukin-6 receptor (IL-6) and Janus kinase (JAK) in the patients with rheumatoid arthritis (RA). [Methods] We evaluated disease activities in RA patients for 52 (W) weeks after starting administrations of IL-6 (N=192) and JAK (N=153). [Results] The mean CDAI of IL-6 and JAK groups were 22.6 and 20.6 at baseline (BL) (p=0.080), 15.9 and 13.4 at 4W (p=0.023), 11.4 and 10.4 at 12W (p=0.199), 9.17 and 11.1 at 52W (p=0.047), respectively. CDAI significantly decreased after 4W from BL in both groups (p<0.05), however CDAI of JAK group was significantly lower at 4W and higher at 52W than IL-6 group. When looking at the clinical courses in both groups in only first line using, the mean CDAI of IL-6 (N=82) and JAK (N=42) groups were 22.9 and 21.7 at BL (p=0.311), 15.2 and 11.4 at 4W (p=0.032), 10.7 and 6.7 at 12W (p=0.007), 8.8 and 6.9 at 24W (p=0.101), 8.2 and 8.9 at 52W (p=0.342), respectively. CDAI significantly decreased after 4W from BL in both groups (p<0.05), however CDAI of JAK group was significantly lower at 4W and 12W than IL-6 group. [Conclusions] Both of IL-6 and JAK had good and quick clinical efficacy, although JAK significantly improved disease activity at early stage after starting administration than IL-6.

## W29-3

**The clinical efficacy of switching therapy between biological agents and JAK inhibitors in the patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate the clinical efficacy of switching therapy between biological agents and JAK inhibitors (JAK) in the patients with rheumatoid arthritis (RA). [Methods] We evaluated the disease activities for 52 weeks (W) in RA patients who received the switching therapy from CTLA4-Ig (ABT) to JAK (ABT-JAK group, N=10), from TNF inhibitors (TNF) to JAK (TNF-JAK group, N=37), from IL-6 inhibitors (IL-6) to JAK (IL-6-JAK group, N=24), from JAK to TNF (JAK-TNF group, N=4), and from JAK to IL-6 (JAK-IL-6 group, N=5). [Results] The mean SDAI/CDAI of ABT-JAK, TNF-JAK, IL-6-JAK, JAK-TNF, and JAK-IL-6 groups were 29.3/20.6, 24.1/18.1, 19.9/19.7, 32.2/30.2, and 25.0/20.9 at baseline (BL), and 12.1 (p=0.018)/11.5 (p=0.046), 7.8 (p<0.001)/7.4 (p<0.001), 15.0 (p=0.104)/14.7 (p=0.095), 6.6 (p=0.009)/6.0 (p=0.009), and 6.6 (p=0.002)/6.5 (p=0.001) after 52W (vs BL), respectively. The disease activities significantly decreased after 4W in TNF-JAK and JAK-IL-6 groups, and after 12W in JAK-TNF group, and after 52W in ABT-JAK group, however, did not significantly decreased after 52W in IL-6-JAK group. [Conclusions] In this study, it might be considered that the switching therapy from ABT or TNF to JAK and from JAK to IL-6 or TNF could be effective when RA patients need switching therapy.

## W29-4

**Comparative study of the effects of JAK inhibitors to cycle -the ANSWER study-**

Toshihisa Maeda[1], Shinya Hayashi[13], Naoki Nakano[13], Tomoyuki Kamenaga[13], Takaichi Okano[2], Iku Shirasugi[2], Sadao Jinno[2], Yuzuru Yamamoto[2], Yo Ueda[2], Hirotaka Yamada[2], Keisuke Nishimura[2], Mai Yamashita[2], Sho Sendo[2], Eriko Yamamoto[2], Wataru Yamamoto[3], Koichi Murata[4], Takayuki Fujii[4], Kenichiro Hata[5], Ayaka Yoshikawa[5], Kosuke Ebina[6], Yuki Etani[7], Naofumi Yoshida[8], Hideki Amuro[8], Ryota Hara[9], Masaki Katayama[10], Motomu Hashimoto[11], Tadashi Okano[12], Masanori Tsubosaka[13]

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Conflict of interest: None

[Objective] Five JAK inhibitors are available in treatment Rheumatoid arthritis (RA) in Japan, and each drug has its own characteristics, but there are cases in which JAK inhibitor treatment is not successful. To compare and examine the effects of switching to another JAK inhibitor in cases where JAK inhibitors did not respond. [Methods] For patients with RA who received a JAK inhibitor, Tof or Bar, after 2013 and who did not respond, and were able to receive treatment with another JAK inhibitor for at least 24 weeks. The efficacy was compared between the drugs. [Results] There were 70 patients in the Tof group and 85 patients in the Bar group. Changes from Tof were made in 44 patients (62.8%) for Bar, 8 patients (11.4%) for Pef, 12 patients (17.1%) for Upa, and 6 patients (8.6%) for Fil. There were changes from Bar in 15 cases (17.6%), Pef in 19 cases (22.4%), Upa in 35 cases (41.1%), and Fil in 16 cases (18.8%). Although the drug change was found to be effective in SDAI, CDAI, and DAS28_CRP, there were no differences between the drugs. There was also no difference between the drugs in HAQ. [Conclusions] The results suggest that administering another JAK inhibitor to patients in whom JAK inhibitor treatment is ineffective can be effective, but there is no difference between the drugs.

## W29-5

**Effect of prior biologic DMARDs on discontinuation of JAK inhibitors due to inefficacy in Rheumatoid arthritis**

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Conflict of interest: None

[Objective] The aim of this study was to examine the effect of prior treatment with biological DMARDs (bio) on the discontinuation of JAK inhibitors (JAKi) due to inefficacy during the course of treatment for rheumatoid arthritis (RA). [Methods] 103 cases in which JAKi was administered for RA were included in this study. Prior treatment bios are divided into three types: TNF inhibitor (TNFi), IL6 inhibitor (IL6i), and CTLA4-Ig, and log-rank test and Cox proportional hazard analysis were performed. [Results] Bio was used prior to JAKi in 85 of 103 patients (82.5%), of which 53 (51.5%) for TNFi, 36 (35.0%) for IL6i, and 27 (26.2%) for CLTL4-Ig. In comparison of the discontinuation rates due to inefficacy, there was no significant difference between those with a history of TNFi use vs. those without, and for IL6i and CTLA4-Ig, the discontinuation rate was significantly higher with a history of use (p=0.04, p= 0.03). The hazard ratio (95% CI) of IL6i and CTLA4-Ig use history for JAKi discontinuation was 2.66 (1.01-7.02) for IL6i and 2.84 (1.06-7.57) for CTLA4-Ig. However, IL6i use history was found to be insignificant after adjustment for MTX use. [Conclusions] A history of CTLA4-Ig use was suggested to increase the risk of discontinuation due to ineffectiveness in RA treatment with JAKi.

## W29-6

**Investigation of the effectiveness of JAK inhibitors by pre-b/tsDMARD treatment**

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Conflict of interest: None

[Objective] We investigated the effectiveness of Janus kinase inhibitors (JAKi) for rheumatoid arthritis (RA) with or without prior b/tsDMARD treatment. [Methods] We analyzed 460 cases that had been treated with JAKi (baricitinib: 239 cases, peficitinib: 67, upadacitinib: 86, filgotinib: 68). We examined the rate of achieving SDAI remission at 24 weeks. [Results] There were 162 patients in naïve group and 298 patients in switch group. The baseline SDAI was significantly higher in the naïve group (20.8±12.6) compared to the switch group (17.9±12.2). The remission achievement rate was significantly higher in the naïve group (46.1%) compared to the switch group (30.3%). In the switch group, the remission achievement rate was 32.1% for those with prior treatment using only one medication (n=111) and 29.3% for those with prior treatment using two or more medications (n=186). Among those with a history of IL-6 inhibitor use (n=120), the remission rate was 28.6%, while among those with a history of JAKi use (n=110), it was 36.5%. The use of two or more medications with different mode of action (n=141) had a remission rate of 28.8%. [Conclusion] The naïve group exhibited a significantly higher remission achievement rate compared to the switch group.

## W30-1

**Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Rheumatoid Arthritis (RA): Results from a Randomized Phase 3 Study (Encore)**

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Conflict of interest: Yes

[Objective] Our objective was to assess direct and indirect (ie, by inflammation surrogates) effects of treatment with upadacitinib (UPA) or adalimumab (ADA) vs placebo (PBO) on pain in patients (pts) with RA. [Methods] SELECT-COMPARE was, randomized, double-blind, phase 3 study in pts with RA who had active disease despite methotrexate treatment. Observed case analysis was performed for change from baseline (BL) in Patient's Global Assessment of pain (PtGA). A multiple mediator analysis for UPA and ADA vs PBO on pain assessed as PtGA or TJC28 was conducted. Indirect effect on pain was assessed based on ESR, CRP, and SJC28. [Results] 1629 pts were included in this analysis (UPA, n=651, PBO, n=651, ADA, n=327). PtGA improved with UPA vs PBO from BL to week (wk) 2 (-18.0 vs -7.5), wk 12 (-32.1 vs -15.7), and wk 26 (-41.4 vs -30.8), all $P<0.001$. Improvement in TJC28 was also greater (all $P<0.05$) with UPA and ADA vs PBO at weeks 2, 12, and 26. UPA and ADA vs PBO showed similar indirect effect on PtGA and TJC28, whereas UPA showed a greater direct effect than ADA. [Conclusions] UPA and ADA resulted in rapid and significant improvements vs PBO. Indirect effects on PtGA or TJC28 improvement were similar between UPA and ADA; however, direct effect was up to two times greater with UPA vs ADA.

## W30-2

**Evaluation of Response to Adjuvanted Recombinant Zoster Vaccination in Patients with Rheumatoid Arthritis Receiving Upadacitinib: Results From a Randomized Trial Sub-study (Encore)**

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Conflict of interest: Yes

[Objective] To assess the immunogenicity of RZV in pts with RA receiving UPA 15 mg QD with background MTX. [Methods] Eligible adults with RA enrolled in the ongoing SELECT-COMPARE study received two RZV doses, administered at the baseline and wk12 visits. The humoral response and cell-mediated immunogenicity to RZV were evaluated at wk4 and 16. [Results] Of the 95 pts who received ≧ 1 RZV dose, 93 (98%) received both RZV doses (mean age (sd): 62.4 (7.5), median dura-

tion (range) of UPA exposure: 3.9 (2.9-5.8) years). At baseline, all but 2 pts were receiving concomitant MTX and half were taking an oral CS. One pt discontinued UPA by wk16. Satisfactory humoral responses to RZV occurred in 64% [95% CI: 55-74] of pts at wk4 and 88% [81-95] at wk16. Age and concomitant CS use at baseline did not affect humoral responses at wk16. Nearly two-thirds achieved a cell-mediated immune response to RZV (wk4: n = 21/34, 62% [45-78]; wk16: n = 25/38; 66% [51-81]). Within 30 days post-vaccination of either RZV dose, no serious AEs or HZ were reported. [Conclusions] More than three-quarters of pts with RA receiving UPA 15 mg QD on background MTX achieved a satisfactory humoral response to RZV at wk16. Age and concomitant CS use did not negatively affect RZV response.

## W30-3

**Long-term Safety of Upadacitinib in patients with Rheumatoid Arthritis: Comparison between Japanese and Overall Populations in the Integrated Analysis of Clinical Trials**

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Conflict of interest: Yes

**Objective**: To evaluate long-term safety of upadacitinib (UPA) in Japanese (JP) pts with RA in clinical trials. **Methods**: Using pooled data from 1 Ph2b/3, 2 Ph3 studies for JP population and 6 Ph3 studies (incl JP pts) for overall population, incidences of AE, SAE, AE of special interest for up to 5 yrs were assessed and compared in JP (UPA7.5 mg [Japan only approval]/15 mg) and overall population (UPA15 mg). **Results**: 121/126 JP pts received UPA7.5/15 mg with 1584.0/1549.5 (median, days) exposure. EAIRs (n/100PY [95%CI]) of AE, SAE in UPA7.5/15 mg were 195.9 [162.6-234.1]/193.9 [161.5-230.8], 7.8 [5.4-11.1]/11.1 [8.1-14.9] in JP, and 133.2 [128.3-138.3], 8.3 [7.7-9.0] in the overall. There was 1 death in each group. EAIRs of Herpes Zoster (HZ), serious infection (SI), malignancy in UPA7.5/15 mg were 7.0 [4.6-10.0]/9.6 [6.8-13.2], 3.3 [1.9-5.5]/4.0 [2.4-6.3], 0.2 [0.0-1.2]/1.5 [0.6-3.1] in JP, and 2.7 [2.4-3.1], 2.8 [2.4-3.1], 1.0 [0.8-1.3] in the overall. EAIRs of AE/HZ were higher in JP population compared to the overall. Within JP population, EAIRs of AE showed similar values while those of SAE, HZ, SI, malignancy were numerically higher in UPA15 mg compared to 7.5 mg. **Conclusions**: Long-term UPA safety profile in JP population was generally similar to previous reports with no new safety signals.

## W30-4

**Retrospective chart review evaluating the effectiveness and safety of switching to peficitinib (PEFI) in patients with RA and an inadequate response to bDMARDs: JASPER (Japan post-marketing study of peficitinib use in RA patients) -switch study**

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Conflict of interest: Yes

**Objective:** To evaluate the effectiveness and safety of switching to PEFI in patients with RA and an inadequate response to bDMARDs (bDMARDs-IR) in real-world clinical practice in Japan. **Method:** Data from a post-marketing survey of PEFI in Japan, which registered all patients administered with PEFI from its launch in July 2019 to March 2022, were retrospectively analyzed. Patients with bDMARDs-IR (DAS28-ESR ≧3.2 after 12 weeks of ≧1 bDMARD treatments) were selected by the medical chart review in 23 centers. **Result:** A total of 76 patients had bDMARDs-IR with a median (min-max) age of 74.5 (36-87) years and RA duration of 8.42 (1.6-50.0) years. Concomitant MTX was used in 15 patients, and 56 patients completed 24 weeks of PEFI treatment. Significant decreases of DAS28-ESR from baseline were observed at Week 4, 12 and 24 ($p<0.0001$). The primary endpoint of change in DAS28-ESR from baseline to Week 24 was -0.94±1.24 (95% CI: -1.24 to -0.64, $p<0.0001$). There was no report for the incidence of serious infections such as herpes zoster, pneumonia, sepsis, malignancy, and thrombosis during the 24 weeks. **Conclusion:** The effectiveness and safety of switching to PEFI after bDMARDs-IR were shown in this study. Switching to PEFI was suggested to be useful in Japanese patients with RA and bDMARDs-IR.

## W30-5

**Decreased peripheral monocyte and neutrophil count associate with drug persistency in rheumatoid arthritis patients treated with a Janus kinase inhibitor**

Eri Shishido[1], Yu Matsueda[1], Ayano Ando[1], Nana Kinoshita[1], Yosuke Sakamoto[1], Shunsuke Kyoda[1], Hirotomo Asakura[1], Risa Shindo[1], Kazuma Ino[1], Yoshiro Kanayama[1], Yasuhiro Hasegawa[1], Tomoki Tanaka[1], Tatsuhiko Wada[1], Yoshiyuki Arinuma[1], Sumiaki Tanaka[2], Kenji Oku[1], Kunihiro Yamaoka[1]

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Conflict of interest: None

[Purpose] we aimed to clarify the relationship between changes in leukocyte fractionation and drug persistence rate after administration of molecular-targeted therapy in RA. [Methods] RA patients who initiated JAKi in 2020-2021, TNFi or IL-6i in 2017-2018 were included in the analysis. Patients were grouped to increased group and decreased group based on leukocyte fractionation at 1 month (m) or 3 m of treatment, with an observation period of 3 years. Drug persistency was compared with Kaplan-Meier curves. [Results] Within the TNFi and IL-6i groups, no difference in drug persistency was observed among the increased/decreased group with any leucocyte fractionation at 1 m and 3 m. However, among the JAKi treated patients, mono and neu decreased group at both 1 m (mono: $p=0.002$, neut: $p=0.03$) and 3 m (mono: $p=0.009$, neu: $p=0.004$) demonstrated significantly higher persistency compared to increased group. The only significant difference in patient background between the increased/decreased group was the proportion of patients previously treated with at least 2 molecular-targeted therapies. ($p=0.03$) [Conclusion] Change in numbers of mono and neu following JAKi initiation may be useful to estimate drug persistency in addition to the number of prior molecular-targeted therapy.

## W30-6

**Validity of prognostic nutritional index as a predicting indicator of prognosis of patients with rheumatoid arthritis after throwing biologic or targeted synthetic disease-modifying anti-rheumatic drug**

Ichiro Yoshii

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Conflict of interest: None

[Objective] The study validates prognostic nutritional index (PNI) as a predicting indicator after biological or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD). [Methods] Patients with rheumatoid arthritis (RA) who b/tsDMARDs simultaneously for 1 year were picked up. They were grouped according to the action of the drugs. Mean values of 28-joints disease activity score at 1 year (DAS@1Y) and the improvement at 3 months (iDAS) for each drug were calculated. The relationships between these values and PNI were evaluated statistically. Sensitivity and specificity (Sens/Spec) for the acquisition of deep remission in DAS@1Y regarding the cut-off index (COI) of the PNI for each group were evaluated. [Results] A total of 364 patients were included in the study: 159 for TNF inhibitor (TNFi), 53 for IL-6 inhibitor (IL6i), 58 for CTLA4-Ig, and 94 for JAK inhibitor (JAKi). iDAS in the IL6i, JAKi, and whole patients significantly correlated with the PNI positively, and DAS@1Y in the TNFi and the whole patient significantly correlated with

the PNI negatively. The IL6i group had significant COI with significant Sens/Spec. The whole patient and JAKi demonstrated no significant COI. [Conclusions] The PNI is suggested as a valuable predicting indicator after b/tsDMARD when IL6i.

## W31-1

**Factors Contributing to Improvement of Locomotion Syndrome Risk with Total Knee Arthroplasty**

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Conflict of interest: None

(Objective) TKA for knee osteoarthritis (OA) is one of the methods to improve LS. The purpose of this study was to investigate the factors related to the improvement of locomotion (L) by TKA. (Methods) Patients with knee OA who underwent TKA between 2020 and 2022 and were followed up postoperatively were included. The LS was evaluated by the rise test, 2-step test, and Loco 25 postoperatively. In addition, Knee Society Score (KSS), quadriceps strength, knee range of motion, gait speed, fatigue, and physical activity was measured and statistically analyzed in relation to LS (Results) Among 159 patients (132 women), L level 3 (135), 2 (17), and 1 (5), while L level 3 (84),2 (56), and 1 (13) at one year postoperatively. The standing test, 2-step test, and Loco 25 all showed improvement after surgery, and Loco 25 was most correlated with improvement in the degree of locomotion. All other factors improved significantly at 1 year postoperatively, and multivariate analysis of whether or not Loco 25 improved showed that KSS was the only factor that affected the improvement of L. (Discussion) This suggests that not only numerical improvement of motor function but also psychological changes accompanying the improvement of motor function may influence the improvement of locomotion level after TKA.

## W31-2

**The incidence of Limbs and Pelvis Fragility Fracture after operated Total Knee Arthroplasty and Rheumatoid arthritis, Osteoporosis**

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Orthopedic, Rheumatism, Nagoya Medical Center

Conflict of interest: None

[Objective] Total Knee Arthroplasty (TKA) has increased because senior citizen keep and improve bodily functions. However super-aging society have task of fragility fracture. We considered that one of the complications of TKA and Rheumatoid arthritis. [Methods] We had TKA (1485 Patients, 1976 knee) surgery first time between Sep/2009 and Jul/2022. The rate of occurrence of Fragility Fracture is calculated by Kaplan-Meier. The age of surgical operation was separated 4 parts (under 70,70-under 75,75-under 80, 80 or over) and Fracture rate is calculated by person year law. [Results] The average age was 73.1 years old and female are 80.3%. Full follow-up was 6300 years old. RA patients were 368. Fragility Fractur that required surgery are 70, the average age was 79.7 years old. The cumulative incidence rate of Fragility Fracture increases with age increase. There was no significance difference between RA patients and non-RA patients in the Fragility Fracture and Osteoporosis treatment was the same. [Conclusions] When Surgery after TKA was over 80 years old, the Fragility Fracture rate increased. The Fragility Fracture rate of TKA patients is expected to be high and Osteoporosis treatment is necessary.

## W31-3

**Pain relief effect and imaging changes after PRP treatment for knee osteoarthritis**

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Conflict of interest: None

[Objective] We examined the relationship between improvement in pain and changes in radiographic and MR images after administration of APS, so-called the next-generation PRP, for knee osteoarthritis. [Methods] The subjects were patients whose imaging and NRS could be evaluated before and at 6M and 12M after APS administration. On X-ray images, patients were divided into three groups according to changes in joint space: open/constant/narrow, and on MR images, patients were divided into three groups according to changes in joint fluid volume: decreased/constant/increased. The degree of NRS improvement was compared among the three groups. [Results] There was no significant difference in NRS improvement between the three groups of joint space changes on radiographic images, but there was a significant difference between the three groups of joint fluid volume changes on MR images. Therefore, the improvement in pain after administration of APS did not indicate inhibition of arthritis progression on radiographic images, and the improvement in pain was significantly related to the decrease in joint fluid volume, suggesting that the pain-relieving effect of APS was due to its anti-inflammatory effect. [Conclusions] Pain relief in APS was associated with improvement of joint edema on MR imaging.

## W31-4

**Association between Central Sensitization and Postoperative Pain after Total Knee Arthroplasty and Cluster Analysis in Patients with Knee Osteoarthritis**

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Conflict of interest: None

[Objective] This study investigated the relationship between central sensitization (CS) and postoperative pain in knee osteoarthritis (KOA) patients who underwent total knee arthroplasty (TKA). We also conducted cluster analysis of patient characteristics. [Methods] We performed TKA on 27 knees with KOA. Preoperatively, we recorded Central Sensitization Inventory (CSI), European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L), Forgotten Joint Score (FJS-12), The Knee Society Score (KSS 2011), Knee Joint JOA Score, Loco-Check, and the 25-question geriatric locomotive function scale (GLFS-25), and pain intensity (NRS) up to 48 hours post-op. Hierarchical cluster analysis (Ward's method) was performed. [Results] The overall female ratio was 88.9%, and the mean age was 75.6 years at the time of surgery. The Cluster analysis divided patients into two main groups based on CSI, EQ-5D-3L, FJS-12, KSS functional score, and GLFS-25. Within each group, some patients scored significantly worse in EQ-5D-3L and NRS, yielding four clusters. [Conclusions] Despite subclinical CSI scores in over half of TKA cases, our findings suggest associations with post-op pain, quality of life, and locomotive syndrome. EQ-5D-3L is also valuable for assessing patient characteristics.

## W31-5

**Elucidation of the mechanism of pain and stiffness in knee osteoarthritis focusing on endothelin-1**

Hirotaka Tsuno[1,2], Nobuho Tanaka[2], Masashi Naito[3], Mitsuyasu Iwasawa[3], Satoru Ohashi[3], Hiroshi Furukawa[5], Naoshi Fukui[2,4]
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Conflict of interest: None

[Objective] To elucidate the mechanism of pain and stiffness in OA synovium focusing on ET-1. [Methods] Synovial tissue was collected from 27 knees of 23 patients with knee OA during TKA. Based on preoperative examination and interview, patients were divided into (1) 6 cases with synovial tenderness and 12 cases without synovial tenderness, or (2) 6 cases with obvious stiffness and 11 cases without stiffness. Gene expression of ET-1, ETAR, NGF, TrkA, and ACTA2 were evaluated using qPCR.

Synovial cells were isolated and maintained in monolayer or in three-dimensional culture using collagen gel. Recombinant protein of ET-1 was added to the cells, and gene expression of ACTA2 was examined. [Results] Genes of ET-1, ETAR, NGF, and TrkA were significantly upregulated in the group with synovial tenderness. ET-1, NGF, TrkA, and ACTA2 were significantly more highly expressed in the group with stiffness. There was a significant positive correlation between the expression of NGF and TrkA and that of ET-1, ETAR and ACTA2, respectively. In synovial cells maintained in three-dimensional culture, the expression of ACTA2 was significantly enhanced by the addition of ET-1. [Conclusions] ET-1 may induce the expression of NGF and myofibroblasts in synovial tissues, resulting in pain and stiffness.

## W31-6

**Biologically active TGF-b1 is abundantly released from osteoarthritic cartilage by compressive loading and may possibly be involved in synovial pathology**

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Conflict of interest: None

[Background] In OA, factors released from cartilage may be involved in synovial changes. [Objective] To identify factors released from OA cartilage and could cause synovial changes. [Methods] Macroscopically degenerated and preserved cartilages were obtained from 12 end-stage OA knees. These cartilages were placed in culture media of the amounts corresponding to the tissue weights, and 1 MPa of load was applied 60 times repeatedly to obtain released factors. The amounts of TGF-β1, β2 and β3 released into the media were determined by a Luminex, and the amounts of active TGF-β were determined by an assay using HEK-Blue TGF-β Cells. Then an experiment using primary cultured synovial cells was performed to examine if the released factors were biologically active. [Results] By loading, approximately 4 ng of TGF-β1, but little TGF-β2 or β3, was released per 1 g of the cartilage tissue. The assay using the HEK cells indicated that 1.8-3.7 ng of active TGF-β was released from these cartilages. The experiments using the synovial cells exhibited that the expression of *PLAU* and *SERPINE1* was indeed enhanced by active TGF-β released from the cartilages. [Conclusions] This study has shown that active TGF-β1 was released from OA cartilage at biologically significant levels by loading.

## W32-1

**Age-related Treg dysfunction in arthritic environments**

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Conflict of interest: None

[Objective] To clarify age-related changes of Tregs in RA patients and GIA mice. [Methods] 1) The percentage of Tregs in peripheral blood of untreated RA patients were measured by FCM and the correlation between age and the Treg ratio was analyzed. 2) GIA was induced in young and old mice after Treg depletion, and the arthritis scores were compared. 3) Suppression assay and OCR measurement were performed using Tregs from young and old naïve or GIA mice. 4) $CD4^+$ T cells sorted from each lymph node were analyzed by scRNA-seq. 5) Responses of young and old Tregs to TCR stimulation with or without IFN-β were evaluated. [Results] 1) There was a significant positive correlation between age and the percentage of Tregs. 2) The arthritis was significantly worsened in the young mice, while the old mice showed little worsening of arthritis with Treg depletion. 3) Although old naïve Tregs showed higher suppressive function, the old Tregs had low inhibitory function under GIA condition. 4) Type I IFN signaling was more enhanced in old Tregs. 5) Old Tregs showed altered activity under IFN-β treatment compared to young Tregs. [Conclusions] It was suggested that the different responsiveness to Type I IFN among young and old Tregs was related to aged Treg dysfunction under the arthritis condition.

## W32-2

**Anti-citrullinated osteopontin antibody enhances the binding of osteopontin to synovial cells and aggravates rheumatoid arthritis**

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Conflict of interest: None

[Objective] To identify autoantibodies in RA and to investigate their involvement in the pathogenesis of RA and their role as biomarkers. [Methods] Autoantibodies to various proteins were detected by ELISA using sera from RA patients. Using FLS and IgG purified from serum, we verified the binding activity of OPN and the induction of inflammatory signals via anti-citrullinated (cit-)OPN antibodies. We also examined the effect of antibodies on arthritis using mouse models of arthritis immunized with cit-OPN, and investigated the positivity rate of anti-citrullinated (cit-) OPN antibodies and clinical characteristics in RA patients. [Results] We screened the sera of 30 RA patients and found that 60.0% of the patients were positive for anti-cit-OPN antibodies. IgG from patients with anti-cit-OPN antibodies enhanced the binding activity of OPN to FLS. OPN also induced the production of MMPs and IL-6 in TNF-stimulated FLS, and IgG from patients positive for anti-cit-OPN antibody enhanced this induction. Validation using sera from 224 RA patients showed that the positive rate of anti-cit-OPN antibody was about 44%. [Conclusions] Anti-cit-OPN antibodies could be involved in enhancing proliferation and inflammatory signaling by increasing the binding activity of OPN and FLS.

## W32-3

**Antigen-nonspecific differentiation of peripheral helper T cells in the context of rheumatoid arthritis**

Ryosuke Tsurui[1], Hisakata Yamada[1,2], Kazuhiro Kai[1], Takahide Sakuragi[1], Yasuharu Nakashima[1]

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Conflict of interest: None

[Objective] Polyclonal PD-1+ CXCR5- Tph cells infiltrate in the joints of rheumatoid arthritis (RA). In this study, we examined whether Tph can be induced in an antigen-nonspecific manner by IL-7, which elicits homeostatic proliferation of T cells. [Methods] Peripheral blood mononuclear cells (PBMCs) of healthy subjects were cultured in the presence of IL-7 without antigenic stimulation. Flow cytometric analysis of surface antigens and intracellular cytokines and gene expression analysis of sorted cells were performed by comparing with Tph cells in RA joints. The effects of synovial fluid (SF) from RA patients on the differentiation and chemotaxis of Tph cells were examined. [Results] CD4 T cells in PBMCs from healthy subjects proliferated and expressed PD-1 in response to IL-7. These cells were CXCR5 negative, produced CXCL13 and IL-21, and expressed Blimp1 and Maf, like Tph cells in RA joints. The Tph-like cells showed an ability to migrate to RA SF, which further promoted the development of Tph-like cells. [Conclusions] Tph cells can be induced in an antigen-nonspecific manner by IL-7, which is enhanced by RA SF. This might account for the infiltration of polyclonal Tph cells in RA joints.

## W32-4

**Development of new treatments for intestinal pathobionts associated with rheumatic diseases**

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Conflict of interest: None

[Objective] The relationship between various diseases including rheumatic diseases and intestinal pathobionts has become clear. However, antibiotics are not suitable for regulating intestinal commensal pathogens because they are not bacteria-specific control methods and have the potential to promote dysbiosis. [Methods] Bacterial and viral genomes were extracted from human feces and subjected to shotgun sequencing. By combining a huge amount of sequence data, we identified the relationships between intestinal bacteria and intestinal phages. Based on this information, the sequences of the lytic enzyme were identified. The lytic enzymes were synthesized, and their host bacteria-specific lytic activity was investigated. [Results] Until now, less than 1% of intestinal phages could be classified, but with the newly developed analysis pipeline, it has become possible to classify about 90% of them. This made it possible to identify the relationships between intestinal bacteria and intestinal phages, which led to the identification of previously unknown bacterium-specific lytic enzymes. [Conclusions] Using host bacteria-specific phage therapy will not only advance research on rheumatic diseases mediated by intestinal pathobionts, but may also lead to future clinical applications.

## W32-5

**Identification of cellular targets of JAK inhibitors to exert bone-protective effects, osteoclasts or osteoblasts?**

Masatsugu Komagamine[1,2], Noriko Komatsu[1], Kazuo Okamoto[3], Kotaro Matsuda[1], Tsutomu Takeuchi[2,4], Yuko Kaneko[2], Hiroshi Takayanagi[1]
[1]Department of Immunology, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, [2]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, [3]Department of Osteoimmunology, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, [4]Saitama Medical University, Saitama, Japan

Conflict of interest: Yes

[Objective] Bone protective effects of JAK inhibitors (JAKi) have attracted much attention. We aimed to elucidate either osteoclasts or osteoblasts JAKi act on to exert bone-protective effects on three types of bone damage in RA. [Methods] We administered JAKi to CIA mice and performed histological analysis on the calcaneus, distal femur, and spine. We also examined their effects on osteoblast and osteoclast differentiation in vitro. [Results] JAKi administration reduced osteoclast number at all the bone sites. Osteoblast number was increased in the calcaneus, distant from the inflamed synovium, periarticular bone and spine, but not in the calcaneus in proximity to the inflamed synovium. In vitro, ALP-positive cells were decreased under pro-inflammatory cytokines and increased only by the addition of high concentrations of JAKi. JAKi suppressed osteoclastogenesis in the co-culture system and abrogated the suppressive effect of IFN-g on osteoclastogenesis. [Conclusions] The effects of JAKi on osteoclasts and osteoblasts depend on local inflammatory conditions. JAKi exert osteoprotective effect mainly by suppressing osteoclastogenesis in joint erosion, while JAKi suppress osteoclastogenesis and promote osteoblastic bone formation in periarticular osteopenia and systemic osteoporosis.

## W32-6

**CCL2 facilitated osteoclastogenesis and osteogenesis in young and aged murine MSC-macrophage co-cultures**

Masakazu Toya[1,2], Masanori Tsubosaka[2], Shoji Baba[1], Satoru Harada[1], Taro Mawatari[1], Stuart B Goodman[2]
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Conflict of interest: None

[Objective] "Inflammaging" is continuous systemic low-level chronic inflammation, which impairs the initiation of bone regeneration in the elderly. CCL2 promotes osteogenesis by facilitating the migration of macrophages during acute inflammation. We hypothesized that CCL2 would also enhance bone regeneration in aged cells and investigated the therapeutic effect of CCL2 using young and aged cells. [Methods] MSCs and macrophages were co-cultured, then ALP and Alizarin Red staining were performed. Primary bone marrow cells were cultured, then TRAP staining and real-time RT-PCR were performed. In the CCL2-treated group, cells were cultured with CCL2 for 24 hours. Tukey's or Kruskal-Wallis tests were performed depending on the normal distribution. [Results] Young cells showed higher osteogenic ability than aged cells. The CCL2-treated group showed greater osteogenesis in young and aged cells. In both cells, the number of TRAP-positive cells and the expression of *C-fos* and *Dc-stamp* were increased in the CCL2-treated group. [Conclusions] CCL2 facilitated osteoclastogenesis and osteogenesis not only in young but also in aged cells. Modulation of CCL2 could potentially facilitate the initiation of bone regeneration in impaired aged cells, which might provide a novel anti-aging therapy.

## W33-1

**The predictive factor for flare during MTX reduction is the baseline mTSS, and joint destruction one year later is more likely to progress compared to cases with continued reduction**

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Conflict of interest: None

[Objective] To report the final results of a prospective trial (UMIN 000028875) of factors contributing to joint destruction progression at 48 weeks after MTX reduction (discontinuation). [Methods] The study included 113 patients (previously 79) who maintained low disease activity for 24 weeks or more after MTX administration, with a DAS28-CRP score below, and PDUS Grade 1 or less in both hands on ultrasound examination (26 regions). MTX reduction was carried out every 2-3 months based on "shared decision-making between patients and physicians." RA patients were divided into groups based on the degree of reduction: Flare prevention group (F group; 22 patients), low-dose reduction group (L group; 37 patients), and high-dose reduction group (G group; 54 patients). [Results] Significant differences were observed in MTX administration at 12 months (F vs. L, G, $P < 0.05$), ΔmTSS/year (F vs. G, $P < 0.05$), baseline CDAI value (L vs. G group, $P < 0.05$), 12-month CDAI, SDAI (F vs. G, $P < 0.05$, F vs. L, $P < 0.05$), 12-month D-VAS (F vs. L, G, $P < 0.01$). [Conclusions] The predictive factor for flare during MTX reduction is the baseline mTSS, and joint destruction is more likely to progress one year later compared to cases with continued reduction.

## W33-2

**The impact of administration route on the continuance rate of MTX in rheumatoid arthritis**

Yukiko Takakuwa, Seido Ooka, Hiroko Nagafuchi, Yoshiki Ishizaki, Tatsuya Kawasaki, Machiko Mizushima, Takayasu Ando, Shotaro Suzuki, Kumiko Tonooka, Misato Kawakami, Nobuyuki Endo, Kohei Yoshioka, Etsushi Toyofuku, Sho Mori, Futaba Miyaoka, Keiichi Sakurai, Kazuko Yamazaki, Masaaki Mori, Kimito Kawahata
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Conflict of interest: None

[Objective] In Japan, differences in the method of administration of MTX may contribute to differences in the continuation rate. Therefore we investigated the differences. [Methods] We retrospectively compared the

disease activity and adverse events for cases introduced to MTX, dividing them into oral (PO) and subcutaneous administration (SC) groups. [Results] PO of 282 cases and SC of 50 cases (SC-Naive: 20, SC-Switch: 30) were extracted. At 6 months of administration, doses of 14 mg or higher were observed in 3% of the PO group, while doses of 12.5 mg or higher were observed in 25% of the SC group. The CDAI for the SC group, which was 54% with scores of 11 or higher at the start of treatment, decreased to 24% after 6 months. During the switch to SC, 23 cases experienced digestive organ symptom, which all resolved after the switch to SC. Post-administration, cases with AST (U/L) levels exceeding 31 were 24% for PO and 8% for SC, while cases with ALT levels exceeding 41 were 19% for PO and 8% for SC. Discontinuation due to side effects was 10% for PO and 2% for SC. Excluding dose reduction and discontinuation due to side effects, the continuation rate was 77% for PO and 90% for SC ($p<0.05$). [Conclusions] MTX-SC may have a higher continuation rate compared to MTX-PO.

## W33-3

**Subcutaneous injection therapy with MTX in rheumatoid arthritis can be a potential phase 1 treatment**

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Conflict of interest: None

[Objective] Oral methotrexate (MTX) is widely used as a fundamental drug for RA treatment. However, many can not take it in sufficient amounts due to side effects such as gastrointestinal symptoms. On the other hand, the recently introduced MTX subcutaneous injection formulation in Japan is expected to have fewer gastrointestinal symptoms than oral formulations and is anticipated for future clinical applications. [Methods] We examined the efficacy and safety of the MTX subcutaneous injection formulation used for more than 3 months in 16 cases of MTX-resistant RA. For Efficacy, RA disease activity and mTSS were measured. [Results] Of the 16 cases, 6 cases have adverse event +worsening RA, 6 cases had worsening RA. The average dose of oral MTX was 9 mg per week, and folic acid was used at an average of 2.6 mg per week. The average volume of the subcutaneous injection MTX formulation was 10 mg per week at the start of administration and 12.8 mg at 6 months, with 8 cases using the maximum amount (15 mg syringe). The DAS28-CRP improved from 3.76 before administration to 3.26 at 1 month and 3.18 at 3 months. Moreover, gastrointestinal symptoms, hair loss, and liver dysfunction improved. [Conclusion] The MTX subcutaneous injection can be a valuable phase 1 treatment therapy.

## W33-4

**Characteristics and prognosis of patients with methotrexate-associated lymphoproliferative disorders (MTX-LPD) that does not resolve spontaneously after MTX discontinuation**

Miyu Wakatsuki[1], Hiroyuki Yamashita[1], Yuya Akiyama[1], Setsuko Oyama[1], Shintaro Aozaki[1], Ryo Kuwata[1], Misa Yamaji[1], Takuya Harada[1], Kyoko Motomura[1], Yusuke Nakamichi[1], Yuji Yoshida[2], Hiroshi Kaneko[1]
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Conflict of interest: None

[Objective] To investigate the risk factors and prognosis for LPD not regressing spontaneously after MTX discontinuation. [Methods] We compared 22 cases of Regressive-LPD and 16 cases of Persistent-LPD among 38 patients diagnosed with MTX-LPD out of 1373 RA. We also compared the characteristics of 11 survivors and 5 died patients with Persistent-LPD. [Results] In univariate analysis, there were no differences in age, gender, duration of rheumatoid arthritis, RF, anti-CCP antibody, CRP, duration and dose of MTX use, and stage of LPD, but Persistent-LPD had significantly higher LDH and lower Lymphocyte recovery at one month after MTX withdrawal. Multivariate analysis revealed an increase in lymphocyte count of < 220/ μL one month after MTX withdrawal was associated with risk of LPD being persistent ($P$=0.02, OR 7.12). The log-rank test revealed LDH > 250 was a risk factor for death ($P$=0.02). Tocilizumab was the most common biologic used after the onset of LPD (6 cases), and there were no cases of LPD relapse after tocilizumab administration. [Conclusions] An increase in lymphocyte count of < 220/ μL one month after MTX withdrawal is a risk factor for LPD being persistent. High LDH level is a risk of death in Persistent-LPD. Tocilizumab could be safely used after the onset of LPD.

## W33-5

**Examination of the validity of the Japanese Society of Hepatology' "Nara Declaration" and Fib-4 Index in liver fibrosis in patients treated with MTX**

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Conflict of interest: None

[Objective and Methods] MTX-induced liver injury is thought to progress from fatty liver to steatohepatitis and liver fibrosis. The Nara Declaration of Jpn. Society of Hepatology states that if serum ALT exceeds 30, chronic liver disease (CLD) is suspected, and in the case of fatty liver, liver fibrosis should be evaluated using the Fib-4 Index. We compared Fib4 and Liver Fibrosis Index (LFI) by US elastography in 66 patients with ALT below 30 (non-CLD group) and 50 patients with ALT above 31 (CLD group) who were evaluated for fatty liver by US. [Results] FIb4 and LFI did not differ significantly between the two groups. In FIb4, cases above the cutoff of 1.3 accounted for 68% of the non-CLD group and 66% of the CLD group. In LFI, cases above the cutoff of 2.0 accounted for 23% of the non-CLD group and 29% of the CLD group. Cases above the cutoff were significantly more common in FIb4 than in LFI. There was no significant difference in Fib4 in the degree of fatty liver found on US, but LFI increased significantly with the enhancement of the degree of fatty liver. [Conclusions] Fib4 is largely influenced by age and increases in high levels in older patients. It is overestimated in older RA patients. US elastography may be more useful for evaluating fibrosis in RA patients.

## W33-6

**The risk factors for liver fibrosis in rheumatoid arthritis patients with nonalcoholic fatty liver disease (NAFLD)**

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Conflict of interest: None

[Objective] Methotrexate (MTX), a key drug in the treatment of rheumatoid arthritis (RA), has been indicated to have the potential to progress liver fibrosis in patients with nonalcoholic fatty liver disease (NAFLD). In this study, we investigated risk factors for liver fibrosis, including MTX, in RA patients with NAFLD. [Methods] Among 564 RA patients who participated in our Nagahama Cohort from March 2017 to August 2023, 368 patients with a history of NAFLD or abdominal CT/echo were included, and divided into 2 groups according to the presence of NAFLD to examine risk factors. [Results] Comparing RA patients with NAFLD (n=79, 21.5%) and without NAFLD (n=289, 78.5%), we found that the rates of men (40.5% vs 26.8%, p=0.015), diabetes (17.7% vs 7.4%, p<0.01) and obesity (53.2% vs 20.7%, p<0.0001) were higher in the NAFLD group than in the other. There was no significant difference of patients with MTX (48.1% vs. 38.5%, p=0.136). The FIB4-Index (age-adjusted) of MTX naïve NAFLD patients was compared with (n=23) or without MTX (n=18). There was an increase from 1.16 to 1.76 (p<0.001) in the MTX group. [Conclusions] In RA patients with NAFLD, obesity and diabetes are risk factors, and it is

possible that liver fibrosis may progress after MTX administration.

## W34-1

**A study of cervical ankylosis and its effect on cervical rotation angle in Ankylosing Spondylitis~from the T-ASK study~**

Ryo Sato[1], Kenji Kishimoto[2], Shuji Asai[1], Mochihito Suzuki[1], Junya Hasegawa[1], Yusuke Ono[1], Hironobu Kosugiyama[1], Kenya Terabe[1], Shiro Imagama[1]
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Conflict of interest: None

[Background] In ankylosing spondylitis (AS), it is important to know which ankylosis of the cervical spine affects the angle of rotation. [Objective] The purpose of this study was to investigate the effect of the cervical spine on the angle of cervical rotation and the site of cervical spine stiffness in patients with AS. [Methods] Of 81 AS patients enrolled in the T-ASK study from January 2005 to October 2022, 22 patients whose cervical spine could be evaluated by CT and whose cervical rotation angle was measured at that time were included. C0/1 to C7/Th1 were evaluated by CT and the presence of ankylosis was assessed. Cervical rotation angles were divided into >70 degrees, 20-70 degrees, and <20 degrees based on BASMI. [Results] The patient background was 80% male, age 38.8±14.8 years, 55% HLA-B27 positive, and mean disease duration The mean disease duration was 12 years. >Among the 13 patients with 20-70 degrees, 7 (53%) had at least one ankylosis at C1/2, C2/3, and C3/4, and all patients had ankylosis of the intervertebral joints. [Conclusions] In the present study, intervertebral joint stiffness, especially at C1/2, C2/3, and C3/4, had more influence on the decrease of cervical rotation angle. Detailed imaging evaluation is important to maintain the function of AS patients.

## W34-2

**Assessment of diagnostic performance of SAPHO syndrome by analysing imaging data using a large-scale language model**

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Conflict of interest: Yes

[Objective] The aim of this study is to test the diagnostic performance of SAPHO syndrome by analysing bone scintigraphy using a large-scale language model. [Methods] 151 patients who underwent bone scintigraphy for suspected SAPHO syndrome between January 2007 and December 2022 were retrospectively reviewed. ChatGPT was used as the large-scale language model. The diagnostic performance of the large-scale language model was verified by comparing cases judged to have SAPHO syndrome that fulfilled Kahn's classification criteria based on a combination of diagnostic imaging data and skin lesions such as palmoplantar pustulosis with cases diagnosed with SAPHO syndrome by rheumatologists based on all clinical information. The diagnostic performance of the large-scale linguistic model was verified. [Results] There were 79 patients with a diagnosis of SAPHO syndrome. Analysis using Japanese imaging data showed a low sensitivity of 13.9%. The analysis using English had a sensitivity of 83.5%, specificity of 69.4% and diagnostic accuracy of 76.8%, suggesting that the analysis using a large-scale language model in English may be more useful. [Conclusions] The usefulness of the analysis of bone scintigraphy in the diagnosis of SAPHO syndrome using a large-scale language model is suggested.

## W34-3

**Structural damage to the sacroiliac joint in ankylosing spondylitis**

Junya Hasegawa[1], Kenji Kishimoto[2], Mochihito Suzuki[1], Ryo Sato[1], Hironobu Kosugiyama[1], Kenya Terabe[1], Shuji Asai[1], Shiro Imagama[1]
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Conflict of interest: None

[Objective] Sacroiliac joint changes are important featueres in the diagnostic criteria for ankylosing spondylitis (AS) on x-ray. The purpose of this study was to investigate the distribution of sacroiliac joint changes in Japanese patients. [Methods] From 2004 to 2022, 58 cases in which the sacroiliac joint could be evaluated by CT were included. The sacroiliac joints were divided into ventral, central, and dorsal segments, and the presence of bone erosion, osteosclerosis, joint space narrowing, and ankylosis were examined. [Results] The mean age of the patients was 45 years, 77% were male, the mean time to diagnosis was 10 years, and the HLA-B27 positivity rate was 48%. Bone erosion was significantly more common on the iliac side. Dorsal erosions were also significantly more common on the iliac side. Osteosclerosis was significantly more common on the iliac side. In the central region, there were also significantly more cases on the iliac side. There was no significant difference in the incidence of joint space narrowing and ankylosis of the sacroiliac joint between the right and left sides. [Conclusion] Sacroiliac joint lesions in patients with ankylosing spondylitis were more likely to occur on the iliac side than on the sacral side with respect to bone erosion and bone sclerosis.

## W34-4

**Association between HLA typing and clinical characteristics of spondyloarthritis**

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Conflict of interest: None

[Background] The association between spondyloarthritis (SpA) with HLA has been reported. In Japan, a different HLA pattern is observed compared to overseas studies. There are limited on other SpA other than ankylosing spondylitis (AS). [Methods] We investigated patients with SpA who underwent HLA-B typing from 2012 to 2023. We examined their final diagnosis, symptom domains, treatment, inflammatory findings, imaging results, and their association with HLA-B. [Results] The final diagnosis showed 9 patients with AS, 8 with psoriatic arthritis (PsA), 5 with reactive arthritis (ReA), and 22 with undifferentiated SpA (uSpA). Compared with the general population, significantly prevalent HLA patterns were: B27,51 for AS; B37,48 for PsA; B55,60 for ReA; and B35,52,54 for uSpA. In AS, B27 was most associated with active axial involvement, enthesitis, and uveitis. B51,52,61,62 were also similar. In PsA, B7,61 was associated with peripheral arthritis and enthesitis. In ReA, B51,55 were associated with peripheral domain, with B7,35,65 also prevalent. For uSpA, B35,52,54,61 had high activity, followed notably by B39,44,60. [Conclusion] Even in uSpA, there are common HLA patterns and phenotypes similar to other SpA. The HLA typing may be useful for revising diagnoses and disease management.

## W34-5

**The significance of fecal calprotectin measurement in patients with spondyloarthritis**

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Conflict of interest: None

[Objective] To clarify the significance of fecal calprotectin (fCAL) mesurement in patients with spondyloarthritis (SpA). [Methods] fCAL was measured in 24 patients with SpA (SpA group) and 33 patients with other rheumatic diseases (non-SpA group) at Kagawa University Hospital from October 2020 to October 2023 by fluorescence enzyme immunoassay. Patients with IBD were excluded in advance. The results were retrospectively analyzed. [Results] fCAL in SpA group was significantly higher than that in non-SpA group (p=0.016). Colonoscopy was performed on 10 patients in SpA group and 13 in non-SpA group, and non-IBD inflamma-

tory findings were found in 1 and 4 patients, respectively. When analyzed excluding these 5 patients, fCAL in SpA group was significantly higher than that in non-SpA group (p=0.005). In SpA group, 7 patients with ankylosing spondylitis (AS) tended to have higher fCAL than 16 patients with non-AS-SpA. fCAL of non-AS-SpA patients tended to be higher than that of non-SpA group. In SpA group, the presence of axial lesion was not associated with fCAL. [Conclusions] Attention should be paid when evaluating fCAL in SpA patients when searching for IBD, as they differ from those in healthy persons. Further study is needed to evaluate the significance of fCAL measurement in SpA.

## W34-6

**Modulation of Serum Biomarkers in Patients with PsA Treated with Risankizumab in the Phase 3 KEEPsAKE 2 Study (Encore Presentation)**

Yoshinori Taniguchi[1], Buvana Ravishankar[2], Preeti Gupta Lal[2], Thierry Sornasse[2], Binhuan Wang[3], Yingtao Bi[4], Mary J Saltarelli[2], Yuni Fang[2], Byron Padilla[2], Joseph F Merola[5], Oliver Fitzgerald[6]

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Conflict of interest: None

**Objectives:** To elucidate the mode of action of Risankizumab (RZB) in PsA patients (pts) by protein biomarker (BM) dynamics in the global phase 3 trial KEEPsAKE 2 **Methods:** Serum samples from pts who participated in the optional BM exploratory analysis in KEEPsAKE 2 (placebo, n=189; RZB 150 mg, n=183) were used. Serum 92 inflammation-related BMs and beta-defensin 2 (BD-2) at baseline (BL), week 4, and week 24 were evaluated. Changes from BL in protein levels, RZB-modulated BMs, and correlations between relative BM levels and disease activity (DA) were analyzed. **Results:** At BL, the relative levels of 10 BMs (CCL20, IL-17A, IL-17C, IL-24, IL-6, S100A12, oncostatin M, VEGF-A, CXCL1 and CSF-1) positively correlated with at ≧1 BL DA measure. IL-6 was significantly and positively correlated with the inflammation marker hsCRP and musculoskeletal endpoint (PASDAS). CCL20, IL-17A, IL-17C, and BD-2 were correlated with BL PASI. RZB significantly decreased IL-17A, IL-17C, IL-6, and BD-2 vs PBO at week 4, with further decreases at week 24. In RZB-treated pts the decrease in IL-6 and BD-2 correlated with improvement of PASDAS and PASI, respectively. **Conclusions:** RZB downregulated BMs associated with musculoskeletal and skin-related DA, and resulted in a favorable clinical response.

## W35-1

**T/B cells specific differentially expressed genes (DEGs) and pathogenic pathways by RNA-Seq between affected salivary glands and peripheral blood in patients with IgG4-related disease (IgG4-RD)**

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Department of Rheumatology, Institute of Medicine, University of Tsukuba

Conflict of interest: None

[Objective] To clarify T/B cells specific DEGs and pathways by RNA-Seq between affected submandibular glands (SMGs) and PBMC in IgG4-RD patients. [Methods] Pathologically confirmed SMGs and PBMC were collected from treatment naïve definite IgG4-RD patients (N=3), subsequently $CD3^+$T/$CD19^+$B cells were sorted. We compared the gene expression of T/B cells between SMGs and PBMC by RNA-Seq. We performed 1) principal component analysis (PCA) and identification of DEGs, 2) validation by qPCR, 3) Ingenuity Pathway Analysis (IPA). [Results] 1) In PCA, gene expression patterns of T/B cells of SMGs differed from those of PBMC. 214 up-regulated and 50 down-regulated DEGs for T cells, 630 up-regulated and 109 down-regulated DEGs for B cells were identified in SMGs compared with PBMC. Up-regulated DEGs in SMGs included several cytokines, chemokines, and transcriptional factors. 2) The mRNA expression of IL-21 and EGR2 in T cells of SMGs was significantly increased than those of PBMC. 3) In IPA, Th1, Th2, IL-17, wound healing, TLR, and SLE signaling were up-regulated in T cells of SMGs. IL-8, IL-15, complement, fibrosis, and SLE signaling were up-regulated in B cells of SMGs. [Conclusions] Using RNA-Seq, we identified DEGs and possible pathogenic pathways in T/B cells from affected SMGs of IgG4-RD.

## W35-2

**The usefulness of ultrasound shear wave elastography in submandibular gland lesions in IgG4-related disease**

Keisuke Nishimura[1,2], Kohe Yo[1], Osamu Iri[1,3], Nozomi Nishimura[1,3], Kaoru Mizukawa[1,2], Keiichiro Kadoba[1,3], Hiroki Mukoyama[1,3], Rintaro Saito[1,3], Takumi Nagamoto[1], Tomohiro Yoshida[1,4], Daisuke Waki[1,5], Hiroyuki Murabe[1], Jun Saegusa[1,2]

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Conflict of interest: None

[Purpose] Ultrasound shear wave elastography (SWE) is a technique to quantify tissue elasticity using shear wave velocity (SWV), and is considered to be a useful noninvasive method for diagnosing fibrosis. We investigated the usefulness of SWE in the evaluation of submandibular gland lesions in IgG4-related disease (IgG4RD). [Methods] Submandibular gland ultrasonography was performed on patients with IgG4RD from April 2016 to December 2022, and age, gender, symptoms, and ultrasound findings were analyzed. Patients with IgG4RD were compared with those with primary Sjogren's syndrome (pSS). [Results] Twenty-nine patients (18 males, 11 females) with IgG4RD and 35 patients (4 males, 31 females) with pSS underwent submandibular gland SWE. Nineteen patients with IgG4RD showed multiple hypoechoic areas in the submandibular gland. The median SWV (IQR) of the submandibular gland was 1.59 (1.43-1.72) in the pSS group and 1.88 (1.59-2.40) in the IgG4RD group, which was significantly higher in the IgG4RD group ($p < 0.001$). The median SWV (IQR) of IgG4RD was 1.59 (1.50-1.70) in the group without sialadenitis and 2.06 (1.79-2.65) in the group with sialadenitis ($p < 0.05$). [Conclusion] SWE of submandibular gland may contribute to the evaluation of disease activity in IgG4-related sialadenitis.

## W35-3

**Investigation of elevated serum IgG4 levels and latent IgG4-related disease in patients undergoing maintenance hemodialysis**

Ichiro Mizushima[1], Sun Hirayama[3], Hiromitsu Akamatsu[1], Megumi Ikeda[1], Kaho Hayashi[1], Anri Mori[1], Hiroaki Saito[1], Akira Sakata[1], Hiroyoshi Yanagisawa[1], Fumitaka Yamamori[1], Hajime Sanada[1], Takuya Suda[2], Daiki Hayashi[1], Yoshinori Takahashi[1], Akihiko Koshino[1], Takahiro Yuasa[1], Shunsuke Tsuge[1], Taichiro Minami[1], Megumi Oshima[1], Ryo Nishioka[1], Kiyoaki Ito[1], Tadashi Toyama[1], Hiroshi Fujii[2], Norihiko Sakai[1], Miho Shimizu[1], Ryoichi Miyazaki[3], Takashi Wada[1], Mitsuhiro Kawano[1], Yasunori Iwata[1]

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Conflict of interest: None

[Objectives] This study aimed to investigate the frequency of serum IgG4 elevation and latent IgG4-related disease in patients undergoing hemodialysis. [Methods] We measured serum IgG4 levels in 227 patients undergoing hemodialysis. Linear regression analysis was used to search for factors related to serum IgG4 elevation. Secondary evaluations were conducted for patients with IgG4 elevation. [Results] The mean serum IgG4 level was 34 mg/dL, and serum IgG4 elevation was observed in 12 patients (5.3%). Univariate linear regression analyses showed that male sex, lower serum CH50 and total cholesterol levels, anti-nuclear antibody positivity, absence of hypertension, and smoking history were associated with serum IgG4 elevation. Age- and sex-adjusted analyses extracted the

same factors except for smoking history as significant. One of the 12 was diagnosed with IgG4-related retroperitoneal fibrosis, which was a cause of renal failure in the patient. [Conclusions] In patients undergoing hemodialysis, serum IgG4 elevation is more common in men and those with smoking history or some immunological abnormalities. A small proportion of patients with serum IgG4 elevation actually have latent IgG4-RD, leading to the necessity of recognizing IgG4-RD as a cause of renal failure.

## W35-4

**A case of IgG4-related periaortic architis with normal serum IgG4 and left recurrent nerve palsy**

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Conflict of interest: None

46-year-old man He had hypertension and dyslipidemia, and had been suffering from hoarseness since July, On August 4, back pain appeared. Suspecting aortic dissection, a contrast-enhanced CT scan was performed, which showed soft shadows around the ascending to arch aorta, brachiocephalic artery, left common carotid artery, and left subclavian artery origin, and stenosis of left common carotid artery. A PET-CT scan was performed, which showed an accumulation in the same area, suggesting aortic periaortitis. Although his blood IgG4 level was normal, CT-guided needle biopsy was performed and IgG4/IgG ratio of more than 50% and numerous IgG4-positive cells. Prednisolone 55 mg/day (0.8 mg/kg) was started, back pain and hoarseness improved, and the periaortic soft shadow was disappeared. Vascular lesions caused by IgG4-related diseases usually occur in the aorta and its branches, and are classified into IgG4-related aortitis. IgG4-related periaortitis, in which soft shadows are observed around the aorta. The former is more common in the thoracic aorta and the latter in the abdominal aorta, and high levels of IgG4 in the blood. The present case of IgG4-associated periaortitis was an atypical case and the diagnosis was difficult to make.

## W35-5

**IgG4-Related Disease With Pericardial Effusion: Case Reports and Literature Review**

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Conflict of interest: None

[Case summary] A 72-year-old man presented to his family doctor with exertional dyspnea, non-productive cough and leg edema in last November. Chest X-ray reveled enlarged heart and bilateral pleural effusion. His condition didn't improve though he was started on diuretics, so he underwent computed tomography examination that revealed pericardial effusion in this March. The serum level of IgG4 was 135 mg/dL, and the pericardium biopsy revealed extensive infiltration of IgG4-positive plasma cells, which was diagnosed as IgG4-associated pericarditis. He lost 10 kg after pericardial drainage and pericardiectomy, but leg edema and congestive hepatopathy didn't improve completely. Therefore, we started prednisolone 40 mg/day and his symptoms and liver dysfunction graduatelly improved. [What is new and conclusion] Although there are a wide variety of organs affected by IgG4-related disease, pericardial is not typical organ listed in the EULAR/ACR classification criteria published in 2019. However, IgG4-associated pericarditis has been reported recently, suggesting that the pericardium may also be an important target organ. In this report, we present a case in which pathological results led to the diagnosis of IgG4-associated pericarditis, which we consider a valuable case.

## W35-6

**A case of Erdheim-Chester disease with pericardial effusion that required differentiation from IgG4-related disease**

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Conflict of interest: None

A 69-year-old woman with bilateral knee pain developed shortness of breath, weight gain, and leg edema. CT scan showed pericardial effusion, bilateral pleural effusion, renal capsule thickening, and increased aortic soft tissue density. Serum IgG4 was 60.4 mg/dl. IgG4-related disease was suspected but renal biopsy showed few IgG4-positive cells. Instead, histiocyte clusters were found, suggesting Erdheim-Chester disease (ECD). The infiltrating histiocytes were CD68 (+) S100 (-), and BRAF V600E was weakly positive. Bone scintigraphy revealed abnormal accumulation in both forearms, distal parts of both femurs, and both tibias, raising suspicion for ECD. Bone biopsy did not reveal any foamy histiocytes, but infiltration of histiocytes that were CD68 (+) CD1α (-) S100 (-) was observed, leading to a comprehensive diagnosis of ECD. Prednisolone 50 mg/day was started for pericardial effusion but the effect was poor, requiring further pericardial drainage. The plan is to start PEGINFα in the future. "Coated aorta", "hairy kidney" which are referred to as periaortitis and thickening around the renal capsule are seen, posing a problem in differentiating from IgG4-related disease. It is important to keep this disease in mind and share information with pathologists with specific immunostaining.

## W36-1

**Association of Biological Agents with Changes in Bone Density in Patients with Rheumatoid Arthritis**

Yuki Segawa[1], Takayuki Fujii[2,3], Koichi Murata[2,3], Hideo Onizawa[3], Kosaku Murakami[4], Akira Onishi[3], Masao Tanaka[3], Akio Morinobu[5], Shuichi Matsuda[2]
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Conflict of interest: None

[Objective] Cytokines such as TNF-α and IL-6 are known to adversely affect bone metabolism in rheumatoid arthritis (RA) by promoting osteoclast differentiation and causing bone resorption. It has been reported that TNF inhibitors significantly improve bone mineral density in ankylosing spondylitis, but there are few reports in RA. In this study, we investigated the usefulness of biologic agents in bone mineral density in RA patients. [Methods] Patients who underwent at least two bone mineral density tests between 2012 and 2019 and were not using osteoporosis products were included in the analysis, divided into four groups: TNF inhibitor group (TNFi), IL6 inhibitor group (IL6i), T cell activation inhibitor group (ABT), and no biological agents use group (Control). In order to minimize changes due to differences in gender and age, we use Z-score. [Results] The TNFi and ABT groups showed significantly higher Z-scores in the femur (p-values 0.005, 0.004) and forearm (p-values 0.033, <0.001), compared to the Control group. In the lumbar spine, all groups showed an increase in Z-score, suggesting the influence of progressive spinal degeneration and compression fracture. [Conclusions] TNF inhibitors and T-cell activation inhibitors may be useful in improving bone mineral density in RA patients.

## W36-2

**b/tsDMARDs do not affect osteoporotic changes in patients with rheumatoid arthritis: FIRST registry**

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Conflict of interest: None

Objective: To elucidate the differential effects of b/tsDMARDs on bone metabolism in patients with RA in a real-world cohort. Methods: This was a prospective observational study. RA patients were enrolled at the time of 1st b/tsDMARDs administration. Bone mineral density (BMD) and bone turnover markers (BTMs) were measured during the 52-week observation. The end-points were differences in changes in BMD according to b/tsDMARD type, and the correlation between BMD and BTMs. Results: A total of 1,164 patients were enrolled. b/tsDMARDs improved RA disease activity CDAI 25.8 at baseline to 4.4 at weeks 52. Patients not receiving anti-osteoporotic agents (anti-Op) at week 0 experienced a significant decrease in both femoral neck (0/26/52 weeks: 0.659/0.649/0.646 g/cm3) and radial (0.510/0.507/0.500) BMD, despite maintaining low CDAI levels. None of b/tsDMARDs type preserved BMD. Conversely, patients receiving anti-Op at week 0 maintained stable BMD throughout the study. Although BTMs were changed by b/tsDMARDs, the changes were unrelated to those in BMD. Conclusion: Our study showed the progression of Op in RA patients during b/tsDMARDs treatment without anti-Op. BTMs may not reflect BMD change. Regular monitoring of BMD in RA should be considered for early management of Op.

## W36-3

**Anti-NF-kappaB peptide derived from nuclear acidic protein attenuates ovariectomy-induced osteoporosis in mice**

Taihei Miura[1], Yuki Etani[2], Makoto Hirao[3], Takaaki Noguchi[1], Akira Miyama[4], Gensuke Okamura[3], Kenji Takami[5], Atsushi Goshima[6], Takuya Kurihara[1], Yuji Fukuda[1], Seiji Okada[1], Kosuke Ebina[1,2]
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Conflict of interest: None

[Objective] Nuclear factor-kappa B (NF-κB) is a transcription factor activated with aging. It plays a key role in the development of osteoporosis by promoting osteoclast differentiation and inhibiting osteoblast differentiation. In this study, we developed a small anti-NF-κB peptide called 6A-8R from a nuclear acidic protein (also known as macromolecular translocation inhibitor II, Zn2+-binding protein, or parathymosin) that inhibits transcriptional activity of NF-κB without altering its nuclear translocation and binding to DNA. [Methods and Results] Intraperitoneal injection of 6A-8R attenuated ovariectomy-induced osteoporosis in mice by inhibiting osteoclast differentiation, promoting osteoblast differentiation, and inhibiting sclerostin production by osteocytes in vivo with no apparent side effects. Conversely, in vitro, 6A-8R inhibited osteoclast differentiation by inhibiting NF-κB transcriptional activity, promoted osteoblast differentiation by promoting Smad1 phosphorylation, and inhibited sclerostin expression in osteocytes by inhibiting myocyte enhancer factors 2C and 2D. [Discussion and Conclusion] These findings suggest that 6A-8R has the potential to be an anti-osteoporosis therapeutic agent with uncoupling properties.

## W36-4

**Deletion of the metallothionein 3 in bone marrow-derived macrophage accumulates the intracellular zinc2+ level and regulates the ROS via the NRF2 pathway, affecting osteoclast survival and differentiation**

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Conflict of interest: None

[Objective] The metal-binding protein metallothionein (MT) maintains metal ion homeostasis, especially zinc and manages cellular redox levels. Though the metabolism of metal ions plays an essential role in osteoclastgenesis, the mechanism remains unclear. [Methods] We carried out tests using murine bone marrow-derived macrophage to examine the function of MT in osteoclastogenesis. [Results] MT genes were significantly upregulated upon differentiation from osteoclast precursors to mature osteoclasts in response to RANKL stimulation, and MT3 expression was particularly pronounced in mature osteoclasts among MT genes. The knockdown of MT3 in osteoclast precursors demonstrated a remarkable inhibition of differentiation into mature osteoclasts. In preosteoclasts, MT3 knockdown suppressed the activity of MAPK and NF-κB signaling pathways upon RANKL stimulation, leading to affect cell survival. Additionally, ROS levels were decreased, and intracellular $Zn^{2+}$, NRF2 and the downstream antioxidant proteins were more highly expressed in the MT3 preosteoclast knockdowns. [Conclusions] By modulating ROS through the NRF2 pathway, MT3 plays a crucial role in regulating osteoclast differentiation and survival, acting as a metabolic modulator of intracellular $Zn^{2+}$.

## W36-5

**The efficacy of Romosozumab for localized periosteal femoral thickening which precede atypical femoral fracture**

Hiroe Sato[1,2], Naoki Kondo[3], Eriko Hasegawa[1], Yoichi Kurosawa[1], Ayako Wakamatsu[1], Yukiko Nozawa[1,2], Daisuke Kobayashi[1], Takeshi Kuroda[1,2], Ichiei Narita[1]
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Conflict of interest: None

[Objectives] Localized periosteal femora thickening (LPT) can precede atypical femoral fracture (AFF) and higher LPT height is a risk for complete and incomplete fracture. When LPT is detected, discontinuation of bisphosphonate (BP) is necessary and surgical treatment is considered in cases with pain or dreaded line at the top of LPT. Teriparatide therapy is reported to be effective in fracture cases but Romosozumab (ROM) effect has not been well examined. [Methods] Eight patients with LPT treated with ROM were included. After excluding 3 patients, remaining 5 patients were analyzed. [Results] Five patients were all women and LPT was observed in both femora (n=3) and in right femora (n=2). The median age (min-max) at starting ROM was 59 (50-71) years, prednisolone dose was 9 (3-10) mg/day, the duration from LPT detection to ROM initiation was 4.7 (2.1-8.0) years and the duration from BP discontinuation to ROM initiation was 4.5 (0-5.9) years. After ROM therapy, four patients were used BP. The change of LPT height after ROM initiation was <0.5 mm/year in all LPT but that after ROM discontinuation was increased >0.5 mm in 3 femora of 2 patients who used BP. [Conclusions] LPT height was not much changed during ROM use, but it got high in some cases using BP after ROM discontinuation.

## W36-6

**Efficacy of long-term treatment with denosumab for osteoporosis in rheumatic diseases**

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Conflict of interest: None

[Objective] To assess the long-term efficacy and safety of denosumab (DMAb) in patients with rheumatic diseases (RD). [Methods] One hundred and sixty-five patients with RD who received DMAb from 2013 to 2022 were included in this study. Clinical date, bone mineral density (BMD), medications prior to DMAb and adverse events were obtained from medical records and analyzed retrospectively. [Results] The mean ± SD age was 67.9 ± 10.7 years, 152 were female, and 113 were on gluco-

corticoids (GC) therapy (prednisolone dose; 5.7 ± 8.8 mg/day). Lumbar spine BMD (L-BMD) and femoral neck BMD (F-BMD) was analyzed up to 7 years and 3 years, respectively. The BMDs significantly increased over time [the mean percent change of L-BMD from baseline at 7 years: 16.8%, F-BMD change at 3 years: 10.5%]. Comparing patients with and without GC, L-BMD change at 7 years was not significantly different (with GC: 17.5%, without GC: 16.0%). Compared by prior therapy, L-BMD change at 7 years was greatest in the patients receiving bone-forming agents. Two cases of osteonecrosis of the jaw, 5 vertebral fractures, and 3 non-vertebral fractures were observed during DMAb treatment. [Conclusions] Long-term treatment with DMAb, with or without GC, was shown to be effective in RD patients.

## W37-1

**Analysis of clinical features in eosinophilic granulomatosis with polyangiitis treated with Mepolizumab: a single center experience**

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Conflict of interest: None

[Objective] Mepolizumab (MPZ) has been increasingly used in Eosinophilic granulomatosis with polyangiitis (EGPA) since 2018 in Japan. Therefore, we conducted a retrospective analysis of the clinical database of the 38 patients of EGPA treated with MPZ in our hospital. [Methods] 38 EGPA patients have been treated with MPZ and followed for at least 6 months since 2018 (up to Aug 2023) were analyzed for clinical course, including remission rates. Remission was defined as BVAS 0 at 6 months. Disease flare defined as increased disease activity required intensification of immunosuppressive therapy. [Results] Of the 38 patients (18 ANCA positive and 20 negative), 11 patients (9 newly diagnosed or 2 relapsing diseases) received a remission induction with MPZ and 27 patients received maintenance MPZ therapy. The mean age onset was 56±12 years and BVAS 12.1±18.1. All patients used GC, and some required additional treatment [(GC pulse 79%, cyclophosphamide (CY) 39%, IVIG 39%)]. After 6 months of therapy, the achievement rates of GC dose below 5 mg/day was 50% and improvement of sensory disorders was 44%. While no flare-up and no-death was observed. [Conclusions] These results showed that MPZ is effective and has an acceptable safety profile in relatively EGPA patients in daily practice.

## W37-2

**Interim Analysis of Post-marketing Surveillance Study of Mepolizumab in Patients with Eosinophilic Granulomatosis with Polyangiitis (EGPA)**

Shingo Nakayamada[1], Asami Abe[2], Michiaki Takagi[3], Nobunori Takahashi[4], Atsuo Nakajima[5], Ayako Nakajima[6], Keiichiro Nishida[7], Takao Fujii[8], Etsuko Hayashi[9], Yukiko Yanagita[9], Mitsuhiro Yoshida[9], Masataka Kuwana[10], Nami Okamoto[11], Yoshiya Tanaka[1]

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Conflict of interest: Yes

[Objective] To collect the safety data of mepolizumab for patients with EGPA in Japan. [Methods] All EGPA patients treated with mepolizumab after May 2018 were included. The longest observation period was 96 wks. The incidence rate (IR, per 100 person-years) of adverse events (AEs) was evaluated. [Results] As of 31 July 2023, 691 cases were included for safety analysis (691, 542, and 397 at wks 12, 48, and 96). The patient characteristics were 58.6% female, 61 yrs of age, EGPA duration of 2.3 yrs, and observation period of 93.4 wks (median). The total person-years was 977.4. The IRs of AEs and serious AEs were 71.21 and 26.30. The most common serious AEs (number of events) were EGPA (25), asthma (21), pneumonia (15) and pneumonia bacterial (13). The IRs of hypersensitivity, infection and malignant tumor (AEs of special concerns) were 4.09, 14.84 and 0.51, respectively. Serious AEs were 0.61, 6.14 and 0.51, respectively, and 4 AEs resulting in death were reported in 3 patients: circulatory collapse, sepsis, bladder cancer and malignant tumor (2 malignant tumors were reported in the same patient). [Conclusions] No new concerns have been detected up to the present in comparison with the known safety profile of mepolizumab. (Funding: GSK, 208505).

## W37-3

**Retrospective observational study of 19 cases with otitis media with ANCA associated vasculitis**

Natsumi Nagao[1], Yu Funakubo Asanuma[1], Keita Okamoto[1,2], Hiroaki Yazawa[1], Takuma Wada[1], Kazuhiro Yokota[1], Yasuto Araki[1], Yuji Akiyama[1], Toshihide Mimura[1]

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Conflict of interest: None

[Objective] To elucidate the clinical course of otitis media with ANCA associated vasculitis (OMAAV). [Methods] We retrospectively examined clinical features in 19 patients diagnosed with OMAAV. These patients visited otolaryngologists and/or rheumatologists from July 2013 to July 2023 at our hospital. [Results] The average age was 67.9 years, and the time from onset of OMAAV to the treatment initiation averaged 2.9 months. Among them, 8 had localized middle ear involvement, and 11 had systemic vasculitis. Hearing impairment types included mixed hearing loss in 14, conductive in 4, and sensorineural in 1 case, with 17 patients experiencing bilateral, and 3 being deaf. Two patients were PR3-ANCA positive, 16 were MPO-ANCA positive, and one was positive for both ANCA types. All patients received initial treatment with corticosteroids, and 13 patients were concomitant with immunosuppressive therapy. Hearing improved in 15 of 18 patients (83%) with both pre- and post-treatment hearing assessments, with the median 5-tone average hearing level decreasing from 69 dB to 40 dB ($p<0.001$). [Conclusions] The utilization of the 2015 OMAAV diagnostic criteria and collaboration with Otorhinolaryngologist may have allowed for relatively early treatment, and hearing improved in 80% of patients.

## W37-4

**Analysis of clinical features in ANCA-associated vasculitis treated with Avacopan: a single center experience**

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Department of Nephrology and Rheumatology, Kyorin University

Conflict of interest: None

[Objective] Avacopan (AVA) has been used in ANCA-associated vasculitis (AAV) from 2022. Therefore, we conducted a retrospective analysis of the clinical database of the AAV-patients in our hospital. [Methods] Nineteen patients [9 (47%) females)] followed since 2022 (up to Aug 2023) were analyzed for clinical course, including remission rates. Remission was defined as BVAS 0. GC Pulse, RTX, and AVA were used for induction therapy. PSL was begun at a dose of 0.4-1.0 mg/kg/day and then tapered off at 12 weeks. [Results] AVA was used in 19 patients with AAV (10 MPO-MPA, 7 MPO-GPA, 1 PR3-GPA and 1 double positive-GPA), 12 newly diagnosed, 4 relapsing disease and 3 maintenance phases. The mean age was 72.2±11.5 years, At the start of AVA, BVAS 12.2±8.1, CRP was 0.95±1.99 mg/dL and the dose of PSL was 32.2±20.7 mg/day. At week 12, 24 and 48, percentages of participants who could discontinue PSL were 26%, 42%, 57% and remission rates were 84%, 83%, 86%, respectively. Though one patient died from pneumonia, no patients requiring maintenance dialysis. AVA was discontinued in 4 patients (1 death, 1 liver disor-

der and 2 abdominal symptoms). [Conclusions] These results showed that AVA may be effective and have acceptable safety profiles in relatively elder AAV patients in daily practice.

## W37-5

**Five cases of ANCA-associated vasculitis in which additional treatment with avacopan was ineffective**

Soichiro Kubota[1,2], Moe Watanabe[1,2], Nakako Mabuchi[1,2], Ryosuke Ito[1,2], Yoshiaki Kobayashi[1,2], Shunichiro Hanai[1,2], Daiki Nakagomi[1,2]
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Conflict of interest: None

Objective. Abacopan is a selective C5a receptor antagonist and a potential new treatment for ANCA-associated vasculitis (AAV). The ADVOCATE study compared the addition of abacopan to cyclophosphamide pulse (IVCY) or rituximab (RTX) during remission induction with the steroid arm. Although it showed superiority in terms of sustained remission at 52 weeks, the effect of abacopan alone is not clear. Therefore, we examined the effect of single agent abacopan at induction of remission. Methods. We examined the details of 5 cases in which only abacopan was added without using IVCY or RTX or increasing the dose of steroids during AAV relapse. Results. There were 1 case of microscopic polyangiitis and 4 cases of granulomatosis with polyangiitis, 2 females and 3 males, mean age 78 years. Symptoms at relapse were: case 1: hypertrophic meningitis; case 2: high CRP, myalgia and worsening systemic symptoms; case 3: lung mass shadow; case 4: otitis media; case 5: high CRP. In all cases, no clear improvement was observed despite the addition of avacopan only, and three cases worsened. Conclusion. The ADVOCATE study highlights the non-combination of steroids, but it may be difficult to control the disease at relapse with abacopan alone.

## W37-6

**Comparison of the rates of achieving steroid-free status in patients with eosinophilic granulomatosis with polyangiitis (EGPA) treated with or without mepolizumab**

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Conflict of interest: None

[Objective] Mepolizumab has been shown to be beneficial in maintaining remission and reducing steroid in EGPA. However, evidence is lacking concerning the achievement of steroid-free treatment. In this study, we compared the cumulative steroid discontinuation rates in EGPA patients with mepolizumab and controls. [Methods] We retrospectively compared patient backgrounds, courses, and cumulative steroid discontinuation rates over 3 years of treatment in EGPA patients diagnosed at our and affiliated hospitals after May 2018 treated with (i) or without (ii) mepolizumab, and those diagnosed before 2015 (historical control, (iii)) (Gray's test). [Results] In the mepolizumab treated group (i), 6 patients of 16 patients achieved steroid-free status after 3 years of treatment. In the group (ii), 2 of 16, and in the historical control group (iii), 3 of 28 achieved steroid-free status, respectively. Cumulative rates of steroid discontinuation were 0.446, 0.286, and 0.046 ((i) vs. (iii), $p<0.01$), and the median times to achieve steroid-free status were 19.5, 28.5, and 30 months, respectively. [Conclusions] Mepolizumab group achieved steroid-free status at a higher rate and in a shorter period of time as well. Mepolizumab is likely to be useful in achieving steroid-free status in EGPA.

## W38-1

**Treatment Outcomes according to Performance Status in Patients with MPO-ANCA-Positive Microscopic Polyangiitis**

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Conflict of interest: None

[Objective] This study evaluated the treatment outcomes according to performance status (PS) in patients with MPO-ANCA-positive microscopic polyangiitis (MPO-MPA). [Methods] This observational study included patients with MPO-MPA with serum creatinine levels <5.0 mg/dL, who were treated at Iwate Prefectural Central Hospital and enrolled in the RemIT-JAV-RPGN study. The primary endpoint was a composite of death and kidney replacement therapy. We defined PS 0-1 as the good PS group and 2-4 as the poor PS group and performed survival time analysis. [Results] Of the 331 patients, 205 and 126 were divided into the good and poor PS groups, respectively. The incidence of the primary endpoint was 3.6/100 person-years (PY) in the good PS group and 15.6/100 PY in the poor PS group. PS was an independent prognostic factor after adjustment. After propensity score matching, the hazard ratios of glucocorticoid alone were 2.14 (95%CI 0.39-11.68) in the good PS group and 0.78 (0.26-2.31) in the poor PS group compared with the concomitant immunosuppressive agents. Conclusion: In patients with MPO-MPA, prognosis was worse in the poor PS group than in the good PS group. The effect of combination therapy with immunosuppressive agents may be smaller in the poor PS group than in the good PS group.

## W38-2

**Eight cases of new-onset microscopic polyangiitis and granulomatosis polyangiitis treated with a 1000 mg dose of rituximab twice as an induction therapy: a descriptive study**

Kazuya Matsumoto[1], Yoshia Miyawaki[1], Natsuki Kubota[1], Yuya Terajima[1], Kei Hirose[1], Kenta Shidahara[1], Takato Nakadoi[1], Shoichi Nawachi[1], Yu Katayama[1], Takayuki Katsuyama[1], Eri Katsuyama[1,2], Mariko Narazaki[1], Yoshinori Matsumoto[1], Ken-ei Sada[1,3], Jun Wada[1]
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Conflict of interest: None

[Objective] This study examines safety of the 1000 mg rituximab (RTX) administrated twice as an induction therapy in newly diagnosed microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA) patients. [Methods] We analyzed data from MPA/GPA patients received 1000 mg RTX twice every two weeks between January 2016 and October 2023. We collected information on age, gender, disease type, disease activity (BVAS), treatment, comorbidities, remission, and adverse events following treatment over a minimum one-year follow-up. [Results] Eight new-onset MPA or GPA patients were monitored. The average age was 72.7 years (SD 3.9) with seven women (87.5%). The median BVAS was 14.5 (IQR 4.6). The median follow-up duration was 2.2 years (IQR 1.4-3.4). All patients achieved remission within four weeks, with one (12.5%) experiencing a relapse at 41 months post-treatment. There were no deaths on the observation period. However, two relatively elderly patients with impaired renal function or pulmonary involvement suffered serious infections. [Conclusions] This study shows promising safety results for 1000 mg RTX in new-onset MPA/GPA patients. Nevertheless, additional research is warranted to investigate the long-term safety, particularly in elderly patients and those with comorbidities.

## W38-3

**Reduced glucocorticoid-related adverse events with a PEXIVAS reduced-dose glucocorticoid regimen**

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Conflict of interest: None

[Objective] In ANCA-associated vasculitis, our hospital changed from the conventional protocol (CP), gradual reduction of prednisolone (PSL) 1 mg/kg for at least 2 weeks, to the PEXIVAS protocol (PP), the reduced-dose regimen, in the latter half of 2020. We assessed the relapse rate and glucocorticoid-related adverse events (grAEs) in both protocols. [Methods] We retrospectively reviewed 17 cases treated with PP, and 33 cases treated with CP for MPA/GPA and followed up for 78 weeks. [Results] All patients received cyclophosphamide or rituximab for remission induction. The mean age was 71.5 years 76.5 years for the PP and CP groups, respectively. Twelve (70.6%) patients with PP and 26 (78.8%) patients with CP were followed up for 78 weeks. Treatment enhancement was required for four and seven patients in the PP and CP groups, respectively, due to relapse or insufficient response. The mean PSL dose at 78 weeks was lower with PP than with CP (4.7 mg vs. 6.3 mg, p=0.02). Fewer grAEs were observed in the PP group than in the PP group, including serious infections requiring hospitalization (2/17 vs. 14/33, p<0.05), new compression fractures (2/17 vs. 8/33), and new-onset diabetes (3/17 vs. 12/33). [Conclusions] The PEXIVAS protocol reduced grAEs.

## W38-4

**High incidence of drug-induced liver injury in patients with ANCA-associated vasculitis using Avacopan**

Kentaro Mori[1], Tsuyoshi Shirai[1], Tomoyuki Mutoh[2], Mamoru Narita[1], Yosuke Hoshi[1], Tomoaki Machiyama[1], Yusho Ishii[1], Hiroko Sato[1], Tomonori Ishii[1], Hiroshi Fujii[1]
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Conflict of interest: None

[Objective] This study investigated the incidence of drug-induced liver injury (DILI) due to Avacopan. [Methods] 22 patients with ANCA-associated vasculitis (AAV) using Avacopan in our related institutions were included, and their clinical information was evaluated. [Results] 8 of 22 cases presented with DILI. 5 cases were microscopic polyangiitis (MPA), and 3 cases was granulomatosis with polyangiitis (GPA). Sulfamethoxazole/trimethoprim was used in most of cases. DILI was rapidly improved in 6 cases. However, in a 75-year-old patient with MPA, an increase of direct bilirubin (D-bil) and hepatobiliary enzymes were observed four weeks after the use of Avacopan during remission induction, and liver biopsy revealed vanishing bile duct syndrome (VBDS). Despite the cessation of Avacopan and the use of ursodeoxycholic acid, D-bil remained above 10 mg/dL for five months. Another case was a 68-year-old woman with MPA who was treated with Avacopan during remission induction. Five weeks later, an increase in D-bil and liver enzymes were observed, and VBDS was suspected. [Conclusions] DILI due to Avacopan could occur frequently in Japanese, and fatal DILI such as VBDS seemed not rare. The case should be adequately selected, and contributing factors needed to be proven.

## W38-5

**Is the glucocorticoid-free possible by the early phase use of mepolizumab (MEP) as remission induction in patients with eosinophilic granulomatosis with polyangiitis (EGPA)?**

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Conflict of interest: Yes

[Objective] To verify whether glucocorticoid-free therapy can be achieved in EGPA patients treated with mepolizumab. [Methods] We retrospectively investigated the medical records of 26 EGPA patients treated with MEP until the end of September 2023 and statistically analyzed. [Results] Observation period: 752 people/month. The therapeutic positioning of MEP is initial/re-induction of remission in 15 cases and maintenance in 11. At the start of MEP, average eosinophil count was 2047, CRP 0.36, and PSL dose 26.2 mg/day. Five cases were treated with immunosuppressants. By the final observation, PSL was discontinued in 10 cases, and the period to discontinuation was median 19 months. The factor contributing to PSL discontinuation in all cases was the eosinophil count at the start of MEP (P = 0.015). Furthermore, when first-time remission induction cases (N = 12) were stratified and compared by the time of MEP initiation, PSL discontinuation was significantly achieved in cases where MEP was started within 4 weeks of the start of treatment. (P=0.017) [Conclusions] We found that it is possible to achieve glucocorticoid-free by combining MEP within 4 weeks from the start of remission induction treatment.

## W38-6

**Glucocorticoid tapering effect in patients with eosinophilic granulomatosis with polyangiitis treated with mepolizumab**

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Conflict of interest: None

Objective: To evaluate the long-term efficacy of add-on mepolizumab (MEP) to standard of care (SoC) in eosinophilic granulomatosis with polyangiitis (EGPA) patients. Methods: Information was collected retrospectively up to 36 months for EGPA patients on prednisolone (PSL) who started add-on MEP and continued for at least 12 months. Relapse rate; PSL increase due to disease activity (BVAS: Birmingham Vasculitis Activity Score), PSL dose, and BVAS were evaluated. Factors contributing to achieving PSL 4 mg/d or PSL-free were calculated using the Cox proportional hazards model. Results: BVAS improved from 3 (median) to 0 in 29 patients analyzed, with a PSL 4 mg/d rate of 64.3% (N=18, P<0.001) and a PSL-free rate of 50.0% (N=14, P<0.001) at the end of observation. Baseline eosinophil count ≧100/μL was identified as a factor contributing to achieve PSL 4 mg/day (hazard ratio 3.922, 95% CI 1.077-16.50, P=0.038). However, there were no detectable factors for achieving PSL-free. Relapse occured in 7 patients, 2 of whom required reinduction therapy with high-dose PSL and immunosuppressive agents. Conclusions: The addition of MEP to EPGA patients with residual eosinophils and disease activity while on PSL is expected to improve disease activity and significantly reduce PSL.

## W39-1

**Diagnostic accuracy of muscle MRI for muscular vasculitis in anti-neutrophil cytoplasmic antibody-associated vasculitis**

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Conflict of interest: None

[Objective] To assess the positive predictive value (PPV) of a muscle MRI for muscle biopsy (MB) and describe the muscle MRI features of systemic vasculitis. [Methods] We included AAV patients underwent muscle MRI at diagnosis or recurrence in our center between 2009 and 2020. The proof of muscular vasculitis was based on the presence of necrotizing vasculitis on MB. As previously reported in polyarteritis nodosa, muscle MRI findings were classified into diffuse, patchy, perivascular, and myofasciitis. We calculated PPV and compared characteristics of the patients with MB positive and with MB negative. [Results] Among 68 with a muscle MRI performed, 62 had a positive finding of muscle MRI. Of the positive MRI results, 35 presented diffuse, 21 patchy, 6 perivascular, and 39 myofasciitis. Open biopsy was performed in 36, and needle biopsy was performed in 6. 31 were positive for MB, 10 were negative. PPV was 75.6%. Comparing MB positive and negative patients, MPA, receiving open biopsy, the diffuse pattern, and myofasciitis pattern were significantly higher in MB positive. [Conclusions] Muscle MRI can predict the positivity of MB and muscular vasculitis with a high probability and specific MRI findings (diffuse and myofasciitis) can predict a positive muscle biopsy with high probability.

## W39-2

**Urinary Dickkopf-3 in patients with microscopic polyangiitis**

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Conflict of interest: None

[Objective] Dickkopf (DKK)-3 is a potent inducer of renal fibrosis. However, its role in microscopic polyangiitis (MPA) remains unknown. In this study, we measured urinary DKK-3 in patients with MPA to test if urinary DKK-3 could be a biomarker for MPA. [Methods] Twenty-three patients with MPA treated in our department for the past two years were enrolled in this study. Urinary DKK-3 was measured using ELISA. Correlation of urinary DKK-3 with renal function, renal histological parameters, and several biomarkers were examined (Ethical approval number 2487). [Results] Compared to healthy individuals, urinary DKK-3 was significantly increased in patients with MPA (1.02 ± 0.06 vs. 14.8 ± 2.46 ng/mL, $p<0.001$). There were significant correlations of urinary DKK-3 with serum Cr level, eGFR, urinary NGAL, and urinary beta2-MG, but not with urinary protein level, MPO-ANCA, CRP, urinary KIM1, urinary NAG. No significant correlation between urinary DKK-3 and the degree of tubular atrophy or interstitial fibrosis was observed. Immunostaining revealed that DKK-3 was localized in proximal tubules and interstitial infiltrating cells. [Conclusions] Urinary DKK-3 might be a biomarker reflecting renal inflammation in MPA.

## W39-3

**Clinical characteristics of adult-onset IgA vasculitis at our hospital**

Yuki Kuroda, Hiromitsu Asashima, Naoki Sugita, Akiyoshi Rai, Akira Kawashima, Fumina Kawashima, Daiki Tabuchi, Ryota Sato, Taihei Nishiyama, Satoshi Akao, Hirofumi Toko, Ayako Ohyama, Mizuki Yagishita, Ayako Kitada, Saori Abe, Haruka Miki, Yuya Kondo, Hiroto Tsuboi, Isao Matsumoto
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Conflict of interest: None

<Objective> To clarify clinical characteristics of adult-onset IgA vasculitis. <Methods> We examined patients with adult-onset IgA vasculitis, who admitted to our department between Apr 1985 and Sep 2023. 1) background, 2) clinical symptoms, 3) laboratory data, and 4) induction therapies were evaluated. <Results> 1) 20 patients (46.8±4.9 years old, 12 males/8 females) were identified. There was no difference in age between males and females. 2) Purpura was observed in all cases, and abdominal pain (85%), renal manifestations (70%), arthralgia (5%) and fever (45%) were observed. Urine casts were detected in all the cases of renal manifestations, and hematuria (60%) and proteinuria (55%) were observed. 3) IgA antibody was elevated in 9 cases (514.3±14.3 mg/dl, 45%) and factor 13 was decreased in 13 cases (41.6±4.9%, 81.3%). There was no relationship between the proportion of involved organs and laboratory tests. 4) PSL was used in 15 cases (40.3±5.0 mg/day, 80%) and 6 cases (30%) were treated with immunosuppressants. Only four cases (20%) recovered without any treatment. <Conclusion> All of adult-onset IgA vasculitis involved purpura and most cases had abdominal pain. Half of them elevated IgA titers and factor 13 was decreased in 80% of them. Most patients were treated with steroids.

## W39-4

**Validity evaluation of the 2022 ACR/EULAR classification criteria for ANCA-associated vasculitis in Japan**

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Conflict of interest: None

[Objective] This study aimed to evaluate the validity of the 2022 ACR/EULAR classification criteria for ANCA-associated vasculitis (AAV) when targeting AAV patients in Japan. [Methods] This study included a total of 432 AAV patients, including MPA, GPA, and EGPA, by the conventional method (hereinafter "cMPA," "cGPA," and "cEGPA," respectively) at three medical institutions in Japan between 2000 and 2023. The usefulness of the new criteria was assessed after applying the criteria to these patients. [Results] In cMPA, cEGPA, and cGPA population, 146 of 147, 142 of 144, and 97 of 141 patients were reclassified as MPA, EGPA, and GPA, respectively. Among the cGPA patients, some patients with pulmonary nodules, sinusitis, chronic otitis media, or interstitial pneumonia were reclassified as MPA. However, all patients with intraorbital masses or intracranial nodules were reclassified as GPA. Among the cMPA patients, most patients with alveolar hemorrhage and pauci-immune glomerulonephritis were reclassified only as MPA. [Conclusions] The new criteria were more likely to reclassify MPO-ANCA-positive cGPA patients as MPA. Moreover, PR3-ANCA-positive cGPA patients were likely to present with recurrent or severe organ involvement, and all of them were reclassified as GPA by the new criteria.

## W39-5

**Clinical Features of Eosinophilic Granulomatosis with Polyangiitis with Peripheral Neuropathy: multicenter REVEAL cohort study**

Yuichi Masuda[1], Shogo Matsuda[1], Takuya Kotani[1], Ayana Okazaki[1], Ryosuke Tsuge[2], Atsushi Manabe[2], Tomoki Taniguchi[2], Ryosuke Hiwa[2], Mayu Shiomi[3], Ryu Watanabe[4], Wataru Yamamoto[5], Motomu Hashimoto[4], Tohru Takeuchi[1]
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Conflict of interest: None

[Objective] To elucidate the clinical characteristics of patients with Eosinophilic Granulomatosis with Polyangiitis (EGPA) with peripheral neuropathy. [Methods] We focused on patients newly diagnosed with EGPA, registered in the multi-center cohort, for whom BVAS (Birmingham Vasculitis Activity Score) before treatment could be evaluated. EGPA was diagnosed based on the ACR/EULAR 2022 classification criteria. We compared the clinical features of patients with EGPA with and without each motor neuropathy (MN) and sensory neuropathy (SN) in BVAS. [Results] The following values are presented as medians. Out of 107 patients with EGPA, 72 met the inclusion criteria. The age was 61.5 years, 40.3% were male, and 43.1% were MPO-ANCA positive. The serum CRP level was 3.3 mg/dL, and the total BVAS was 17.0. MN was observed in 68.1%, and SN in 86.1%. In the group with MN, serum CRP levels and total BVAS were significantly higher ($p = 0.0030$ and 0.0068, respectively) compared to the group without MN. In the group with SN, white blood cell counts, serum CRP levels, and total BVAS were significantly higher ($p = 0.033$, 0.029, and 0.0022, respectively) compared to the group without SN. [Conclusion] Systemic inflammation might be associated with both MN and SN in patients with EGPA.

## W39-6

**The Association of Serum IgG4 Levels at Diagnosis with Clinical Features in Eosinophilic Granulomatosis with Polyangiitis**

Atsushi Manabe[1], Ryosuke Hiwa[1], Mikihito Shoji[1], Tomoki Taniguchi[1], Keiichiro Kadoba[1], Tsuneyasu Yoshida[1], Mirei Shirakashi[1], Hideaki Tsuji[1], Koji Kitagori[1], Shuji Akizuki[1], Ran Nakashima[1], Hajime Yoshifuji[1], Yuichi Masuda[2], Ayana Okazaki[2], Shogo Matsuda[2], Takuya Kotani[2], Wataru Yamamoto[3], Mayu Shiomi[4], Ryu Watanabe[4], Motomu Hashimoto[4], Akio Morinobu[1]
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cal Immunology, Osaka Medical and Pharmaceutical University

Conflict of interest: Yes

Objective: This study aimed to examine the association between serum IgG4 levels and clinical characteristics in patients with eosinophilic granulomatosis with polyangiitis (EGPA). Methods: 27 EGPA patients from the REVEAL cohort, with IgG4 measurements at diagnosis, were divided into two groups based on a median IgG4 level of 376 mg/dl. Clinical features and outcomes were compared. Results: The high IgG4 group (>376 mg/dl) was younger (60.0 [48.0-63.0] years vs. 67.5 [54.5-74.0] years, p=0.037) with higher platelet counts (34.3 [26.6-40.9] vs. 22.5 [14.4-31.3], p=0.019). No differences were found in BVAS, FFS, or organ involvement. The high IgG4 group showed higher relapse-free survival (log-rank test: p=0.020), with more relapses due to asthma and eosinophilia (60% vs. 37%). IgG4 correlated positively with eosinophils and IgE (ρ=0.30, 0.26) and negatively with MPO-ANCA (ρ=-0.40). In 15 without relapses vs. 12 with relapses, the relapse-negative group had higher IgG4 (mg/dl) (417.0 [353.5-637.0] vs. 312.0 [122.6-375.2], p=0.010) and showed a tendency of higher IgE (U/ml) (1820 [1361-3115] vs. 606 [543-1193], p=0.053). Conclusion: EGPA patients with high IgG4 levels at diagnosis are younger, have higher platelet counts, and exhibit lower relapse rates.

## W40-1

**Peripheral immune cells in patients with Deep Remission 12 months after induction therapy for active lupus nephritis**

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Conflict of interest: Yes

[Objective] To elucidate the characteristics of peripheral immune cells associated with Deep Remission (DR), within 12 months after induction therapy (IT) for active lupus nephritis (LN). [Methods] We prospectively assessed peripheral blood before and 12 months after IT and compared the patients with DR defined as urine-protein creatinine ratio (UPCR) ≦0.15 g/gCr, with those with complete response (CR) as UPCR ≦0.5g/gCr and non-achievement of CR. [Results] 52 patients (28, 16 and 8 in the DR, CR and non-CR, respectively) were enrolled. Before IT, the DR group had significantly lower proportions of Tfh, CD16-monocytes and basophils and higher HLA-DR+CD8+cells, NKT-like cells, B cells, plasmacytoid dendritic cells and CD16+monocytes compared to the CR group, and higher HLA-DR+CD8+cells and B cells and lower basophils compared to the non-CR group. After IT, the proportions of plasmablasts, plasma cells, CD16+monocytes significantly decreased, and those of CD8+cells, NKT-like cells, CD16-monocytes and basophils increased only in the DR group. At 12 months of treatment, the DR group had lower proportions of Th17, Tfh and plasma cells than the CR group. [Conclusions] Peripheral B cells, Tfh, plasma cells, NKT-like cells, monocyte fractions and basophils characterize achieving DR.

## W40-2

**The prognosis of mixed-type lupus nephritis depends on morphological changes due to epithelial deposits**

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Conflict of interest: None

[Objective] Using light microscopy (LM) or immunofluorescence (IF), combined proliferative and membranous lupus nephritis (LN) is defined as class III/IV lesion and diffusely distributed membranous lesion in ISN/RPS 2003, and was reported with a poor prognosis. We examined the differences in the evidence of membranous lesions by LM or IF, and the presence of renal remission (RR) 3 years after biopsy and end-stage renal disease (ESRD) at the last observation. [Methods] During 2005-2022, we retrospectively evaluated 43 cases divided into membranous findings on LM (diffuse spike or bubbling) (LM group; n = 30) and those on IF (IgG granular deposition) (IF group; n = 13). RR was defined as a spot urine protein/creatinine ratio <0.5 g/g Cr and normal serum Cr or an increase in serum Cr within 10% of the pretreatment value. [Results] The mean age 41.1 ± 14.6 years (male: female = 9:34), disease duration 6.9 ± 7.1 years, urine protein/Cr ratio 4.1 ± 3.1 g/Cr, serum Cr 0.96 ± 0.43 mg/dl. After 3 years, 69.2% of cases in the IF group achieved RR and had no ESRD, while those in the LM group was lower at 30.0% (p=0.0163), and 5 cases (16.7%) developed ESRD (p=0.0489). [Conclusions] The mixed type, as defined by LM, had a significantly poor prognosis than the one determined by IF.

## W40-3

**Correlation between histopathological type and clinical data of 90 patients with kidney biopsy proven lupus nephritis**

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Conflict of interest: None

[Objective] The site of lupus nephritis (LN) damage is thought to be mesangial in class I and II, endothelial in class III and IV, and epithelial in class V. LN class III/IV+V, which has both endothelial and epithelial damage, is more damaging than a single disease type. [Method] We investigated the correlation between histopathological types and clinical data in 90 patients with kidney biopsy proven LN from 2001 to 2022. [Results] There were 20 male cases and 70 female cases, with an average age of 48.5 years. Renal histology classification was class I:10, class II:9, class III:19, class IV:12, class V:8, III/IV+V:32. For I, II, III, IV, V, III/IV+V, dsDNA antibody, Sm antibody, and RNP antibody were 27.7: 61.7:117.4:93.0:2.5:87.8 IU/mL, 48.8:18.8:52.9:2.0:17.7:3.0 U/mL, and 3.6:48.7:73.1:8.3:17.3:28.7 U/mL. Proteinuria and PSL dose were higher in the following order: I/II, III/IV, and V/(III/IV+V). [Conclusions] dsDNA antibodies affect mesangial disorders and endothelial disorders, and RNP antibodies and Sm antibodies are high in class III, but low in class IV. As the range of damage expands from mesangial, endothelial, to epithelial damage, proteinuria becomes more severe, so it was considered necessary to increase the intensity of treatment.

## W40-4

**Clinicopathological features associated with renal flare in lupus nephritis pure class V**

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Division of Rheumatology, Keio University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Objective] To identify predictive factors for relapse in patients with lupus nephritis (LN) pure class V. [Methods] We retrospectively reviewed patients with LN pure class V who visited our hospital from 2012 to 2023 and achieved remission with remission induction therapy. Patients were divided into two groups according to relapse, and clinical characteristics were compared. Remission, deep remission, and relapse were defined as UPCR<0.7, <0.15, and >1.0 g/gCr, respectively. [Results] 28 patients were included. The mean age was 42.6 years, 24 (86%) were female, and 21 (75%) were new-onset. During the mean follow-up of 73.2 months, 3 (10.7%) relapsed at a mean of 40 months after remission. There were no differences in the treatment, the proportion of new-onset LN, or the use of antihypertensive drugs. The relapse group showed a lower rate of deep remission (0% vs 80%, p=0.003), higher smoking rate (66% vs 8%, p=0.027), anti-dsDNA antibody titer (145 vs 43 IU/mL, p=0.046), proportion of chronicity index ≧3 points (66% vs 16%, p=0.045), and stronger IgG staining (2.3+ vs 1.6+, p=0.039). [Conclusions] Non-achievement of deep remission, smoking, high anti-dsDNA antibody, chronicity index ≧3 and stronger IgG staining were associated with relapse of LN pure class V.

## W40-5

**Long-term outcomes of lupus nephritis with low-level proteinuria: a multicenter, retrospective study**

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Conflict of interest: None

[Objective] To clarify the long-term prognosis of lupus nephritis (LN) with low-level proteinuria (LLP). [Methods] We included 144 LN from ten hospitals. LLP was defined by a urine protein: creatinine ratio (UPCR) of ≦1 g/gCr based on previous reports. [Results] Compared with high-level proteinuria (HLP, UPCR>1), LLP (n=67 [46.5%]) had significantly improved renal function at the time of renal biopsy, and low activity index and chronicity index (CI) while the frequency of class III/IV was similar (79.1% vs. 84.4%, $p$=0.409). In LLP, cyclophosphamide usage was less, and the incidence of end stage renal disease (ESRD) (3.0% vs. 13.0%, $p$=0.036) or death (3.0% vs. 16.9%, $p$=0.006) during the total observation period (median, 72 months) were low. Kaplan-Meier analysis showed significant differences in the incidence of ESRD and death between the groups. Multivariate Cox regression analysis revealed that the significant risk factors for ESRD were high CI and hypertension, whereas those for death were increased age and HLP. [Conclusions] Patients with LN and LLP had favorable long-term renal and life outcomes. As these patients have substantial active pathological lesions, renal biopsy in the early phase with LLP could enable early diagnosis and treatment and thus improve prognosis.

## W40-6

**A case of systemic lupus erythematosus with podocyte infolding glomerulopathy**

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Conflict of interest: None

[Case] A 22-year-old woman complained vomiting and diarrhea for a year ago, and proteinuria and hematuria appeared around the same time. She also had recurrent symptoms of cystitis. She developed fever, recurrent symptoms of cystitis, and findings of nephrotic syndrome for 3 months ago. A simple CT scan revealed multiple lymphadenopathy, intestinal edema, and pleural effusion, so she was referred to our hospital. She was found to be positive for antinuclear antibody, anti-ds-DNA antibody, and hypocomplementemia. The renal biopsy revealed podocyte infolding glomerulopathy. She was diagnosed as systemic lupus erythematosus (SLE) with nephritis, cystitis, and enteritis, and treated with glucocorticoids, mycophenolate mofetil, and tacrolimus. Then, her gastrointestinal symptoms and cystitis symptoms improved. [Conclusions] Podocyte infolding glomerulopathy is a rare histopathological change. Many of the cases reported so far lack clinical findings, suggesting the importance of renal biopsy. In addition, many of the case reports we examined responded well to immunosuppressive therapy. In this report, we describe a case of such a rare pathological finding.

## W41-1

**Outcome of patients treated with immunoadsorption plasmapheresis for lupus nephritis at our hospital**

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Conflict of interest: None

[Objective] We examined the clinical benefit of immunoadsorption plasmapheresis (IAPP) in patients with lupus nephritis treated at our hospital. [Methods] We retrospectively examined the clinical course of 7 patients (2 males and 5 females) treated with IAPP for lupus nephritis at our hospital from February 2011 to February 2023. [Results] Median pre-treatment SLEDAI score was 23 (16-26), and all patients had proteinuria with a urine protein to urine creatinine ratio > 3.5 g/gCr. Renal histology was type III in one case, type IV in four cases, type III+V in one case, and type IV+V in one case. All patients received high-dose glucocorticoids (GC) (3 patients received methylprednisolone pulse therapy) and immunosuppressive drugs (tacrolimus, mofetil mycophenolate, cyclophosphamide pulse), and 2 patients received belimumab. After IAPP (3 to 4 sessions), hypocomplementemia improved (median C3 27 to 45 mg/dl, C4 3 to 12 mg/dl) and anti-ds-DNA antibodies decreased (median 167 to 10 IU/ml), and IC-C1q decreased in all 5 cases in which it was measured. [Conclusions] In lupus nephritis, the addition of IAPP is an effective option for patients with high levels of immune complexes and anti-ds-DNA antibodies who are refractory to treatment with glucocorticoids and immunosuppressive drugs.

## W41-2

**Characteristics of Lupus Nephritis Cases Where Steroid Discontinuation was Possible**

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Toranomon Hospital, Kajigaya, Japan

Conflict of interest: None

[Objective] The CORTICOLUP trial suggests using 5 mg/day prednisolone may reduce SLE relapse risk. However, in practice, steroids are aimed to be discontinued using immunosuppressants, but the effectiveness is unknown. We studied lupus nephritis cases that could cease steroid use. [Methods] We reviewed 13 lupus nephritis cases from 2009-2022 in our hospital who stopped steroids. Relapse post-discontinuation and clinical details were evaluated. [Results] Among patients, 1 was male; 12 were female, with the average onset age being 37. At discontinuation, 8 had low C3 levels; 7 had low C4, and 6 high ds-DNA levels. Average follow-up was 46.0 months (range 26.5-65.5). HCQ was used in 1 case; Tac in 9; and MMF in 8. 3 of the 13 relapsed post-steroid cessation. 2 of the 9 Tac users relapsed, but none from the 8 on MMF. [Conclusions] Reports indicate that serologically active but clinically quiet lupus nephritis and HCQ duration can influence relapse post-steroid cessation. Our study had a high relapse risk, but MMF users didn't relapse. MMF reportedly suppresses plasma and Th1 cells, hinting at its potential benefit in steroid discontinuation.

## W41-3

**Dapagliflozin for rheumatic musculoskeletal diseases patients with chronic kidney disease**

Hironari Hanaoka, Jun Kikuchi, Kazuoto Hiramoto, Mitsuhiro Akiyama, Yasushi Kondo, Shuntaro Saito, Yuko Kaneko
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: None

[Objective] To elucidate the effectiveness of dapagliflozin, a SGLT-2 inhibitor, on renal function in patients with rheumatic musculoskeletal diseases (RMDs) complicated by CKD and identify factors associated with the response to dapagliflozin. [Methods] We conducted a retrospective analysis of patients with RMDs and CKD who were treated with dapagliflozin for more than a year. The good response was defined as an improvement in eGFR slope per year after dapagliflozin treatment compared to that before treatment. Additionally, we investigated the response rate and its predictive factors. [Results] In this analysis, 43 patients were included. The average eGFR slope demonstrated a significant improvement after dapagliflozin treatment compared to that before the treatment ($p<0.01$). A good response rate was 69.8% and was associated with low average levels of C-reactive protein, a high frequency of ARB use, and a low frequency of tacrolimus use compared to non-response ($p=0.03$, $p=0.01$, and, $p<0.01$, respectively). [Conclusions] Dapagliflozin is effective for RMDs patients with CKD for preventing deterioration of renal function. Antihypertensive treatment with ARBs and inflammation control without tacrolimus was associated with a high likelihood of favorable response to dapagliflozin.

## W41-4

**Comparison of lupus mesenteric vasculitis and protein losing enteritis in SLE**

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Conflict of interest: None

[Objective] We aim to clarify the clinical features of gastrointestinal involvements in SLE patients by comparing lupus mesenteric vasculitis (LMV) and protein losing enteritis (PLE). [Methods] We retrospectively extracted 40 cases with gastrointestinal disorders from 382 SLE admissions (218 patients) from 2003 to 2023. Then we focused on the LMV group and the PLE group, and assessed their clinical features. [Results] In total, 14 female patients were included: nine LMV and five PLE. Also, seven out of 13 hemophagocytic syndrome patients had gastrointestinal disorders. There were no significant differences in age, smoking history, organ lesions, positivity for autoantibodies, SLEDAI scores at diagnosis. The LMV group had significantly higher frequency for abdominal pain (p=0.003), nausea (p=0.003). The PLE group had higher frequency for anasarca (p=0.002) and lower level for serum albumin (0=0.0059) and total protein (p=0.019). There was a higher tendency in the PLE group to use cyclophosphamide or mycophenolic acid for remission induction therapy (p=0.086). The maximum dose of prednisolone, the achievement ratio of remission evaluated by LLDAS, mortality rates were not different. [Conclusions] PLE is difficult to control and needs IVCY or MMF.

## W41-5

**The effectiveness of belimumab in systemic lupus erythematosus in our hospital**

Natsuki Sakurai[1], Ryusuke Yoshimi[1,2], Chiharu Hidekawa[1], Naoki Suzuki[1], Yuji Yoshioka[1], Kana Higashitani[1], Soichiro Adachi[1], Yuki Iizuka[1], Ayaka Maeda[1], Lisa Hirahara[1], Chikara Honda[1], Kodai Kitahori[1], Kento Ichikawa[1], Naoki Hamada[1], Yutaro Soejima[1], Hiroto Nakano[1], Kaoru Minegishi[1], Yohei Kirino[1], Hideaki Nakajima[1]
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Conflict of interest: None

[Objective] Belimumab (BLM) is known to have effects on improving disease activity and reducing corticosteroid dosage. Here, we investigated the effectiveness and usage history of BLM at our hospital. [Methods] SLE patients prescribed BLM at our hospital from September 2017 to July 2023 were collected. We compared treatment and laboratory data at when BLM was introduced and one year after its introduction. [Results] 39 patients were included (84.6% female, median age at BLM introduction 37.1-year-old (IQR 31.2-47.7), median duration of illness 10.3 years (2.9-21.3), neuropsychiatric SLE 38.5%, lupus nephritis 61.5%, anti ds-DNA antibody positivity 94.9%). By BLM, the median dose of prednisolone (PSL) decreased from 10 to 6 mg/day (p=0.002). Furthermore, anti ds-DNA antibody titer (29 to 11 IU/mL, p=0.002) and hypocomplementemia (CH50: 31.9 to 40.9 U/mL, p=0.009) was improved, but there was no significant improvement in renal involvement. In the subgroup analysis, 15 patients with PSL dose < 7.5 mg/day at the time of BLM introducing, anti ds-DNA antibody titer and hypocomplementemia was improved and there was a trend of reduced PSL dose (5 to 4.3 mg/day). [Conclusions] In our study, BLM improved anti DNA antibody and hypocomplementemia and reduced corticosteroid dose.

## W41-6

**Clinical characteristics and efficacy of patients with systemic lupus erythematosus (SLE) treated with Anifrolumab (ANF)**

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Conflict of interest: None

[Objective] To clarify the clinical characteristics, therapeutic efficacy, and safety of ANF in patients with SLE. [Methods] We retrospectively examined patient background, reasons for induction, changes in SLEDAI-2K and PSL dosage after induction, and adverse events in 13 SLE patients who received ANF at our department from October 2022 to September 2023. [Results] Mean age was 48.5±20.4 years, mean disease duration was 2.3±3.0 years, mean SLEDAI-2K score was 7.0±4.2, mean anti-DNA antibody titer was 43.9±113.0 IU/ml, and mean PSL dose was 16.3±18.0 mg/day before introduction. Inadequate response to prior therapy in 6 patients, maintenance of remission in 2 patients, steroid reduction in 2 patients, and as adjunctive therapy during induction of remission in 3 patients. Mean SLEDAI score was 0.7±1.3 at 1 month and 0 at 3 months after induction, and mean PSL dose was 8.2±11.2 mg/day at 1 month and 2.1±3.9 mg/day at 3 months after induction. One case of blistering resolved after discontinuation. There were no serious adverse events. [Conclusions] The efficacy and safety of ANF in patients with SLE of moderate severity or less was suggested, and its efficacy was also suggested in combination with high-dose PSL in some patients with severe disease.

## W42-1

**Effectiveness and safety of JAK inhibitors with and without methotrexate in patients with rheumatoid arthritis in a real-world setting**

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Conflict of interest: Yes

[Objective] This study aimed to compare the effectiveness and safety of JAK inhibitors (JAKis) with and without methotrexate (MTX) in patients with rheumatoid arthritis (RA). [Methods] The study utilized data from a multicenter registry and included 216 patients treated with JAKis with MTX and 180 patients treated with JAKis without MTX. Patients were observed for a minimum of 24 weeks, and propensity score matching was employed to mitigate potential treatment-selection bias. [Results] A total of 119 matched pairs of patients were identified. The log-rank test revealed no significant differences in the cumulative discontinuation rate due to insufficient response or adverse events between the MTX (+) and (-) groups. At baseline and at 4, 12, and 24 weeks, no significant differences in the SDAI scores were observed between the two groups. However, at the 12-week mark, the MTX (+) group demonstrated a significantly higher rate of remission according to SDAI (48% vs. 31%, P=0.009) compared to the MTX (-) group. [Conclusions] This 24-week observational study suggests that concomitant use of MTX may assist RA patients treated with JAKis in achieving early remission.

## W42-2

**Effectiveness of JAK inhibitors in elderly-onset rheumatoid arthritis**

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Conflict of interest: None

[Objective] This study utilized the Tsurumai Biologics Communication Registry (TBCR) to investigate the efficacy of Janus kinase inhibitors (JAKi) in elderly-onset RA (EORA). [Methods] We examined 460 cases had received JAKi treatment over 24 weeks. EORA was defined as RA onset at the age of 65 or older (E group: 105 cases), while younger-onset RA (YORA) before the age of 65 (Y group: 355 cases). The characteristics of EORA were assessed. Patients backgrounds, disease activity (SDAI), persistence rates, and herpes zoster incidence were compared between two groups. [Results] The E group had a higher proportion of males, shorter duration of illness, lower eGFR values, lower anti-CCP antibody and RF positivity rates, a higher rate of glucocorticoid use, and a lower rate of prior b/tsDMARDs use. The mean SDAI values significantly improved to 8.0±9.2 (E group) and 8.4±8.6 (Y group) at 24 weeks, with no significant differences between two groups. The remission achievement rate at 24 weeks was 35.0% (E group) and 36.0% (Y group). The persistence rates up to 24 weeks were 71.1% (E group) and 78.5% (Y group). The incidence of herpes zoster was 5.95 (per 100 person-years) (E group) and 4.94 (Y group). [Conclusions] The efficacy of JAKi in EORA was not significantly different from that in YORA.

## W42-3

**Efficacy, Safety and Drug Continuation Rate of Janus Kinase inhibitor in Elderly Patients with Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] Janus kinase inhibitors (JAKi) have been shown to be effective, but there are concerns about their use in elderly patients due to adverse events such as infections, cardiovascular events, and malignancies. We evaluated the efficacy, safety, and continuation rate of JAKi in elderly patients with rheumatoid arthritis (RA). [Methods] We classified 119 RA patients who initiated JAKi at Saitama Medical University Hospital between October 2014 and June 2023 into two groups: below 65 years (n=49) and older than 65 years (n=70), according to the starting age. [Results] Patient characteristics (younger/elderly group) was as follows: mean age (52/75 years), mean disease duration (95.5/141.5 months, p=0.039), methotrexate users (63.3/20.0%, p<0.001), prednisolone users (34.7/42.9%, p=0.447), DAS28-ESR (4.80/5.28, p=0.096). DAS28-ESR improved significantly in both groups 12 weeks after treatment initiation (p<0.001/<0.001). The 12-month continuation rate was lower in the elderly group (74.4 /49.2%, p=0.008), with more adverse events (36.4/54.5%), while lack of efficacy was less common (54.5/42.4%). [Conclusions] In elderly RA patients the efficacy of JAKi was not inferior to that in younger patients, but the continuation rate was significantly lower.

## W42-4

**Actual rheumatoid arthritis patients started on JAK inhibitors in our hospital**

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Conflict of interest: None

Objective: To report on the efficacy and safety of JAK inhibitors in patients initially selected for Recommendation Phase 2. Methods: From July 2013 to March 2023, we started 92 patients who initially selected among 544 patients who could be followed for at least 6 months. Results: 1) CDAI remission rate at 6 months and continuation rate at 1 year were JAK inhibitors > non-TNF inhibitors > TNF inhibitors. During the observation period, 48.5% of patients continued, 25.5% moved to the second drug, and 18.5% discontinued. Discontinued cases by remission were 7.5%, steroid discontinuation rate was 88.5%, and 30.5% of all cases relapsed. 2) For the second drug, 65.4% of all cases switched to a drug with a different mechanism of action, and 34.6% switched to another JAK inhibitor. 3) The mean duration of use of b/tsDMARDs after the second drug was the same as that of other b/tsDMARDs. 6) The rate of conversion to D2TRA patients was TNF inhibitor > non-TNF inhibitor > JAK inhibitor. There was no difference in the incidence of adverse events. Conclusion: The high efficacy and persistence rate of JAK inhibitors as first-line agents and the low transition rate to D2TRA patients demonstrated the superiority of JAK inhibitors in achieving RA treatment goals. Translated with DeepL.

## W42-5

**Effects of JAK inhibitor on kidney and liver function in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] JAK inhibitors (JAKi) are useful medication in the treatment of patients with rheumatoid arthritis (RA). JAKi may cause renal and hepatic dysfunction depending on the excretion route. In this study, we investigated changes in renal and hepatic function in RA patients using JAKi. [Methods] We analyzed 291 RA patients with JAKi. We evaluated renal and hepatic function using creatinine (Cre), eGFR, AST and ALT at 0, 4, 12, 24, 36, 52 weeks. We classified baricitinib and filgotinib as JAKi with renal excretion (JAK R), and tofacitinib, peficitinib, and upadatinib as JAKi with hepatic excretion (JAK H). We investigated the relationship between type of JAKi and renal and hepatic function in RA patients with or without MTX using repeated ANOVA. [Results] In 291 RA patients with JAKi, there were 167 patients (JAK R 75, JAK H 92) with MTX and 124 patients (JAK R 42, JAK H 82) without MTX. In the analysis for RA patients with JAKi without MTX group, there were significant interaction between changes in Cre, eGFR and ALT and type of JAKi. [Conclusions] In this study, we found a significant relationship between the excretion route of JAK inhibitors and changes in renal and hepatic function. It is important to select JAK inhibitors according to the patient's renal and he-

patic function.

## W42-6

**Baricitinib inhibits bone erosion progression in rheumatoid arthritis in HR-pQCT**

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Conflict of interest: Yes

[Objective] Baricitinib has been shown to inhibit bone erosion on X-ray in rheumatoid arthritis. The purpose of this study was to investigate the changes in bone erosion in more detail by using HR-pQCT, and to capture changes in bone erosion volume, etc., which could not be measured previously. [Methods] Clinical evaluation, mTSS, ultrasonography, MRI, HR-pQCT, and biomarkers were evaluated at baseline, 6 and 12 months after the start of Baricitinib in 14 patients who consented to receive Baricitinib at our hospital. The change from baseline was measured at the second and third metacarpals and wrist joints on the symptomatic side. The change from baseline was examined by the Wilcoxon rank-sum test. [Results] The median age of patients was 65.5 years, duration of disease was 77 months, and DAS28-ESR was 4.95. Clinical disease activity and ultrasound findings significantly decreased from baseline after Bari initiation. mTSS mean change at 12 months was 0.83. Bone erosion volume worsened in 6 but improved in 2 at 12 months. The mean change in volume of bone erosions at 12 months was 1.08 mm3, depth 1.12 mm, and width 0.02 mm. [Conclusions] Baricitinib seems to be useful for the inhibition/repair of joint structure destruction.

## W43-1

**Our experience with TNF-alpha inhibitors and IL-6 inhibitors in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To evaluate the efficacy of TNF-α and IL-6 inhibitors for rheumatoid arthritis (RA). [Methods] Disease activity, mHAQ score, and persistence rate were investigated in 78 patients with RA TNF-α or IL-6 inhibitors for at least 52 weeks. [Results] The mean age was 65.5 (±18.0) years and 69 patients (88.5%) were female. Switch cases included 11 (29.7%) on TNF-α inhibitors and 10 (24.4%) on IL-6 inhibitors. The mean concomitant methotrexate dose was 6.3 (±2.4) mg for TNF-α inhibitors and 5.5 (±3.3) mg for IL-6 inhibitors. The mean DAS28-ESR at weeks 0 and 24 was 5.41 (±1.40) and 3.44 (±1.38) for TNF-α inhibitors and 5.51 (±1.57) and 2.42 (±1.10) for IL-6 inhibitors, respectively. The mean mHAQ score was 0.83 (±0.63), 0.54 (±0.58) for TNF-α inhibitors and 1.02 (±0.67), 0.85 (±0,68) for IL-6 inhibitors. The mean DAS28-ESR at 0 and 24 weeks for switch patients was 5.29 (±1.53) and 3.92 (±1.69) for TNF-α inhibitors and 4.49 (±2.01) and 3.12 (±1.17) for IL-6 inhibitors, respectively. The mean mHAQ score was 0.79 (±0.83), 0.65 (±0.69) for TNF-α inhibitors and 1.08 (±0,78), 1.06 (±0.75) for IL-6 inhibitors. [Conclusions] TNF-alpha and IL-6 inhibitor treatment rapidity decreased the disease activity in patients with RA. Switch patients showed slow improvement compared to Bio-naïve patients.

## W43-2

**The clinical efficacy of inhibitors of interleukin-6 receptor, Sarilumab and Tocilizumab, in the patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate the clinical efficacy of Sarilumab (SAR) and Tocilizumab (TCZ) in patients with rheumatoid arthritis (RA). [Methods] We evaluated disease activities in RA patients for 52 weeks (w) after starting administrations of SAR (N=40) and TCZ (N=152). [Results] The mean DAS28-CRP of SAR and TCZ groups were 4.45 and 4.49 at baseline (BL) (p=0.407), 2.89 and 3.43 at 4W (p=0.012), 2.37 and 2.88 at 12W (p=0.010), 2.42 and 2.64 at 24W (p=0.157), 2.49 and 2.56 at 36W (p=0.363), 2.27 and 2.57 at 52W (p=0.064), respectively. DAS28-CRP significantly decreased after 4W in both groups (p<0.05). When looking at the clinical courses in both groups in only using as second line biologic agents (Bio), the mean DAS28-CRP of SAR (N=16) and TCZ (N=55) groups were 4.15 and 4.47 at BL (p=0.154), 2.62 and 3.57 at 4W (p=0.007), 1.95 and 2.99 at 12W (p<0.001), 2.04 and 2.79 at 24W (p=0.022), 2.07 and 2.59 at 36W (p=0.048), 1.93 and 2.64 at 52W (p=0.008), respectively. DAS28-CRP significantly decreased after 4W in both groups (p<0.05), however, DAS28-CRP after 4W in SAR group were significantly lower than TCZ group. [Conclusions] Both of SAR and TCZ had good and quick clinical efficacy, especially in first line using. However, SAR had stronger clinical efficacy than TCZ in second line using.

## W43-3

**The efficacy of mono therapy of TNF inhibitors, IL-6 inhibitors, CTLA4-Ig, and JAK inhibitors as first line using in patients with rheumatoid arthritis from the data of ANSWER cohort**

Kenji Mamoto[1], Motomu Hashimoto[2], Tadashi Okano[3], Yutaro Yamada[1], Shinsuke Yamada[2], Ryu Watanabe[2], Kazuo Fukumoto[2], Takaho Gon[2], Masao Katsushima[2], Wataru Yamamoto[4], Kosaku Murakami[5], Koichi Murata[6], Yuri Hiramatsu[7], Takuya Kotani[7], Yuki Etani[8], Yasutaka Okita[9], Naofumi Yoshida[10], Hideki Amuro[10], Takaichi Okano[11], Mai Yamashita[11], Ryota Hara[12], Yuji Nozaki[13], Tetsu Itami[13], Hiroaki Nakamura[1]

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Conflict of interest: None

[Objective] To investigate the persistence rate and clinical efficacy of TNF inhibitors (TNF), IL-6 inhibitors (IL-6), CTLA4-Ig (ABT), and JAK inhibitors (JAK) in first line using without MTX in patients with rheumatoid arthritis (RA). [Methods] We evaluated and compared the persistence rate and disease activities for 52 weeks after starting administrations between RA patients with TNF (N=120) and with IL-6 (N=112), ABT (N=159), JAK (N=29) as first line without MTX from the data of ANSWER cohort. [Results] The persistence rate for 52 weeks (W) were 60.8% in TNF, and 75.9% in IL-6 (p=0.01), 77.9% in ABT (p<0.01), 79.3% in JAK (p=0.04) (vs TNF). The mean DAS28CRP and CDAI at baseline were 4.40, 20.24 in TNF, and 4.28, 18.79 in IL-6, and 4.36, 20.05 in ABT, and 4.12, 16.70 in JAK, respectively. There were no significant differences between TNF and IL-6/ABT/JAK. The mean DAS28CRP and CDAI after 52W were 2.91, 10.31 in TNF, and 2.18 (p<0.01), 7.51 (p<0.01) in IL-6, 2.61 (p=0.03), 7.80 (p=0.01) in ABT, 2.07 (p<0.01), 4.74 (p<0.01) in JAK (vs TNF), respectively. [Conclusions] We confirmed that the persistence rate and clinical efficacy of IL-6, ABT, and JAK in first line using without MTX were better than TNF mono therapy in real clinical data as the guidelines recommended in Phase II therapy.

## W43-4

**Consideration on the Selection of Biologic Agents for Rheumatoid Arthritis Patients Based on Intraoperative Synovial Pathology**

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Conflict of interest: None

[Objective] In Phases II and III of rheumatoid arthritis (RA) treatment, there are no clear criteria for selecting biologic agents. We hypothesized that understanding each patient's synovial phenotype might be instrumental in predicting the choice of an effective agent. [Methods] Since 2018, surgeries were performed on 39 patients classified with RA (7 males, 32 females) with an average age of 72.3 years. Immunohistochemical staining of intraoperatively obtained synovium categorized the samples into Lymphoid type (L type) predominant in CD3,4,20, Myeloid type (M type) predominant in CD68, Mixed type, and Low inflammatory type (Low type) when no staining was present. L type was preferentially treated with anti-IL-6 agents, and M type with TNF inhibitors. [Results] Out of the patients, 15 were L type, 7 M type, 1 Mixed type, and 16 Low type. Among the 23 cases other than Low type, improvements were observed in all cases with respect to CRP, DAS28 (ESR), and CDAI within an average of 26 weeks post-administration, resulting in low disease activity or better. [Conclusions] With the increasing varieties of targeted drugs for RA and more choices available, understanding the synovial phenotype in pathology appeared to be linked to predicting the choice of an effective biologic agent.

## W43-5

**Usefulness of certolizumab pegol useful rheumatoid arthritis with high rheumatoid factor**

Takahiro Yamano[1], Kazunori Yamada[1,2], Haruka Iwao[1], Tomoyuki Sakai[1], Isao Matsushita[3,5], Hiraku Motomura[4], Toshiki Kido[5], Makoto Horita[6], Yasuo Katsuki[7], Shinichi Kato[8], Satoshi Nakazaki[8], Hiroshi Fujinaga[9], Tetsuo Watanabe[9], Masahiro Konishi[10], Ichiro Mizushima[10], Mitsuhiro Kawano[10], Takashi Murayama[8], Yasufumi Masaki[1]
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Conflict of interest: None

[Objective] Rheumatoid factor (RF) binds to the Fc region of biological DMARDs and may attenuate the drug's effects. We investigate whether certolizumab pegol (CZP), an anti-TNF alfa antibody without Fc region, is effective in patients with high RF. [Methods] Patients who received TNF inhibitor at least once from the database of the Fukui Ishikawa Toyama Database of Rheumatoid Arthritis, a multicenter study in Hokuriku region, were included. The reduction in DAS28CRP and percentage of responders in the EULAR response criteria at 3 months after initiating treatment were compared between the CZP and non-CZP groups. Statistical software is EZR, and Mann-Whitney U test and Fisher's exact test were used. [Results] There were 288 patients who received TNF inhibitor at least once, and 61 patients were in the CZP group. Using propensity score matching, although the reduction in DAS28CRP was not different between the two groups, the CZP group showed a significant decrease in DAS28CRP compared to the non-CZP group in the group with high RF (RF>200 IU/mL) (p=0.006). All patients with high RF in the CZP group are responders. [Conclusion] CZP may be more effective than other TNF inhibitors in patients with high RF.

## W43-6

**Analysis of changes in Antigen specific ACPA Antibody Titers and Response to Therapy -from the result of ORIJIN study, a multicenter prospective observational study of Japanese patients with active Rheumatoid arthritis newly treated with abatacept (ABT)**

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Conflict of interest: Yes

[Objective] To investigate the relationship of the treatment response and changes in specific ACPA antibody titer in the patients with active RA newly treated with abatacept (ABT). [Methods] Patients with active RA scheduled to receive ABT were prospectively observed at 8 centers, and disease activity was evaluated. The antibody titers were measured using a 13 types of citrullinated antigen peptides custom multiplex bead array (MagPlexTM). The relationship between therapeutic response and antibody titer was investigated. [Results] The SDAI remission rate after ABT administration in 92 patients was 22.8% and 29.3% at 12 and 24 months, respectively, and the rate of achieving low disease activity (SDAI < 11) was 64.1% and 74.7% at 12 and 24 months, respectively. The continuation rates of ABT at 12 and 24 months were 84.8% and 65.2%, respectively. Antibody titers to citrullinated fibrinogen (Fibrinogen A 211_230) at 12 and 24 months in the low disease activity achievement group (364.7 ± 585.2, 249.6 ± 308.1) were significantly lower compared with the non-remission group (961.1 ± 1330.7, 1074 ± 1423.1) ($p < 0.05$, Wilcoxon signed rank test). [Conclusions] The antibody titers against citrullinated fibrinogen may be related to the therapeutic efficacy of ABT, and further studies are needed.

## W44-1

**Therapeutic effect of rituximab on skin symptoms of systemic sclerosis ~Up to 4 years~**

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Conflict of interest: None

[Objective] In September 2021, the indication for RTX was expanded to SSc. Our department has previously treated patients with diffuse skin sclerosis SSc (dcSSc), who have rapidly progressing skin sclerosis and are complicated by PH and ILD from an early stage, with a high risk of affecting life prognosis, using RTX. The study was approved by the ethical review committee and informed consent was given. We retrospectively examined the course of skin hardening, including cases in which RTX was started after the expansion of indications. [Methods] 14 SSc patients met the 2013 ACR/EULAR classification criteria, 7 males and 7 females. The disease type was dcSSc in 13 cases and lcSSc in 1 case. Average age was 53.3 ± 21.1 years. Disease duration was 7.8 ± 9.1 years. TSS was 23.7 ± 8.2. [Results] TSS was 14.6 ± 10.0 (n = 14) after 1 year from the start of RTX administration, 12.8 ± 8.9 (n = 12) after 2 years, and 10.6 ± 8.3 (n = 7) after 3 years from the start. There was a significant decrease in TSS. Four years have passed for the three. Two of them had a relapse and their TSS increased to 15.0±11.5. [Conclusions] RTX may be more effective in younger patients. It is necessary to accumulate more cases to determine which conditions are more appropriate for the use of RTX.

## W44-2

**Characteristics of patients with systemic sclerosis with dysphagia**

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Conflict of interest: None

[Objective] To determine the prevalence of dysphagia in SSc and the association with clinical features. [Methods] SSc patients examined by videofluoroscopic swallowing study (VFSS) were consecutively involved. Presence of esophageal (E), pharyngeal (P) and gut involvement (G) were defined by VFSS, respectively. Dysphagia was also identified by the existence of residue by VFSS and aspiration and/or penetration evaluated by the Penetration Aspiration Scale (PAS). Univariate and multivariate analysis were examined to extract the risk factors. [Results] Fifty SSc were enrolled. Based on the PAS, 42% were with penetration, 4% with aspiration, and 54% those without. By uni- and multivariate analysis, aspiration/penetration was associated with pharyngeal ($p<0.02$) and esophageal residue ($p<0.01$), diarrhea ($p<0.01$), and UCLA GIT-2.0 ($p<0.05$). In GI involvements, P was found in 82%, 98% of P had E and 54% of P had G. Interestingly, the E+P+G+ group was younger onset ($p<0.03$), frequently found with aspiration and/or penetration ($p< 0.01$) and with higher UCLA GIT-2.0 ($p<0.01$) compared with E+P+G- group. [Conclusions] Dysphagia is not an independent GI component and can find in half of SSc patients. GI involvement seem to start from pharyngeal and/or esophageal lesions and then reach to gut lesion.

## W44-3

**Abnormal Laboratory Findings at the Onset of Scleroderma Renal Crisis**

Hiromitsu Akamatsu, Anri Mori, Megumi Ikeda, Kaho Hayashi, Hiroaki Saito, Akira Sakata, Hiroyoshi Yanagisawa, Fumitaka Yamamori, Akihiko Koshino, Hajime Sanada, Daiki Hayashi, Taichiro Minami, Yoshinori Takahashi, Shunsuke Tsuge, Shiori Nakagawa, Megumi Oshima, Keisuke Horikoshi, Ryo Nishioka, Takahiho Yuasa, Todashi Toyama, Akinori Hara, Kiyoaki Ito, Shinji Kitajima, Ichiro Mizushima, Sakai Norihiko, Miho Shimizu, Mitsuhiro Kawano, Yasunori Iwata, Takashi Wada
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Conflict of interest: None

(Objective) This study evaluated the clinical findings at the onset of scleroderma renal crisis (SRC) and investigated the frequency of each finding that are considered typical. (Methods) Clinical findings at the onset of SRC were collected in 15 patients with SRC diagnosed at our hospital between October 2007 and July 2023. Various laboratory data considered as typical were investigated. (Results) Of 97 SSc patients, 15 (16%) developed SRC. Hypertension was present on admission in 80% of cases; both PRA and PAC exceeded upper limit of normal in 67% of cases. All patients had elevated LDH. Hp was decreased in 87% of cases, while 13% had fragmented red blood cells. Total bilirubin was elevated in 20% of patients, indirect bilirubin in 50%. Urinary protein to creatinine ratio (g/gCr) >1.0 was observed in 53%, urinary β2-microglobulin in 100%, urinary NAG in 53%. (Conclusion) Since SRC cannot be ruled out even with normal PRA and PAC and normal bilirubin, and fragmented red blood cells are not seen in most cases, SRC should remain in the differential diagnoses even with these negative findings.

## W44-4

**Clinical characteristics of 6 cases of systemic sclerosis with lower extremity amputation**

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Conflict of interest: None

[Objective] Microangiopathy causing digital ulcer and various skin manifestations is one of the major pathogenic factors in systemic sclerosis (SSc), while we experience cases with severe ischemia, leading to lower extremity amputation. We analyzed the clinical characteristics to identify the risk factors for lower extremity amputation in SSc. [Methods] Retrospective analysis was performed of 6 cases of SSc with lower extremity amputation in our hospital. [Results] All cases were female. Five cases were limited cutaneous SSc with anticentromere antibody (ACA), and one case was diffuse cutaneous SSc with anti-topoisomerase I antibody. Disease duration from onset to amputation was 20.3 years. Five cases had pulmonary arterial hypertension (PAH). Risk factors for peripheral arterial disease (PAD) included hypertension in 6 cases, dyslipidemia in 4 cases, and diabetes mellitus in 2 cases. Contrast-enhanced CT of the lower extremity showed severe stenosis in the tibial artery region in all cases. [Conclusions] Risk factors for amputation included positive ACA, complications of PAH, and risk factors for atherosclerosis. All cases showed severe stenosis in the tibial artery region, a feature different from PAD which mainly affects the femoral and iliac arteries.

## W44-5

**The impact of anti- survival of motor neuron (SMN) complex antibodies on classification of the disease severity in patients with mixed connective tissue disease (MCTD)**

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Conflict of interest: None

[Objective] We reported the detection of anti- SMN complex antibodies (Abs) in some patients with MCTD. Aim of this study is to evaluate the impact of anti- SMN complex Abs on classification of the disease severity in MCTD patients. [Methods] 70 newly diagnosed consecutive cases of MCTD were enrolled. Serum anti-SMN complex Abs were screened by immunoprecipitation of 35S-methionine-labeled cell extracts, and associations between anti-SMN complex Abs and clinical characteristics were analyzed. [Results] Anti-SMN complex Abs were detected in 36% (25/70). Anti-SMN complex Abs-positive MCTD had a higher prevalence of pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) than negative patients. In the MCTD severity classification defined by ministry of health, labour and welfare, most anti-SMN complex Abs-positive cases were classified as ‘severe’ (80%, 20/25), and almost all (24/25) were ‘moderate’ or higher group to be eligible for benefits. In contrast, half (49%, 22/45) of the negative cases were classified as ‘mild’. Moreover, all

three cases of death within 1 year of the treatment were positive for anti-SMN complex Abs. [Conclusions] Anti-SMN complex Abs are associated with PAH and ILD, and might be useful in predicting severity and prognosis in MCTD.

## W44-6

**The effects of immunosuppressants and pulmonary vasodilators used in the treatment of collagen disease-complicated pulmonary hypertension (CTD-PH) on serum pulmonary hypertension biomarkers**

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Conflict of interest: None

[Objective] To clarify the effects of immunosuppressants (IS) and pulmonary vasodilators (PV) used in the treatment of collagen disease-associated pulmonary hypertension (CTD-PH) on serum PH biomarkers that we have reported. [Methods] Patients suspected of PH and who underwent bicardial catheterization at our facility from 2015 to 2021 were included. Serum was collected from the pulmonary artery and vein at the time of the procedure using a bicardial catheter, and the biomarkers IIL-6, IL-17, IL-12p70, MCP-1 (Ella simple plex), IL-21, and TIMP-1 (ABCAM). was measured by ELISA. The therapeutic effect was evaluated by hemodynamics, WHOFC and RHC. [Results] 56 cases (33 CTD and 23 non-CTD), and 12 CTD-PH and 3 nonCTD-PH in which follow-up RHC was performed after intervention with IS and PV were included. In PH, IL-6 levels were positively correlated with mPAP and WHOFC severity. IL-6 decreased in PH when PV were administered, but there was no change when IS were administered. TIMP-1 was elevated in CTD-PH, especially in SSc. TIMP-1 decreased with additional administration of IS. No changes were observed in either group with PV. [Conclusions] IL-6 reflects the hemodynamics of PH and decreases with improvement with PV. The effects of IS are reflected in change of TIMP-1 rather than IL-6.

## W45-1

**Survey and review of the treatment content, disease activity, and maternal and infant outcomes during the perinatal period for pregnant and childbirth rheumatoid arthritis (RA) patients, 2nd report ~ Analysis by Kansai multicenter ANSWER cohort ~**

Yuri Hiramatsu[1], Eri Nakamura[1], Ayaka Yoshikawa[1], Yumiko Wada[1], Hideyuki Shiba[1], Takuya Kotani[1], Motomu Hashimoto[2], Akira Onishi[3], Kosaku Murakami[4], Masaki Katayama[5], Yonsu Son[6], Hideki Amuro[6], Ryota Hara[7], Toru Hirano[8], Yuichi Maeda[9], Kosuke Ebina[10], Wataru Yamamoto[11], Tohru Takeuchi[1]
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Conflict of interest: None

[Purpose] To investigate and examine differences in treatment content, disease activity, and maternal and infant outcomes in RA patients who have become pregnant and given birth. [Methods] From the Kansai multicenter ANSWER cohort database, we investigated treatment details, disease activity, and maternal and infant outcomes before, during, and after pregnancy in women with RA who gave birth between 2013 and 2023. [Results] A total of 131 cases had live births. The age at delivery was 34.5 years. Term delivery was 92.8%, average delivery week was 39 weeks, and baby weight was 2949 g. Disease activity remained in remission during pregnancy and postpartum in 44% of cases, but disease activity tended to increase after the second trimester in other cases. Regarding treatment before and during pregnancy, 42% and 35% of cases used csDMARD, 39% and 55% used corticosteroids, and 48% and 35% used bDMARD. In cases where bDMARDS was continued even after pregnancy was confirmed, disease activity after the second trimester was significantly lower. Regarding the safety of therapeutic drugs, No poor outcomes were observed. [Conclusion] In RA pregnancies, the content of treatment before pregnancy and in the early stages of pregnancy is related to the activity during pregnancy and after birth.

## W45-2

**Improving clinical collaboration through the Joint Meetings on Pregnancies Complicated by Rheumatic Diseases**

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Conflict of interest: None

[Objective] To improve collaboration between rheumatologists and obstetricians in the management of pregnancies complicated by rheumatic diseases, we initiated joint meetings for information exchange and education of junior doctors. [Methods] Monthly meetings were held at a tertiary centre in FY2022, using a hybrid format due to COVID-19 pandemic. Agendas included delivery reports, pregnancy discussions, infertility case troubleshooting, and improving interdepartmental collaboration. An end-of-year questionnaire assessed the impact of the meetings. [Results] In FY2022, 16 deliveries, 108 pregnancies and 9 infertility cases were discussed in total. No major pregnancey adverse outcomes occurred, with two healthy preterm births. Collaborative improvements included standardised steroid cover and aspirin prescription protocols. Post-meeting surveys showed that 68.4% improved understanding and 94.7% improved collaboration, leading to bi-directional mini-lectures in FY2023. [Conclusion] The meetings improved interdepartmental communication, with ongoing sessions likely to improve mutual understanding and quality of patient care.

## W45-3

**A survey of the status and understanding of pregnancy and childbirth of WoCBA-RA patients**

Ayako Wakamatsu[1], Hiroe Sato[3], Yasufumi Kijima[2], Yoichi Kurosawa[1], Yukiko Nozawa[3], Daisuke Kobayashi[1], Naoki Kondo[2], Takeshi Kuroda[3], Ichiei Narita[1]
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Conflict of interest: None

[Background] Preconception care is important in WoCBA-RA, but unmet needs are not clear. [Methods] We investigated pregnancy and delivery in RA women aged 18 to 45 years old of our hospital. Pregnancy and delivery courses were collected from the medical records. [Results] We evaluated 30 cases. The onset of RA was 27 (22-33) years old [median (quartile)], 11 patients (37%) gave birth after RA onset, childbirth age was 36 (31-37) years old, and 7 (3-9) years had passed since the onset of RA. They were concerned about the effects of medication (73%), heredity (57%), RA itself (53%) on their children, and the inability to raise their children (50%). Some patients lacked basic knowledge; for example, pregnancy and delivery were possible for RA (7%), planning pregnancy is necessary (13%), and RA progression during pregnancy is better if RA activity was suppressed before pregnancy (37%). After childbirth, worsening of RA was observed in 9 cases (82%), and many of them said that childcare was difficult due to pain. [Conclusion] WoCBA-RA patients were more anxious about pregnancy, childbirth and childcare than the medical staff thought. It was necessary to provide repeated information to the patients, including their families, from an early stage in cooperation with obstetricians.

## W45-4

**How are rheumatoid arthritis patients' desires for conception shifting in accord with advances in treatment?**

Ryo Inoue, Sakiko Isojima, Chika Sasakura, Yuko Inoue, Yoko Miura, Mika Hatano, Takahiro Tokunaga, Nobuyuki Yajima
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Conflict of interest: None

[Objective] In this study, we evaluated changes in attitudes toward pregnancy among female rheumatoid arthritis patients of childbearing age using a questionnaire. [Methods] In a cross-sectional study using NinJa2020, a database of rheumatoid arthritis patients, we administered a questionnaire to women aged 50 years or younger regarding changes in the desired number of children due to the onset of rheumatoid arthritis. The proportions of respondents who reported a decrease were compared by the time of onset of disease and by age of onset of disease. The reasons for the decrease were also evaluated. [Results] The analysis was conducted on 280 subjects. The number of patients who reported a decrease was 57% (20/35) for onset before 2000, 47% (63/133) for onset 2001-2011, and 35% (39/112) for onset after 2012. As for the reasons for the decrease, while there was less restraint by physicians and family members, opinions such as "I am worried about to take care of my child" and "I am worried about the effects of the medication on my child" remained. [Conclusion] The decrease in restraints by physicians and family members has had a positive impact on the retention of desire to conceive.

## W45-5

**The current state of fertility treatment and pregnancy outcomes of women complicated with Rheumatoid arthritis or Systemic lupus erythematosus in a single center**

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Conflict of interest: None

[Objective] We analyzed pregnancies with Rheumatoid arthritis (RA) or Systemic lupus erythematosus (SLE), and clarified the current state of fertility treatment and pregnancy outcomes. [Methods] Patients with RA or SLE who were managed from pregnancy planning to delivery from 2007 to 2023 were enrolled. We retrospectively investigated the patients' clinical characteristics, disease activity, treatment agents and pregnancy outcomes. [Results] 36 pregnancies with RA and 41 pregnancies with SLE were analyzed. 11 pregnancies (30.6%) with RA and 5 pregnancies (12.2%) with SLE were established through fertility treatment. The mean time to pregnancy was 11.2±11.1 months in the RA group and 9.1±12.2 months in the SLE group, with no significant difference. The time from trying to conceive to infertility treatment was 5.1±2.9 months in the RA group and 16.8±18.9 months in the SLE group, which was shorter in the RA group (p=0.086). There were no significant differences in age, fertility treatment, or disease activity between fertility treatment and natural pregnancy. [Conclusions] Patients with RA tended to have higher rates of infertility treatment, and they started infertility treatment in a shorter period of time. Further study is needed to determine which patients need fertility treatment.

## W45-6

**Effects of cyclophosphamide administration on ovarian dysfunction in pediatric patients - a systematic review**

Ken-ei Sada[1,2], Takako Miyamae[2,3], Kayoko Kaneko[2,4], Sakiko Isojima[2,5], Kunihiro Ichinose[2,6], Masakazu Matsushita[2,7], Kenji Oku[2,8], Yasunori Iwata[2,9], Keishi Fujio[2,10], Atsuko Murashima[2,11], Ayako Nakajima[2,12], Yoshiya Tanaka[2,13]
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Conflict of interest: None

[Objective] This systematic review aims to assess the effect of cyclophosphamide (CY) administration during childhood on ovarian function in patients with juvenile-onset collagen disease. [Methods] A comprehensive search of the MEDLINE database was undertaken to evaluate relevant literature. [Results] The search, conducted on July 22, 2023, yielded 464 references. After a two-stage screening process, four observational studies focusing on patients with systemic lupus erythematosus were included for assessment. One study found a significant association between CY use and elevated FSH levels indicating ovarian dysfunction (risk ratio: 2.8, 95% confidence interval: 1.7-4.8), while another study found no significant difference in menstrual disorders or amenorrhea with or without CY use. Three studies evaluated FSH levels as an indicator of ovarian dysfunction, two of which reported statistically significant higher in the CY group. None of the studies were adjusted for confounding factors, largely due to limited sample sizes. [Conclusions] Despite limitations including the observational nature of the studies, the results indicate that CY administration in childhood may potentially impact future ovarian function.

## W46-1

**Similarities and differences of cytokine profiles and macrophage activation in patients with anti-MDA5 antibody-positive dermatomyositis, SLE, and adult-onset Still's disease**

Tomoka Hiyama, Kazuhiro Kurasawa, Rika Sato, Yuki Aizawa, Yuhi Yoshida, Anna Hasegawa, Tomoyuki Miyao, Ayae Tanaka, Satoko Arai, Reika Maezawa, Masafumi Arima, Kei Ikeda
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Conflict of interest: None

[Objective] To clarify macrophage-activating mechanisms in patients with anti-MDA5 antibody (MDA5) by comparing cytokine profiles between MDA5, SLE, and adult-onset Still's disease (AOSD). [Methods] The study participants included 39 patients with MDA5, 31 with SLE (9 macrophage activation syndrome [MAS]), and 22 with AOSD (9 MAS). Serum cytokine levels before starting treatment were measured using a multiplex assay. [Results] IL-6, IL-8, IL-10, IL-18, and TNF-alpha were elevated in MDA5, AOSD, and SLE compared to controls; IP-10 was increased in MDA5; IFN-alpha was high in SLE, particularly in MAS; and IL-18 and ferritin were markedly elevated in AOSD. Cluster analysis showed two clusters, AOSD and SLE/MDA5, and the latter was further divided into SLE and MDA5. The principal component analysis also revealed that MDA5 had a cytokine pattern similar to SLE, which differed from AOSD. Ferritin levels were correlated with IFN-alpha and IP-10 in SLE, with IL-6, IL-8, IL-10, IL-18, and TNF-alpha, in addition to IFN-alpha and IP-10 in MDA5, but with no cytokines in AOSD. [Conclusions] Cytokine profiles of MDA5 differed significantly from AOSD and had some similarities to SLE, suggesting different macrophage activating-mechanisms between MDA5, SLE, and AOSD.

## W46-2

**Efficacy and safety of nintedanib in progressive fibrosing interstitial lung disease in patients with connective tissue diseases**

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of NTN in CTDs patients with ILD in our institute. [Methods] Thirteen patients with CTDs who had received concomitant NTN for relapse of ILD in our department by September 2023. Patients were prospectively followed up according to the examination schedule, and KL-6, SP-D, %VC, and K-BILD scores were analyzed at 24 months. [Results] The mean age was 59.3±15.1 years, 4 males and 9 females. Steroid dosage at baseline was 11.1±13.4 mg/day of prednisolone (PSL) equivalent, KL-6 was 1404.0±1244, SP-D was 147.0±98.8 ng/ml, %VC was 70.3±14.9%, and K-BILD score was 72.1±21.1. At 24 months after NTN commencement, the dose of PSL was 5.3 ± 2.6 mg/day, KL-6 was 1096.4 ± 1175.9, SP-D was 137.3 ± 63.2 ng/ml, %VC was 78.2 ± 18.2%, and the K-BILD score was 74.8 ± 18.6. Although there were no significant change from the baseline in each items, PSL dose and %VC were slightly improved. Adverse events were observed in 8 patients. [Conclusions] This study will suggest that concomitant NTN might enable to reduce the dose of PSL and prevent progression of ILD.

## W46-3

**The effectiveness of Nintedanib in preventing progression of PF-ILD based on CT image analysis**

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Conflict of interest: None

[Objective] Nintedanib (NTB), anti-fibrotic drug, has recently been approved for progressive fibrosing-interstitial lung disease (PF-ILD) and widely used for various kinds of ILD including connective tissue diseases (CTD)-ILD. However, the evidence of effectiveness of NTB for PF-ILD has still been unclear. We aimed to unveil the effectiveness for prevention of progression of ILD based on CT image analysis. [Methods] Twenty-one PF-ILD patients in our hospital, who continued NTB over one year and performed CT at least 3 times, were enrolled. We assessed the annual changes of CT scores and the relationships with patients' data. [Results] KL-6, SP-D and oral corticosteroid dose were significantly reduced in a year. The progression speed of ILD was significantly decreased after the start of NTB. Female sex and diarrhea as adverse drug reaction were significantly shown to be good factors for the slowly progressive ILD. Multivariate analysis revealed female sex was the only significant factor. [Conclusions] It was suggested that NTB was effective for preventing progression of PF-ILD, especially in female patients.

## W46-4

**Low-dose Nintedanib for Autoimmune Disease-Related Progressive Fibrosing Interstitial Lung Disease: A Case Series**

Takeshi Kawaguchi[1,2], Haruka Sasaki[1], Risa Kudo[1], Masatoshi Kimura[1,2], Yuki Rikitake[1,2], Kosho Iwao[1], Ayako Aizawa[1], Yumi Kariya[1], Motohiro Matsuda[1], Shunichi Miyauchi[1], Ichiro Takajo[1,2], Kunihiko Umekita[1]
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Conflict of interest: None

[Objective] In INBUID trial, nintedanib (NTD) at doses of 200-300 mg/day was effective in reducing the rate of decline in forced vital capacity (FVC) in patients with progressive fibrosing interstitial lung disease (PF-ILD). However, the efficacy of doses < 200 mg/day has not been proven. We aimed to summarize the clinical characteristics of patients treated with low-doses of NTD. [Methods] Patients with autoimmune disease-related PF-ILD treated with low-doses of NTD at our department from January 1, 2020 to September 30, 2022 were enrolled. We retrospectively examined the patient's clinical characteristics. [Results] NTD was started in 22 patients, of whom the dose was reduced to < 200 mg/day in 3 patients and discontinued in 2 patients. The causes of dose reduction were diarrhea and weight loss, and the causes of discontinuation were liver damage and colonic diverticulum perforation. Two patients received low-dose treatment for 22 months, one patient for 10 months, and all 3 patients are still on treatment. Two patients had increased FVC and decreased KL-6. In one case, FVC, KL-6, and clinical symptoms worsened. [Conclusions] In cases whom the usual dose of NTD cannot be continued, it may be possible to continue at low-dose, which may prevent a decline in respiratory function.

## W46-5

**Treatment experience with nintedanib for connective tissue disease-associated interstitial lung disease**

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Conflict of interest: None

[Objective] In this study, we retrospectively investigated the use of nintedanib for connective tissue disease-associated interstitial lung disease (CTD-ILD). [Methods] Between January 2020 and March 2023, we studied 17 patients with CTD-ILD who had started nintedanib and had been treated for at least 6 months (female 70.6%, age 62.1±11.3 years) to determine patient characteristics, their treatment status, continuation rate, and adverse events. [Results] Underlying diseases were systemic sclerosis in 6 patients, Sjögren's syndrome in 6 patients, anti-ARS antibody syndrome in 4 patients, rheumatoid arthritis and SLE in 2 patients each, and serum KL-6 at induction of nintedanib was 1054 (623, 2045) U/mL, %FVC 74.8 (62.7, 82.9) and %DLCO 53.6 (45.5, 61.9). The rate of continuation of treatment for more than 1 year was 76.5%. KL-6 levels decreased by more than 20% in 7/13 patients (53.8%) when assessed 6-12 months after the start of nintedanib treatment. The dose of nintedanib was 150 mg/day or less in 9/17 patients (52.9%). [Conclusions] Nintedanib was used in CTD-ILD patients of decreased FVC or DLCO, and approximately half of the patients achieved a decrease in KL-6 after administration, but many patients required dose adjustment due to diarrhea or gastrointestinal symptoms.

## W46-6

**Nintedanib usage status in our hospital and attempts to improve nintedanib continuation rate**

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Conflict of interest: None

[Purpose] Understand the status of NTB usage in our hospital and take steps to improve the continuation rate. [Results] We investigated the continuation rate of 65 cases (CTD: 23 cases, Non-CTD: 42 cases) who used NTB at our hospital by April 2023, and found that CTD: 56.5%, Non-CTD: 83.3%. The continuation rate was poor for CTD. In addition, the incidence of side effects was higher in CTD, 65.2% in CTD and 21.4% in non-CTD. The breakdown of side effects was mainly gastrointestinal symptoms, with diarrhea: 73.3%, nausea/vomiting: 60%, and when examined by disease, most were SSc cases. In May 2023, we established a team medical system consisting of doctors, nurses, pharmacists, and rehabilitation departments, and began introducing NTB or providing side effects education and hospitalization. As of September 2023, we have provided introductory training to 6 patients, and it has become easier for patients and medical professionals to share the points that patients are concerned about regarding NTB use, and consultations tailored to individual circumstances are available for continued use. became possible. [Conclusion] Understanding side effects is important for continuing NTB. We will also report on comments from patients and healthcare workers after the introduction.

## W47-1

**100 cases of new onset autoimmune diseases after COVID-19 vaccination in Japan**

Junki Hiura[1], Yusuke Kashiwado[2], Yasutaka Kimoto[3], Masahiro Ayano[3], Hiroki Mitoma[2], Nobuyuki Ono[3], Yojiro Arinobu[3], Hiroaki Niiro[4], Takahiko Horiuchi[5]

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Conflict of interest: None

[Objective] To elucidate the clinical features of new onset autoimmune diseases after COVID-19 vaccination in Japan. [Methods] Questionnaire were sent to 614 departments of rheumatology, all educational facilities of Japan College of Rheumatology (JCR). Clinical information, including background of patients, diagnosis, vaccine type, timeline of onset, symptom, treatment, and outcome, were collected by the questionnaire. [Results] 100 patients were reported in survey. 61% were women, and the mean age was 64.6 years. Rheumatoid arthritis (27 cases) was the most common disease, followed by ANCA-associated vasculitis (19 cases), idiopathic inflammatory myopathies (11 cases), polymyalgia rheumatica (11 cases), and systemic lupus erythematosus and adult onset still's disease (6 cases each). Onset of disease occurred after the first vaccination in 44% of cases, with an average of 7.0 days from vaccination to onset of disease after the first vaccination and 8.8 days after the second vaccination. Joint symptoms were present in 64%, skin symptoms in 23%, pulmonary symptoms in 20%, and muscle symptoms in 19%. Glucocorticoids were used in 81% of cases. [Conclusions] We characterized rheumatic diseases after SARS-CoV2 vaccination.

## W47-2

**Should methotrexate be discontinued during COVID-19 vaccination for patients with rheumatoid arthritis?**

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Conflict of interest: Yes

[Objective] ACR recommended suspension of MTX during COVID-19 vaccination (Vac) to RA patients. We investigated the relationship between MTX use and antibody production. [Method] From 445 RA patients (72 y) and 30 controls (C) (71 y), anti-spike protein antibodies (S titers) and anti-nucleotide antibodies (N titers) were measured. [Results] The analysis was performed on 381 patients, excluding N positive subjects (86 RA, 8 C) as previously infected. The median number of Vac in both groups was 5, and the median S titer was 4190 [IQR; 1250, 10400] U/ml in RA and 6490 [2487.5, 12175] in C (p=0.296). The RA included 52 (14.5%) biologics (Bio) users and 29 (8.1%) JAK inhibitor (JAKi) ones, with MTX use rate of 82.5% and a dose of 10 [8.0, 12.0] mg/week. Therefore, when comparing the S titer between C, RA using Bio/JAKi, and RA without Bio/JAKi, the RA with Bio/JAKi showed significantly lower S titers. (1910 [26.1, 5105], p=0.002 vs C, p<0.001 vs Bio/JAKi non-RA). Multiple regression analysis showed that Bio/JAKi use (β; -0.129, p=0.013), number of Vacs (β; 0.143, p=0.015), and days since last Vac (β; -0.197, p=0.001) were extracted as a significant factor, but MTX dosage was not (β; 0.057, p=0.273). [Conclusion] There is no need to interrupt MTX when administering Vac to RA patients.

## W47-3

**Analysis of risk factors related to severe COVID-19 in patients with rheumatic diseases**

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Conflict of interest: None

[Objective] The aim of this study is to analyze the risk factors related to severe COVID-19 in patients with rheumatic diseases. [Methods] We conducted a retrospective study of COVID-19 patients admitted to our division, and those who were confirmed to have developed COVID-19 in outpatients between February 2020 and October 2023. [Results] A total of 75 patients were included in the study, among whom 32 patients were hospitalized, two were diagnosed with COVID-19 in outpatients of our division, and 41 were diagnosed in other hospitals. 76% of them were female, and the median age was 61. Except for one case, all patients developed COVID-19 after January 2022, when the Omicron variant became predominant. 57 patients were asymptomatic or mild, and 16 were moderate or severe, two were critical. Two patients died from interstitial pneumonia and perforation of the small intestine. In univariant analysis, risk factors for moderate disease or higher were male (p<0.001) and unvaccinated (p=0.04). In hospitalized patients, lactate dehydrogenase was significantly higher in the group with moderate disease or higher (p=0.04). [Conclusions] Most of the COVID-19 patients with rheumatic diseases had favorable outcomes. Male and unvaccinated patients were associated with severe diseases.

## W47-4

**Clinical characteristics of autoimmune diseases that developed or worsened after the COVID-19 vaccination**

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Conflict of interest: None

[Objective] To characterize autoimmune diseases that developed or worsened after the COVID-19 vaccination. [Results] Forty-eight cases were identified, with an age of 65.0±17.6, male-to-female ratio of 20:28, and Pfizer: Moderna: unknown ratio of 30:8:10. The name of autoimmune diseases were as follows: 13 patients with vasculitis syndrome (4 MPA, 2 GPA, 2 IgA vasculitis, 3 unclassifiable, 1PN, 1Takayasu arteritis), 10 with RA (6 negative, 4 positive of RF/ACPA) and 3 exacerbations of RA, 4 with PM/DM, 4 with ITP, 3 with RS3PE, 3 with PMR, 3 with exacerbation of interstitial pneumonia, and others. Five patients had a family history of autoimmune diseases, 23 had mild, 12 moderate, and 13 severe in disease activity. 28 patients were hospitalized, requiring moderate to high dose steroids, and death occurred in 5 patients. Seven cases were untreated with remission at the last observation. [Conclusion] autoimmune diseases that developed after COVID-19 vaccination were particularly affected by vasculitis, arthritis, myositis, and thrombocytopenia. Some cases responded well to treatment, but moderate, severe, and fatal cases were also observed. This study suggests the importance of active questioning and careful observation of vaccination history.

## W47-5

**Vaccination rate, adverse reactions and reasons for non-vaccination of COVID-19 vaccine in patients with rheumatoid arthritis up to fifth dose**

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Conflict of interest: Yes

[Objective] To know the vaccination rate, adverse reactions, and reasons for non-vaccination of COVID-19 vaccine in RA patients. [Methods] We investigated the vaccination rate, systemic adverse reactions, and reasons for non-vaccination in RA patients up to five vaccines. [Results] Information was obtained for 501 cases. Patient background: Mean age 66.5 years, female 372 cases, RA duration 14.2 years. The vaccination rate was 6.8% for non-vaccination, 93.2% for the 1st dose, 88.4% for the 3rd dose, and 47.9% for the 5th dose. Non-vaccination was observed in 13.9% of those aged 0-64, 7.5% of those aged 65-74, and 1.3% of those aged 75. Regarding the declining trend in the vaccination rate, 88.9/95.3/96.4% for the 1st dose, 81.1/91.2/95.0% for the 3rd dose, 25.3/59.6/64.3% for the 5th dose among 0-64 years old/65-74 years old/75 years old and over and

98.7/80.6% for the 1st dose, 97.2/68.1% for the 3rd dose, 62.5/21.5% for the 5th dose among influenza vaccine recipient/non-recipient. Adverse events occurred in 9.2% in the 1st dose, 15.0% in the 2nd dose, 19.4% in the 3rd dose, 16.5% in the 4th dose, and 12.9% in the 5th dose. [Conclusions] COVID-19 vaccination rate has been steadily declining in patients with RA and is influenced by age or patients' perspectives to vaccine.

## W47-6

**COVID-19-related osteonecrosis of the femoral head**

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Conflict of interest: None

[Objective] We report six cases of osteonecrosis of the femoral head (ONFH) following COVID-19 infection treatment. [Methods] We evaluated six cases eight hips of ONFH following COVID-19 infection recovery. [Results] All the patients were hospitalized due to respiratory problems and received corticosteroid (CS) treatment. The total dose of CS administered was 264-795/mg, which is equivalent to prednisolone. Further, the femoral head collapsed 2-15 months later. Five of the six patients had total hip arthroplasty. [Conclusions] Given the possibility of ONFH development, a careful examination is required for the patient complaining of pain around the hip joint after treatment with COVID-19.

## W48-1

**A Study of Satisfaction with Life in General and with Life in Rheumatoid Arthritis Patients-Intergenerational Differences in Unmet Medical Needs as a Factor for Decreased Satisfaction-**

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Conflict of interest: None

[Introduction] This study reports on a survey of factors associated with human life satisfaction in outpatient RA patients. [Methods] 75 RA patients 55.4 (16.0) attending an outpatient clinic were included in the study, and their human life satisfaction were assessed by NRS. The desired treatments to improve satisfaction and whether these treatments were discussed with the patients were investigated. The results were compared between generations in terms of age, duration of disease, SDAI, DAS28 CRP, and HAQ. [Results] There were no differences in satisfaction between generations. Even when patients were in remission, 69% of them requested enhanced drug therapy and 27% requested enhanced rehabilitation. There was a difference in the desired rehabilitation, such as the promotion of social activities in young and middle-aged patients and the maintenance of ADLs in elderly patients. However, many patients were not able to discuss their needs with anyone other than their physicians. [Discussion] Management of disease activity alone does not increase life satisfaction of RA patients. It is necessary to respond to the different unmet medical needs of different generations, such as younger and older age (social activities) and older age (ADL maintenance), by multiple disciplines.

## W48-2

**The Effect of Different Drug Treatments on Skeletal Muscle Mass in Rheumatoid Arthritis**

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Conflict of interest: None

Objective RA is the largest contributor to secondary sarcopenia. We investigated the effect of different drug treatments on skeletal muscle is significant in RA patients. Methods Eighty-one RA patients were included in the study. The treatment groups were divided into TNF inhibitor group (TNF group), IL-6 inhibitor group (IL-6 group), T cell selective co-stimulation group (ABT group), JAK inhibitor group (JAK group), and no b/tsDMARDs treatment group (no treatment group). Skeletal muscle index (SMI) over a one-year period were compared using analysis of variance. Results The mean average age of the patients was 70.8 years, and the mean number of patients by drug treatment was 19 in the TNF group, 11 in the IL-6 group, 18 in the ABT group, 10 in the JAK group, and 23 in the no group. The mean SMI values before and after the study were 5.75/5.37 in the TNF group, 5.66/5.55 in the IL6 group, 5.55/5.62 in the ABT group, 5.49/5.57 in the JAK group, and 6.02/6.19 in the no group. Conclusions The SMI changes were different in each drug treatment. Differences in the mechanism of action of drug therapy affected inflammatory cytokines such as TNF and IL-6, which may have some effect on skeletal muscle.

## W48-3

**Incidence and risk factors of falling in ambulatory patients with rheumatoid arthritis: a prospective study for a year and comparison with 16 years ago**

Naoki Nakagawa[1,2], Keita Nagira[1], Yuta Takasu[1], Chikako Takeda[1], Masako Hayashibara[3], Hiroshi Hagino[4], Hideki Nagashima[1]
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Conflict of interest: None

[Purpose] To study frequency and risk of fall in rheumatoid arthritis (RA) patients prospectively for a year and compare it with our previous study of 16 years ago. [Methods] Among RA patients who visited our outpatient clinic from January to July 2022, 126 female patients aged 50 years and older, were included in this study and investigated the frequency of falls for one year. Anti-rheumatic drugs, disease activity, physical disability assessment (HAQ) and motor function were measured and examined their characteristics. [Results] A total of 124 patients, 90 in the non-fall group (68.2 ± 9.9 years) and 34 (27.4%) in the fall group (70.4 ± 8.9 years) were included. Differences between groups (non-fall vs. fall) were the rate and dose of corticosteroid (CS) (8.9%, 0.2 mg/day vs. 23.5%, 0.6 mg/day) and rate of taking sleeping pills (7% vs. 21%) ($p<0.05$), while multivariate analysis showed that taking sleeping pills was a risk factor for falls (OR 3.6, 95% CI 1.03-13.1, $p=0.045$). Stage, CS, disease activity, and HAQ were decreased compared to those of past study, and function was preserved. [Conclusions] These results suggest that reducing the dose of CS and the control of disease activity can prevent motor dysfunction associated with joint destruction and reduce the frequency of falls.

## W48-4

**Efficacy of locomotion training for elderly patients with rheumatoid arthritis**

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Conflict of interest: Yes

[Objective] The purpose of this study is to investigate the effects of locomotion training on physical function and disease activity in elderly patients with rheumatoid arthritis (RA). [Methods] Of the RA patients aged 60 years or older, 40 patients who were able to walk independently, remained in remission or had low disease activity for at least 6 months were instructed in locomotion training. Within 6 months of initiation, 10 patients discontinued locomotion training. The 30 participants who were able to continue locomotion training for 6 months were included in this study. The gender of the 30 patients was 2 males and 28 females, mean age was 75.9 ± 7.0 years, mean disease duration was 13.2 ± 13.2 years, and mean SDAI was 3.73 ± 2.93. Lower limb muscle strength, 10m walking time, Timed Up & Go Test (TUG), 2-step values and SDAI were evaluated. [Results] Bilateral knee extensor and hip abductor muscle strength increased significantly after 6 months compared to those at the start of the study. The 10m walking time and TUG were significantly decreased, and 2-step value significantly improved after 6 months. Patient's VAS and SDAI were significantly decreased after 6 months. [Conclusions] Locomotion training may be able to improve physical function in elderly patients with RA.

## W48-5

**Report on Makeup and Its Impact on Social Life in Patients with Rheumatoid Arthritis**

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Conflict of interest: None

Introduction However, there are RA patients who are unable to lead a full social life, and we have focused on cosmetic activities as a factor to promote social participation. In this study, we investigated the makeup application status of RA patients at home and its influence on their social participation. Methods. Sixty-four RA patients attending our hospital were included in the study. Median values of social functions of the SF-12 subscale were calculated, and the patients were divided into two groups, high value group and low value group, for statistical validation. The questionnaire was used to evaluate age, years of RA, DAS28CRP, HAQ, locomotor 25, SF-12, and cosmetic process. Results The comparison between groups showed differences in physical function, physical pain ($P<0.05$), daily role function (physical and mental), vitality, and mental health ($P<0.01$) in the HAQ, Loco 25, and SF-12 subscales. Both groups were similar in skin care, while the high group tended to have more make-up and point make-up. Discussion The results of this study suggest that reduced interaction with others may lead to a decline in physical and mental functions. Increasing opportunities to apply makeup and activating interactions with others may contribute to improving the quality of life.

## W48-6

**Online music therapy for patients with rheumatoid arthritis by using chair dance**

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Conflict of interest: None

[Objectives] We have reported that active music therapy improves general health (GH) condition and moods of patients with rheumatoid arthritis (RA). Under COVID-19 pandemic, we switched the activity to online since 2020. In this study, we investigated the effects of online music therapy by using chair dance. [Methods] Zoom online meeting system was recruited. Five songs were sung with a recorded piano accompaniment and 3 were danced sitting in a chair while watching dance videos. GH condition was evaluated by 0-10 NRS, pain by face scale, positive and negative moods, and emotional relaxation were surveyed by self-rating questionnaire including NRS, face pain rating scale, PANAS, and ERS. [Results] Seven female patients with RA were investigated. The median of HAQ-DI was 0.375. The results of before/after the activity were; GH 2.6/2.1, pain 5.9/4.6, positive affect of PANAS 24.6/27.1, and negative affect of PANAS 23.4/16.9, and four subscales of ERS were 11.0,12.4,12.3,11.0, respectively, which showed significant improvement of physical and psychological condition. Neither arthralgia nor fatigue was not induced by chair dance. [Conclusions] On line active music therapy by using chair dance improves the condition of patients with RA under COVID-19 pandemic.

## W49-1

**Clinical Features of Pustulotic Arthro-Osteitis in SPARKLE-J, a New Registry for Spondyloarthritis, Pustular arthro-osteitis and SAPHO syndrome**

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Conflict of interest: None

A new registry for spondyloarthritis, pustulotic arthro-osteitis, and SAPHO syndrome has been established by a large multicenter research group (the Ministry of Health, Labour and Welfare of Japan Research Grant for Intractable Diseases) to improve the standard of care and patient QOL for spondyloarthritis and related diseases, such as ankylosing spondylitis. Its name is SPARKLE-J (**S**pondyloarthritis, **P**AO (pustulotic arthro-osteitis), and SA**P**HO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome Registry lin**K**ed to the nationa**L** databas**E** of **J**APAN. They were 58.0±11.1 years of age, 7.6±5.7 years of duration, 49.9±10.1 years of age at onset, 86.2% female and smoking rate 20.0%. The disease activity was modified ASDAS 2.0±1.1, and the total rate of low disease activity and remission was 48.5%. The mean number of tender and swollen joints was 2.5 and 1.4, and 17.3% had enthesitis. Blood biochemical data showed positivity of CRP 41.2%, RF 15.9%, and HLA B27 0%. mHAQ averaged 0.3±0.4. Comorbidities included focal tonsils in 39.0%, dental focal infection in 22.0%. Treatment for included tonsillectomy in 21.3%, periodontal treatment in 8.6%, and tooth extraction in 3.7%. Regarding drug therapy, 57.5% used NSAIDs, 6.3% steroids, 11.3% sulfasalazine, 12.3% MTX, 23.0% biologics.

## W49-2

**Report of three cases of SAHPO syndrome in which JAK inhibitors were effective**

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Conflict of interest: None

[Objective] We report three cases in which JAK inhibitors were effective against osteoarthritis associated with SAPHO; Synovitis Acne Pustulosis Hyperostosis Osteitis syndrome. [Cases] Case 1: 64-year-old female. After diagnosis of axial arthritis accompanied by palmoplantar pustulosis, TNFα and IL-17 inhibitors were used, but due to early ineffectiveness, the patient was changed to UPA; Upadacitinib. Both back pain and skin rash improved. Case 2: 51-year-old male. After diagnosis of axial arthritis accompanied by giant acne, TNFα and IL-17 inhibitors became ineffective early, so UPA was used, and the giant acne and lower back pain quickly disappeared. Case 3: 24-year-old male. He was diagnosed with rheumatoid arthritis 15 months ago and was treated with MTX and an IL-6 inhibitor, but he developed an increased inflammatory response and severe pain in

both lower limbs. MRI of both lower legs revealed sporadic osteomyelitis, and he was diagnosed with chronic relapsing multiple osteomyelitis. With the administration of BAR; Baricitinib, he quickly noticed that his leg pain disappeared and the inflammatory response decreased. [Conclusion] Although the mechanism of action is unknown, JAK inhibitors may be highly effective treatments for SAPHO.

## W49-3

**SAPHO syndrome with Lincoln sign on bone scintigram**

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Conflict of interest: None

SAPHO syndrome is a disease that causes sterile inflammatory lesions in bones, joints, and skin. Approximately 10% of SAPHO syndrome patients develop diffuse sclerosing osteomyelitis in the oral and maxillofacial regions (particularly the mandible). The Lincoln sign is an image finding on bone scintigraphy in which the mandible appears to have black whiskers due to extensive lesions. Here, we report a case of SAPHO syndrome with Lincoln sign. The case is a 20-year-old Chinese man. He was diagnosed with SAPHO syndrome 3 years ago due to osteomyelitis of the lower jaw and acne on his face. Osteomyelitis was alleviated by administration of pamidronate. However, he had relapsed pain in both mandibles about 7 months ago, and sternum pain also appeared about 1 month ago, so he visited our department for the first time. The mandible was swollen on MRI, and the bone marrow showed low signal intensity on T1-weighted images, indicating osteomyelitis. Bone scintigraphy showed significant uptake in both mandibles (Lincoln sign positive). Within the scope of our search, there were no clinical reports of SAPHO syndrome exhibiting Lincoln sign. We report this case as an important case in that it suggests the need to include SAPHO syndrome in the differential diagnosis of Lincoln sign.

## W49-4

**A case of adult-onset chronic recurrent multifocal osteomyelitis improved by treatment with golimumab**

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Conflict of interest: None

[Case] 55 year old female [Chief complaint] Left sternoclavicular joint pain [History of present illness] The patient had left sternoclavicular joint pain and a mass since X-8. A biopsy of the mass was performed in X-5, and histopathology showed fibrous tissue growth. The cause was not clear, but the symptoms improved with NSAIDs, and the patient was followed up. In X, the patient was referred back due to worsening the sternoclavicular joint pain and an enlarged mass. MRI and bone scintigraphy showed bone marrow edema at sternoclavicular joints. A repeat biopsy of the mass showed nonspecific inflammation. Based on the diagnostic criteria, a diagnosis of chronic relapsing multifocal osteomyelitis (CRMO) was established. The patient was initially treated with NSAIDs and bisphosphonate, and golimumab (50 mg/month) was introduced as a TNF-α inhibitor because of poor improvement. [Clinical Significance] Fewer adult-onset CRMO cases are reported. The efficacy of NSAIDs, bisphosphonate, and some TNFα inhibitors have been reported, but the treatment method has not been established. This case showed the efficacy of golimumab. Further accumulation of cases is necessary to establish the pathogenesis and treatment methods, and we will discuss this issue with the literature.

## W49-5

**A case of pustulotic arthro-osteitis with severe inflammation and acute symptoms**

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Conflict of interest: None

[Introduction] We experienced a case of acute-onset palmoplantar pustulotic osteoarthritis (PAO), which required differentiation from soft tissue tumor, pyogenic arthritis, and pyogenic spondylitis. [Case] A 49-year-old woman was diagnosed with PAO because of swelling of her right knee along with palmoplantar pustulosis. However, she suspected a soft tissue tumor or septic arthritis because the swelling in her right knee was significant, and MRI revealed a wide range of lesions along the femur up to 28 cm proximal to the articular surface. And a lumbar spine MRI showed STIR hyperintensity in the vertebral body around the ventral side of L2/3/4/5 intervertebral disc. Pyogenic spondylitis was suspected, and she was admitted to the hospital as an emergency. Arthroscopic synovectomy was performed to diagnose and treat arthritis in the right knee, and significant synovial hyperplasia was observed. Based on the test results, it was thought that the patient had significant synovitis due to PAO. After she started drug treatment that, his polyarthritis symptoms repeatedly flared up, but he underwent tonsillectomy, dental treatment, and treatment with biological agents, and is currently in remission.

## W49-6

**An Instance of Acute Myeloid Leukemia Erroneously Identified as Chronic Recurrent Multifocal Osteomyelitis**

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Conflict of interest: None

A male patient of 25 years advanced with the cardinal grievance of lumbosacral discomfort. A computed tomography-guided percutaneous needle biopsy was undertaken on the dolorous left iliac osseous structure, yielding histopathological findings congruent with those characteristic of chronic osteomyelitis. Subsequently, multiple foci of accumulation were discernible within the osseous recesses of the pelvis and ribs, as attested by bone scintigraphy. Following this evaluation, a diagnosis of chronic recurrent multifocal osteomyelitis (CRMO) was proffered, instigating the prescription of glucocorticoids and bisphosphonate agents, albeit with circumscribed therapeutic success. To effectuate a more comprehensive assessment and therapeutic plan, the patient was referred to our medical service. The hematological assay disclosed a total white blood cell count of 4,900/μL, encompassing 33.0% blast cells. Although bone marrow aspiration showed dry tap, the sustained emergence of blast cells in the peripheral blood, coupled with the application of flow cytometry, culminated in the adjudication of acute myeloid leukemia (AML) bearing an M0 subtype. Consequently, the patient was expeditiously referred to the hematology department to initiate the imperative chemotherapeutic intervention.

## W50-1

**A Study on Job turnover and Employment of Patients with Rheumatoid Arthritis Using the NinJa Database**

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Conflict of interest: None

[Objective] To explore the factors related to job turnover and employment in patients with rheumatoid arthritis (RA). [Methods] RA patients' data including work status (employed: E or unemployed: U) in two con-

secutive years (2020 / 2021) were extracted from NinJa. Patients were classified according to work status as E/E (n=4741, median age 59 yr, female ratio 71%), U/U (7319, 73 yr, 84%), E/U (299, 67 yr, 74%), and U/E (167, 61 yr, 82%). Disease activity, HAQ-DI, medications, and hospitalization or surgery in both years were compared between E/U and U/E groups. [Results] There was no difference of female ratio, disease duration (median 9 vs. 10 years) between E/U and U/E groups. Patients in E/U were old and had high HAQ-DI in 2020 (0.25 vs. 0.13) compared to U/E. Rate of hospitalization (18% vs. 7%) and surgery (10% vs. 2%) in 2021 was higher in E/U than U/E. There were no significant differences in disease activity and medications in two consecutive years between the two groups. [Conclusions] It was suggested that age, physical impairment and events such as hospitalization or surgery may be associated with job turnover, independent of disease activity or medications.

## W50-2

**Relationship Between Long-Term Care Insurance Application Status and Pathology of Rheumatoid Arthritis Patients**

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Center for Rheumatic Disease, Marunouchi Hospital, Nagano, Japan

Conflict of interest: None

[Objective] To clarify the relationship between the long-term care insurance application status of rheumatoid arthritis (RA) patients and their pathophysiology. [Methods] We investigated the degree of independence in daily life, degree of independence with dementia, and relationship to treatment of RA patients who completed the long-term care insurance doctor's opinion in 2021-2023. [Results] The study population consisted of were 71 patients aged 51-91 (mean 78.4) years. The level of independence in daily life was J in 6 cases, A in 43 cases, B in 20 cases, and C in 2 cases. The dementia independence level was independent in 57 cases, 1 in 2 cases, 2 in 8 cases, 3 in 3 cases, and 4 in 1 case. Disease activity was SDAI 8.6 without cognitive impairment and 6.9 with cognitive impairment (no significant difference). According to the use of methotrexate or biological agents / JAK inhibitors, 26/39 patients (66.7%) had no cognitive impairment and 7/14 patients (50.0%) had cognitive impairment. [Conclusions] Many RA patients apply for long-term care services due to impaired independence in daily life, and it is necessary to consider evaluation of physical disability.

## W50-3

**Survey on Perceptions of Barriers to Regional Medical Collaboration in the Management of Rheumatic Diseases**

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Conflict of interest: None

[Objective] To investigate the awareness of each stakeholder in regional medical collaboration in the management of rheumatic diseases. [Methods] We asked medical institutions with which we collaborate and physicians in our department to fill out a self-administered questionnaire, which was a combination of a 5-point Likert scale and open-ended questions. [Results] Twelve hospitals, 39 clinics, and 10 outpatient rheumatologists in our department responded to the questionnaire. Barriers to referral to our department included "lack of feedback" (33%), "patients not wanting to be referred" (25%), "uncertainty about the appropriateness of referral" (25%) in hospitals, and "difficulty in making appointments" (33%), "uncertainty about the appropriateness of referral" (31%), and "lack of acquaintance with doctors" (23%) in clinics. The physicians in our department pointed out "patients not wanting to be referred" (100%), "not knowing where to reverse referral" (70%), and "concerns about follow-up at the reverse referral site" (70%) as barriers to reverse referral from our hospital. [Conclusions] Physicians at each medical institution considered a lack of communication between facilities and a lack of patient awareness of referral to be the main barriers to regional medical collaboration.

## W50-4

**A Retrospective Study of Muscular Symptoms Associated with the Use of Immune Checkpoint Inhibitors**

Marina Nagata[1], Kumiko Shimoyama[1], Soma Fukami[1], Haruka Yonezawa[1], Yusuke Okubo[1], Shogo Furukawa[1], Ryuhei Yasuoka[2], Noriyoshi Ogawa[1]
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Conflict of interest: None

[Objective] We report on the clinical features of muscular symptoms associated with immune checkpoint inhibitor (ICI) in our hospital. [Methods] Patients who used ICI between January 2022 and September 2023 were identified from the database of our hospital. Patients who were referred for muscular symptoms were analyzed. [Results] One hundred fifty-two patients were treated with nivolumab, two hundred one with pembrolizumab, and forty-three with nivolumab plus ipilimumab. Five patients (two male, three female, mean age: 69.6±9.4 years) were referred to our department (four myositis, one polymyalgia rheumatica). The clinical features of myositis were muscle weakness and elevated serum CK levels but negative for myositis-specific autoantibodies. Discontinuation of ICI resulted in spontaneous recovery in two cases, while two cases complicated by myasthenia gravis and myocardial damage required glucocorticoid pulse therapy. Polymyalgia rheumatica was characterized by muscle pain, elevated serum CRP and normal serum CK level, and showed a good response to small dose of prednisolone. [Conclusion] The presence of comorbidities such as myasthenia gravis or myocardial damage may have a serious impact on the prognosis. It is important to treat patients in collaboration with other departments.

## W50-5

**Can rheumatic diseases be diagnosed with ChatGPT?**

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Conflict of interest: None

[Objective] We aimed to investigate whether ChatGPT can differentiate rheumatic diseases and explore methods for effectively and safely applying ChatGPT in clinical practice. [Methods] We utilized the Azure Open AI service, gpt-3.5-turbo model. We created an input format for medical history, physical examination findings, and test results in English. We asked for the most likely diagnosis (prompt 1), the top three possible diagnoses (prompt 2), and the single most likely diagnosis among five options (prompt 3). We used 20 cases from medical board exams and national medical licensing exams. [Results] The accuracy using medical history and physical examination findings were 55%, 75%, and 85% for prompts 1, 2, and 3, respectively. When including test results, the accuracy was 80%, 85%, and 90% for prompts 1, 2, and 3, respectively. [Conclusions] The exam cases presupposed selecting the most likely diagnosis from the provided choices, which led to challenges when information was limited. However, ChatGPT demonstrated high accuracy in the differential diagnosis of rheumatic diseases. It is crucial to emphasize that the ultimate responsibility for diagnosis lies with the physician, but ChatGPT can serve as a valuable discussion partner.

## W50-6

**A Retrospective Observational Study of Frequency and Risk Factors for Adrenal Insufficiency in Patients with Autoimmune Disease on Low-Dose Glucocorticoid Medications**

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Conflict of interest: None

[Objective] To determine the frequency of adrenal insufficiency (AI) and correlation with glucocorticoid (GC) treatment in patients receiving low-dose GC therapy in our department. [Methods] Patients who had been treated for at least 3 months at a PSL equivalent of 5 mg/day or more, had stable disease activity at a maintenance dose of 5 mg PSL or less, and had adrenal function tests performed between January 2021 and May 2023 were included in the study. The presence of AI, PSL dose, duration of treatment, pulse therapy, and cumulative PSL dose were evaluated. AI was diagnosed based on the criteria of the Japan Endocrine Society, and severe AI group was defined and analyzed separately. [Results] 87.5% of 48 patients met the general criteria for AI. In the group diagnosed with AI, the median PSL dose at the time of evaluation was 3.25 mg, which was significantly higher. Severe AI was identified in 62.5% of the patients, and we observed significant differences in the cumulative PSL dose, baseline cortisol levels, and the presence of pulse therapy, the PSL dose. [Conclusion] Our findings suggest that the frequency of AI remains high even when the PSL dose is reduced to 5 mg or less, suggesting that the severity of AI is related to the cumulative PSL dose.

## W51-1

**A significance of genetic analysis in adult with clinically suspected inborn errors of immunity**

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Conflict of interest: None

[Objective] To Investigate the profile of adult patients with Inborn errors of immunity (IEI): immunodeficiency (ID), autoinflammatory diseases (AID), and autoimmune diseases who underwent genetic analysis. [Methods] Of patients who visited our department from 2018 to 2023, 56 patients who underwent genetic analyses in adulthood were examined. [Results] The mean age at examination was 38.1±14.3 years and 66.7% were female. The total number of patients with suspected ID, AID and atypical autoimmune disease before genetic analysis was 16, 39, and 15. The purpose of genetic analysis was screening for the atypical clinical presentation in 24 patients (ID: 13, AID: 10, atypical autoimmune diseases: 8) and confirming the diagnosis of diseases as expected by clinical course in 32 patients (ID: 3, AID: 29, atypical autoimmune diseases: 7). Genetic analyses confirmed the diagnosis in 27 patients (ID: 7, AID: 21, atypical autoimmune disease: 8), then, treatments were modified based on the genetic analyses in 33 patients. [Conclusions] We revealed the profile of adult patients with IEI in clinical practice. In some adult patients with suspected IEI, genetic analysis led to specific treatments. Future studies are needed to determine the impact of genetic analysis on treatments and prognosis.

## W51-2

**A case of VEXAS syndrome relapsing with diffuse multiple nodular and micronodular shadows in the lungs, which was remitted with PSL 15 mg/day**

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Conflict of interest: None

[Case] A 70-year-old man had fever and high CRP after the COVID-19 mRNA vaccine. He also had infiltrated erythematous nodules, auricular chondritis, leukocytoclastic vasculitis, macrocytic anemia, pancytopenia, vacuoles in bone marrow cells, lung granules, scalp tenderness, conjunctival congestion, and hearing loss. He was suspected of VS. PSL 30 mg/day improved his symptoms except pancytopenia. After reducing PSL to 10 mg/day with tocilizumab, he worsened with chills, cough, and diffuse nodular and micronodular shadows on CT. He was treated for possible miliary TB, bacterial pneumonia, or VS relapse. He recovered with antibiotics and PSL 15 mg/day. TB tests were negative. UBA1 mutation (p. Met41Thr) confirmed VS. [Discussion] About 50% of VS patients have lung lesions, mostly ground-glass opacity, followed by nodular and micronodular shadows in 47% and 38%. They improve with glucocorticoids over 20 mg or immunosuppressants. This case had localized micronodular shadows at first, but diffuse nodular and micronodular shadows later. They resolved with PSL 15 mg/day only. Lung lesions may remit with low PSL doses. He had low platelets, white cells, and high CRP before vaccination, but persistent fever and higher CRP after vaccination, suggesting vaccination triggered VS onset.

## W51-3

**The contributions of deleterious rare alleles in NLRP12 and inflammasome-related genes to polymyalgia rheumatica: links to autoinflammatory disorders**

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Department of Rheumatology, National Hospital Organization Tokyo National Hospital

Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is a chronic inflammatory disease characterized by arthralgia and myalgia of the shoulder and hip girdles, and fever. PMR is linked to autoimmune diseases and autoinflammatory disorders. Exome sequencing has revealed the roles of rare variants in some diseases. Causative genes for monogenic autoinflammatory disorders might be candidate genes for the selective exome analysis of PMR. We investigated rare variants in the coding and boundary regions of candidate genes for PMR. [Methods] Exome sequencing was performed to analyze deleterious rare variants in candidate genes, and the frequencies of the deleterious rare alleles in PMR were compared with those of Japanese population controls. [Results] Deleterious rare alleles in the *NLRL12* gene were associated with PMR ($P$=0.0069, $Pc$=0.0415, odds ratio [OR] 4.49, 95% confidence interval [CI] 1.79-11.27). A multigene panel analysis demonstrated the deleterious rare allele frequency of the candidate genes for autoinflammatory disorders was also increased in PMR ($P$=0.0016, OR 3.69, 95%CI 1.81-7.54). [Conclusions] The deleterious rare allele frequencies of the candidate genes including *NLRP12* were increased in PMR patients, showing links to autoinflammatory disorders in the pathogenesis of PMR.

## W51-4

**Single-cell transcriptomic analysis of secondary Hemophagocytic lymphohistiocytosis**

Hideaki Sofue[1], Wataru Fujii[1], Aki Sakashita[1], Aiko Hirano[1], Hironori Inoue[1], Satoshi Omura[1], Hiroaki Kusuoka[1], Keitaro Saito[1], Takuya Yanagida[1], Yuki Shimada[2], Yu Isoda[3], Yuji Kukida[2], Masatoshi Kadoya[3], Makoto Wada[1], Atsushi Omoto[3], Masataka Kohno[1], Wataru Fukuda[3], Yutaka Kawahito[1]
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Conflict of interest: None

[Objective] To investigate secondary Hemophagocytic lymphohistiocytosis pathogenesis. [Methods] We comprehensively analyzed immune cells in peripheral blood and bone marrow specimens of 11 sHLH patients (3 with autoimmune disease, 4 with malignancy, 3 with infections, and 1 with drug-induced disease) by single-cell RNA sequencing and compared them among disease groups. [Results] Autoimmune diseases (Adult-onset Still's disease and histiocytic necrotizing lymphadenitis) raised neutrophil levels in peripheral blood and bone marrow. One of monocyte subsets overexpressed phagocytosis-related genes, VCAN, CD36, and CCR2. Autoimmune cases showed increased N4BP1 and SGO2 levels, but reduced IL1R2 expression in bone marrow monocytes. [Conclusions] sHLH, secondary to autoimmune disease increased neutrophil counts in peripheral blood and bone marrow. Monocytes with phagocytotic characteristics demonstrated heightened gene expression of adhesion and migration-related genes. IL1R2 gene expression was decreased in bone marrow monocytes in cases of autoimmune disease. These findings may implicate the involvement of the bone marrow monocyte fraction in the pathogenesis of

sHLH.

## W51-5

**A retrospective analysis of 10 patients with joint symptoms following the administration of immune checkpoint inhibitors**

Tomohiro Kuwamoto[1], Ryu Watanabe[1], Tadashi Okano[2], Yutaro Yamada[3], Kenji Mamoto[3], Kota Imaizumi[1], Ryuhei Ishihara[1], Masao Katsushima[1], Kazuo Fukumoto[1], Shinsuke Yamada[1], Motomu Hashimoto[1]
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Conflict of interest: None

[Objective] To elucidate the clinical characteristics and treatment outcomes of patients presenting with joint symptoms associated with immune-related adverse events (irAE arthropathy) following the administration of immune checkpoint inhibitors (ICIs). [Methods] We retrospectively analyzed the clinical course of 10 patients with irAE arthropathy who visited our hospital from January 2017 to April 2023. [Results] The primary diseases were lung cancer in 8 patients, bladder cancer in 1, and gynecological cancer in 1. The ICIs used included anti-PD-1 in 7 (including 3 in combination with anti-CTLA-4), and anti-PD-L1 in 3. The median age at the time of irAE arthropathy was 70 (61-73.5) years, and the duration from ICI administration to onset was 6 (4.25-14) months. Arthritis was observed in 7, while enthesitis was observed in 3. Improvement in joint symptoms was observed in all patients with low-dose prednisolone (PSL, 8±8.2 mg/day). There were two cases showing relapse of enthesitis after resuming ICI or after discontinuation of PSL. [Conclusion] irAE arthropathy was associated with PD-1/PD-L1 blocking antibodies. Not only arthritis but also enthesitis were observed, but treatment response to low-dose PSL was relatively good. We report our experience with a literature review.

## W51-6

**Analysis of cases of rheumatic immune-related adverse events (irAEs) caused by immune checkpoint inhibitors (ICIs) l**

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[1]Department of Medecine, Tokyo Women's Medical University Adachi Medical Center, [2]Department of Dermatology, Tokyo Women's Medical University Adachi Medical Center

Conflict of interest: None

[Objective] Approximately 10% of ICI-treated cancer patients experience rheumatic and musculoskeletal immune-related adverse events (irAEs) with unclear details. [Methods] We analyzed 11 cases of rheumatic irAEs (male/female ratio 6:5, mean age 60.5 ± 12.7 years) in our hospital. [Results] Malignancies included 6 renal cell carcinomas (1 combined with pancreatic cancer), 3 lung cancers, 1 gastric cancer, and 1 uterine cancer. ICIs include nivolumab 6 and pembrolizumab 5. Rheumatic irAE symptoms included arthritis 10, myalgia 1, rash 2. Mean time to onset was 140±120 days. Cases included ANA positivity, anti-TIF1-γ antibody positivity, RF positivity, and anti-CCP antibody positivity; anti-TIF1-γ antibody-positive cases had dermatomyositis, and RF-positive/anti-CCP antibody-positive cases had arthritis. All 11 patients were treated with steroids (10 mg/day in 9 patients, steroid pulse in 1 patient, and 80 mg/day in 1 patient). The steroid response was good in all but 2 patients and could be gradually tapered over a short period of time. Oral antirheumatic drugs were added in 2 steroid refractory cases. [Conclusions] The study anticipates an increase in rheumatic irAEs and highlights the need for specialists to collect and analyze more cases to gain comprehensive insights.

## W52-1

**Correlation between SpO2 at polymyositis-dermatomyositis-associated interstitial lung disease diagnosis and life expectancy**

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Clinical Immunology, Osaka General Medical Center

Conflict of interest: None

[Objective] This study assessed the correlation between SpO2 at the time of PM/DM-ILD diagnosis and life expectancy. [Methods] We retrospectively assessed PM/DM-ILD patients who started therapy at our department between October 2016 and March 2023. Patients were divided into two groups: SpO2<95% (group A) and SpO2>95% (group B) at diagnosis, and compared. [Results] Eight and 27 patients were included in group A and B, respectively. Five (62.5%) and 17 patients (63.0%) were female in groups A and B, respectively. The median age at onset was 68 years (49-70) in group A and 48 years (25-77) in group B, and was significantly higher in group A (p=0.007). The median time from onset to diagnosis was 10 weeks (3-144) in group A and 12 weeks (3-192) in group B, with no statistically significant difference (p=0.84). The positive anti-ARS, anti-MDA5, and anti-TIF1-γ antibody rates were 50%, 37.5%, and 0% in group A, and 40.7%, 40.7%, and 3.7% in group B, respectively. One patient died within six months of PM/DM-ILD in each group (12.5% in group A and 3.7% in group B). Although the proportion of deaths was higher in group A, there was no statistically significant difference (p=0.41). [Conclusions] We found no association between SpO2 <95% at diagnosis and prognosis in patients with PM/DM-ILD.

## W52-2

**Examination of prognostic factors in patients with anti-MDA5 antibody-positive clinically amyopathic dermatomyositis (CADM)**

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Conflict of interest: None

[Objective] To clarify prognostic factors in patients with anti-MDA5 antibody (a-MDA5 Ab) positive CADM. [Methods] The subjects were 17 patients admitted to our hospital from 2011 to 2023. We retrospectively evaluated baseline characteristics and treatment intervention to identify the prognostic factors in all cases and 14 cases with rapidly progressive interstitial lung disease (RP-ILD). [Results] Mean age at diagnosis was 58.8 years, and there were 4 male and 13 female. 6 cases died of RP-ILD, and the mortality rates were 35.3% in all cases and 42.9% in cases with RP-ILD. Cases of death were more likely to be female, older, and had higher a-MDA5 Ab titers and serum IgG levels at baseline than survivor in both all cases and cases with RP-ILD. ROC analysis revealed that the cut-off values of a-MDA5 Ab and serum IgG predicting mortality were 2900 Index and 1474 mg/dl, respectively. Positive rate of anti-Ro52 antibody (a-Ro52 Ab) was 50% (3/6 cases) in survivor and 100% (3/3 cases) in cases of death. A significant positive correlation was observed between a-MDA5 Ab titer and a-Ro52 Ab titer or serum IgG level. [Conclusion] Among a-MDA5 Ab positive CADM patients, those who are elderly, female, have high a-MDA5 Ab titers, serum IgG, and positive for a-Ro52 Ab may have a poor prognosis.

## W52-3

**Analysis of associations among prognostic factors and a prediction model for prognosis of patients with anti-MDA5 positive dermatomyositis**

Aya Shimizu, Kazuhiro Kurasawa, Tomoka Hiyama, Anna Hasegawa, Yuhi Yoshida, Tomoyuki Miyao, Ayae Tanaka, Satoko Arai, Reika Maezawa, Masafumi Arima, Kei Ikeda
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Conflict of interest: None

**[Objectives]** To identify prognostic factors in patients with anti-MDA5 antibody positive dermatomyositis (MDA5-DM), clarify their associations, and create a prediction model. **[Methods]** Patients with MDA5-DM admitted for induction therapy were retrospectively analyzed. Prognostic factors were identified using Cox regression models. The associations among these factors were examined using principal component analysis (PCA), cluster analysis, and path analysis. A prediction model

was created using variables representative of each cluster of prognostic factors. **[Results]** Of 37 patients, 22 died. IL-6, thrombomodulin (TM), and von Willebrand factor (vWF) were identified as prognostic factors, as well as g-GTP, LDH, CRP, ferritin, WBC, KL-6, SP-D, and CT scores. PCA, cluster analysis, and path analysis revealed 2 groups of prognostic factors: g-GTP, LDH, and ferritin; and IL-6, CRP, WBC, KL-6, SPD, and CT scores. We created a prediction model with g-GTP and WBC, selected from the 2 groups. Survival rates of patients with 2, 1, and 0 factors were 0%, 76%, and 90%; the model was validated with an independent set of patients. **[Conclusions]** IL-6, TM, and vWF were found as new prognostic factors. 2 groups of prognostic factors were identified, which can be a basis of an accurate prediction model.

## W52-4

**Factors affecting hospital length of stay in patients with interstitial lung diseases accompanied by anti-MDA-5-positive dermatomyositis**

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Division of Rheumatic Disease, National Center for Global Health and Medicine

Conflict of interest: None

[Objective] Predictors of prolonged hospitalization in patients with anti-MDA-5-positive dermatomyositis (DM) complicated by interstitial lung disease (ILD) are unknown. We aimed to explore them. [Methods] Adult Japanese patients with new-onset anti-MDA-5-positive DM with ILD (n=17) were included from 2010 to 2022. They were treated with combined immunosuppressive therapy with high-dose glucocorticoid, tacrolimus, and cyclophosphamide. Clinical characteristics, known poor prognostic factors, and complications were each examined for correlation with length of hospital stay. [Results] The median age was 52 years, and 47% were female. All 17 patients were discharged alive. The median length of hospital stay was 73 days (95% CI: 36-156 days). Erythrocyte sedimentation rate at admission showed a strong correlation with the length of hospitalization (correlation coefficient: 0.795, $P = 0.002$). The appearance of new shadows during induction remission therapy significantly prolonged the length of hospital stay (51 days versus 170 days; $P < 0.001$). [Conclusions] Our findings indicate that high erythrocyte sedimentation rate on admission and the appearance of new shadows during remission induction therapy prolong the length of hospital stay in anti-MDA-5-positive DM patients with ILD.

## W52-5

**Urinary beta2-microglobulin/N-acetylglucosaminidase ratio as a marker of disease exacerbation in patients with interstitial lung diseases with anti-MDA5-antibody positive idiopathic inflammatory myopathies**

Kazuko Yamazaki, Etsushi Toyofuku, Seido Ooka, Keiichi Sakurai, Machiko Mizushima, Misato Kawakami, Kumiko Tonooka, Yukiko Takakuwa, Shotaro Suzuki, Tatsuya Kawasaki, Takayasu Ando, Yutaka Goto, Nobuyuki Endo, Kohei Yoshioka, Sho Mori, Futaba Miyaoka, Yoshiki Ishizaki, Norihiro Matsumura, Yusei Motonaga, Tomofumi Kiyokawa, Mitsuru Imamura, Harunobu Iida, Sho Sasaki, Yoshioki Yamasaki, Hiroko Nagafuchi, Masaaki Mori, Kimito Kawahata
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Conflict of interest: None

[Objective] Urinary $\beta_2$-microglobulin (U-$\beta_2$MG) reflects increased HLA class I expression induced by inflammatory cytokines. We investigated whether the U-$\beta_2$MG/urinary N-acetylglucosaminidase (U-NAG) ratio could be a marker of disease exacerbation in patients with interstitial lung disease (ILD) with anti-MDA5-antibody-positive idiopathic inflammatory myopathies (anti-MDA5-ILD). [Methods] Patients with anti-MDA5-ILD were admitted from 2016 to August 2023. We classified them into groups of death, survival with plasma exchange (PEX), and survival with no PEX (nPEX), and retrospectively analyzed their U-$\beta_2$MG/U-NAG ratio (urinary creatinine-corrected), anti-MDA5 antibody levels, ferritin, and KL-6. [Results] Of admitted 41 (32 alive, 9 dead) patients, 16 patients measured U-$\beta_2$MG prior to treatment, including 11 females, 3 deaths, 5 with PEX, and 8 with nPEX. All patients received triple therapy (PSL+IV-CY+CNI), 8 received PEX, and 6 received tofacitinib. The median U-$\beta_2$MG/U-NAG ratio was predominantly higher in the death and PEX groups than in the nPEX group (P=0.01). Serum ferritin and KL-6 levels were not significantly different among the three groups. [Conclusions] U-$\beta_2$MG/U-NAG ratio may be a useful marker to determine the disease exacerbation in patients with anti-MDA5-ILD.

## W52-6

**Prognostic serum biomarkers for interstitial lung disease in anti-MDA5 antibody-positive clinically amyopathic dermatomyositis**

Satoko Arai, Kazuhiro Kurasawa, Rika Sato, Yuki Aizawa, Yuhi Yoshida, Tomoka Hiyama, Anna Hasegawa, Tomoyuki Miyao, Ayae Tanaka, Reika Maezawa, Masafumi Arima, Kei Ikeda
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Conflict of interest: None

[Objective] To elucidate the correlation of the time-courses of serum biomarkers with prognosis of interstitial lung disease in anti-MDA5 antibody-positive clinically amyopathic dermatomyositis (MDA5+-CADM-ILD). [Methods] We retrospectively identified 39 patients with MDA5+CADM-ILD who were treated in our hospital and analyzed the associations of the time-courses of KL-6, SP-D, and ferritin with mortality. [Results] 18 patients (46%) died, all of which were due to respiratory failure. Before treatment, median KL-6 level was 757 U/l (18% of patients had a normal value), whereas median SP-D level was 65 U/l (79% had a normal value). The difference in the levels of biomarker between survivors and non-survivors was most significant at the baseline for KL-6 (mean 1125 vs 641 U/ml, p=0.0092) but at the maximum value during follow-up for SP-D (median 389 vs 70 ng/ml, p<0.001) and ferritin (median 5169 vs 697 ng/ml, p<0.001). In a multivariate logistic model, maximum SP-D value was the only independent variable that significantly predicted death (p=0.0066). ROC analysis revealed that the optimal cut-off of maximum SP-D value was 160 ng/ml to predict mortality (sensitivity 88.9%, specificity 100%). [Conclusions] Increase in SP-D during follow-up predicts prognosis of MDA5+CADM-ILD.

## W53-1

**Assessment of negative conversion of anti-ARS antibody in the patient of anti-synthetase syndrome**

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Conflict of interest: None

[Objective] We evaluated the relationship between changes in antibody titer and the clinical course. [Methods] Cases with positive anti-ARS antibodies were included and divided into two groups: negative conversion (N group (gN)) and continuously positive (P group (gP)). We compared antibody titers, the affected organs, and clinical improvement. [Results] Twenty five (gN: 6, gP: 19) patients were included and average age was 64 ± 14.9 years at first measurement. Five in gN and 14 in gP received therapeutic intervention. The initial antibody titer tended to be lower in gN (89 ± 53.3) than in gP (117.3 ± 51.3). Four patients in gN had interstitial lung disease (ILD) alone, and only 1 patient had muscle symptoms, which tended to be fewer than 8 in gP. In cases with solitary ILD, there was a decrease in antibody titer as their improved. There was a case of increased antibody titers with recurrence of ILD. The total number of organ involvement also tended to be lower in gN. No patients were positive for anti-Jo-1 antibodies but were positive for anti-EJ or KS antibodies in the gN. [Conclusion] There were cases that developed negative anti-ARS antibodies, characterized by a small number of organs involved (especially ILD alone), a good response to treatment and positive anti-EJ/KS antibodies.

## W53-2

**Impact of anti-ARS antibodies and immunosuppressants on relapse of patients with anti-synthetase syndrome**

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Conflict of interest: None

[Objective] To clarify the effects of anti-ARS antibodies and immunosuppressants on relapse after initial induction therapy in patients with anti-synthetase syndrome (ASS). [Methods] Participants were consecutive ASS patients who received the first induction therapy in our department. Relapse was judged to occur when physicians decided to intensify the therapy for ASS. Clinical data were collected by reviewing medical records. To identify factors affecting relapse, the Cox regression model was applied. [Results] Fifty-one patients were enrolled in this study. ILD, myositis, and skin involvement were present in 51, 37, and 39 patients. Anti-EJ, Jo-1, PL-12, and PL-7 Abs were detected in 13, 23, 7, and 8 patients. Immunosuppressants were administrated in 26 cases. Relapse occurred in 30 cases (58%). Median time to relapse was 155 weeks. The relapse frequently occurred in patients with anti-EJ and Jo-1 Abs. Immunosuppressants were not identified as a protective factor for relapse (p=0.25). Calcineurin inhibitors suppressed the relapse of myositis (p=0.03) but not ILD (p=0.52). [Conclusions] In ASS, anti-EL/Jo-1 Abs are risk factors for relapse. Immunosuppressants suppress relapse of myositis but not ILD.

## W53-3

**Investigating factors associated with relapse of anti-aminoacyl-tRNA synthetase antibody syndrome: A retrospective cohort study**

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Conflict of interest: None

[Objective] Evaluating factors associated with relapse in patients with anti-aminoacyl-tRNA synthetase antibody syndrome (ASyS). [Methods] (1) Relapses after initial treatment were compared with those of non-relapse. (2) Among each relapse during the entire treatment period, three groups were compared in which the concomitant drug after relapse was a calcineurin inhibitor (CNI) alone, a non-CNI or CNI+non-CNI (multi-target). [Results] (1) Among 38 patients with ASyS, relapse was observed in 26 patients. The duration from the start of induction treatment to the first relapse was 489 days. Patients with relapse had significantly higher CRP and ferritin at the start of treatment than non-relapse patients. (2) CNI alone was used in 37 cases, non-CNI in 8 cases, and multi-target in 16 cases, and the non-relapse period was 784, 393, and 723 days, respectively. There was no difference in CRP and ferritin at the start of treatment or at relapse between CNI alone and multi-target cases, but multi-target was used in patients with many relapses. [Conclusions] ASyS patients have a high rate of late relapse, and the combination of CNI significantly reduces relapse. Multi-target therapy was used in refractory cases, but further studies are needed on effective patients.

## W53-4

**Long-term observation of Pulmonary Function in Anti-ARS Antibody Syndrome**

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Conflict of interest: None

[Objective] The ARS antibody syndrome is associated with a high incidence of interstitial lung disease (ILD), presenting challenges in long-term management. [Methods] We tracked the results and progression of respiratory function tests in patients at our institution from April 2007 to October 2021. [Results] The study involved 175 participants, with an average age of 60.5 years and 113 (65%) being female. Diagnoses included IIM in 51 cases, RA in 4, SjS in 4, IPF in 18, NSIP in 13, and unclassifiable ILD in 76. Over a median observation period of 74 months, the changes in %FVC were as follows: 83 cases (47%) maintained an improvement of 5% compared to the initial %FVC, 23 cases (13%) showed a temporary improvement of more than 5% but eventually showed a change of less than 5%, 13 cases (7%) showed a change of less than 5% throughout the course, 31 cases (18%) showed an improvement of more than 5% during the course but eventually worsened by more than 5%, and 25 cases (14%) did not show improvement during the course and eventually worsened by 5%. [Conclusions] Patients with ARS antibody syndrome often demonstrate initial improvements in respiratory function, but there's potential for deterioration over time. Consideration of a long-term therapeutic strategy is essential.

## W53-5

**Impact of therapies on prognosis in anti-MDA5 antibody-oositive dermatomyositis-associated interstitial lung disease**

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Conflict of interest: Yes

[Objective] This study investigates the prognosis of anti-MDA5 antibody-positive dermatomyositis-associated interstitial lung disease (DM-ILD) patients with poor prognostic factors treated with conventional triple therapy, aggressive multidrug combination therapy, or JAK inhibitor (JAKi) combination therapy. [Methods] We examined consecutive cases from 2011 to 2022. Poor prognostic factors were defined as serum ferritin ≧ 450 ng/mL and AaDO2 ≧30 mmHg. We analyzed three groups: conventional therapy (corticosteroids, calcineurin inhibitors, and IVCY), aggressive multidrug therapy (including blood purification, MMF, and RTX), and JAKi combination therapy. [Results] A total of 33 cases were studied. Patients who died from ILD showed better survival trends in the aggressive therapy (61.5%) and JAKi groups (77.8%) compared to the conventional group (33.3%) (P = 0.38, 0.14, log-rank test). In survivors vs. ILD deaths, the aggressive therapy group had higher serum ferritin and AaDO2 trends (P = 0.11, 0.19), and the JAKi group trended older (P = 0.06). [Conclusions] Aggressive multidrug and JAK inhibitor therapies may improve the prognosis of anti-MDA5 antibody-positive DM-ILD patients with poor prognostic factors.

## W53-6

**Outcome of Triple-Combination Therapy According to Predetermined Protocol in Interstitial Lung Disease with Anti-MDA5-Positive Dermatomyositis**

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Conflict of interest: None

[Objectives] We aimed to investigate the outcome of triple-combination therapy according to a protocol in interstitial lung disease (ILD) with anti-MDA5-positive dermatomyositis (DM). [Methods] Clinical data of 15 consecutive anti-MDA5-positive DM-associated ILD patients treated with a protocol including high-dose glucocorticoids (GCs), tacrolimus, and intravenous cyclophosphamide were retrospectively reviewed and analyzed. The primary end point was 6-month survival. [Results] The 6- and 12-month survival rates were 100%. Over a period of 12 months, amelioration in serum anti-MDA5 titers, serum ferritin levels, and chest high-resolution computed tomography were observed. In addition, median percent-predicted forced vital capacity (%FVC) increased from 77% to 88% ($p$ = 0.17). Prednisolone was initially administered at 1 mg/kg/day, and its median dosages were 16 and 9 mg/day at 6- and 12-month, respectively. GC pulses were administered initially and/or additionally ($n$ = 9 and 3, respectively) at the discretion of the physicians. Cytomegalovirus reactivation was observed in 5 patients, and all the cases were treated successfully. [Conclusion] The protocol including triple-combination therapy seemed effective and well-tolerated in the patients with anti-MDA5-posi-

tive DM-associated ILD.

## W54-1

**Establishment of Animal Models of Dermatomyositis-Specific Autoimmunity-Based Diseases**

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Conflict of interest: Yes

[Objective] Dermatomyositis (DM) is a collagen disease with specific cutaneous manifestations and is a syndrome with a variety of symptoms and severity. We aimed to establish a mouse model of human DM by inducing immune responses to the myositis-specific autoantigens in mice. [Methods] The human TIF1γ full-length protein and mouse MDA5 full-length protein were purified by genetic recombination technology using a baculovirus-insect cell line system, and C57BL/6 mice were immunized with the recombinant proteins along with adjuvants. The TIF1γ-immunized mice were also subcutaneously implanted with cancer cell lines. Pathological analysis of the thigh muscles, ear skin, lungs, and knee joints of the immunized mice was performed. [Results] TIF1γ-immunized mice developed myositis similar to DM in the thigh muscle, which was reproduced by adoptive transfer of CD8 T cells. MDA5-immunized mice developed interstitial pneumonia with fibrosis, which was suppressed by CD4 depletion and not affected by CD8 depletion; T-cell adoptive transfer reproduced pneumonia. [Conclusions] Murine models of TIF1γ-induced myositis and MDA5-induced interstitial pneumonia were established. CD8 T cells and CD4 T cells were pathogenic cells, respectively.

## W54-2

**The role of RasGRP1 in idiopathic inflammatory myopathy**

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Conflict of interest: None

[Objective] Both T cells and macrophages participate in the pathogenesis of idiopathic inflammatory myopathies (IIM). Ras guanyl-releasing protein 1 (RasGRP1), a Ras guanyl exchange factor, plays an important role in differentiation and proliferation of T cells and also in activated macrophages. In this study, we aimed to reveal the role of RasGRP1 in IIM. [Methods] Muscle specimens from six patients with IIM were examined immunohistochemically for RasGRP1 expression concurrently with CD8, CD4 and CD68. Expression of RasGRP1 in C protein-induced myositis (CIM), an animal model of IIM, was evaluated with total RNA obtained from mononuclear cells infiltrated into affected muscles. CIM was induced in wild type and RasGRP1-null mice. [Results] The proportion of CD8, CD4 and CD68 positive cells to the whole mononuclear cells in the muscle tissue was 34%, 42% and 24%, respectively. Among those populations, the rates of RasGRP1+ cells were higher in CD8+ cells (44%) and CD68+ cells (46%) compared to CD4+ cells (19%). The expression of RasGRP1 was elevated sequentially along with the development of CIM. RasGRP1-null mice were resistant to CIM with a decreased number of CD8+ cells in lymph nodes. [Conclusions] RasGRP1 would play a role in IIM and be a possible therapeutic target for IIM.

## W54-3

**Investigation of the usefulness of LRG in evaluation of disease activity in polymyositis/dermatomyositis**

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Conflict of interest: None

[Objective] The expression of leucine-rich α2-glycoprotein (LRG) is induced by many inflammatory cytokines in addition to IL-6. Serum LRG has been reported to be useful as an activity marker for rheumatoid arthritis and inflammatory bowel disease, but there are few reports on idiopathic inflammatory myositis. In this study, we evaluated the usefulness of LRG as a marker of disease activity in polymyositis (PM)/dermatomyositis (DM). [Methods] Blood samples were collected from 24 patients with PM/DM diagnosed according to Bohan and Peter criteria or 2015 Ministry of Health, Labour and Welfare Research Group criteria and scheduled for induction of remission with steroids or immunosuppressive agents before and 6 months after the start of treatment. Disease activity was assessed by CK and CRP and compared to serum LRG. [Results] CK, CRP, and LRG were significantly decreased after treatment in PM/DM overall (P=0.0001, P=0.0050, P=0.0199). CK, CRP, and LRG after treatment in the same patients showed a significant decrease in CK and LRG (P=0.0010, P=0.0469), but no significant decrease in CRP (P=0.0537). However, there were cases in which LRG was high even when CRP was low. [Conclusions] LRG can be a useful serum marker reflecting disease activity in PM/DM.

## W54-4

**Distinct cytokine profile with elevated type I/III interferons in circulation from patients with anti-MDA5 antibody-positive dermatomyositis**

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Conflict of interest: None

[Objective] We explored a characteristic serum cytokine profile in patients with anti-MDA5 antibody-positive dermatomyositis (DM), with a particular focus on type I/III interferons (IFNs). [Methods] Consecutive patients with anti-MDA5$^+$ DM (n=10), anti-synthetase antibodies (n=6), anti-TIF1-γ$^+$ DM (n=6), systemic lupus erythematosus (SLE) (n=6), and COVID-19 pneumonia (n=3), who visited from September 2020 to August 2023, were enrolled. Pre-treatment serum IFN-α, IL-1β, IL-6, and TNF-α were measured by cytometric bead array, while IFN-β, IFN-λ3 were measured by enzyme-linked immunosorbent assay. [Results] IFN-α was elevated in SLE (median 52.2 [IQR 16.5-60.9] pg/mL), while IFN-β was elevated in two patients with classic DM and anti-TIF1-γantibodies (30.6, 76.6 pg/mL). In anti-MDA5$^+$ DM, IFN-α (23.1 [4.1-34.8] pg/mL), IFN-β (10.2 [5.7-11.8] pg/mL), and IFN-λ3 (77.4 [42.4-103.5] pg/mL) were all elevated. COVID-19 was characterized by higher levels of IL-6 and IFN-λ3 was elevated in one patient (26.4 pg/mL). The elevation of IFNs was minimal in patients with anti-synthetase antibodies. There was no significant difference in the level of IL-1β and TNF-α between the diseases. [Conclusions] Patients with anti-MDA5$^+$ DM exhibited a distinct cytokine profile with elevated type I/III IFNs.

## W54-5

**Transcriptome analysis of peripheral blood reveals superiority of the triple combination of baricitinib, rituximab, and tacrolimus therapy (BRT-Tx.) for anti-MDA5 antibody-positive dermatomyositis (MDA5-DM)**

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Conflict of interest: Yes

[Objective] We devised BRT therapy (BRT-Tx) for MDA5-DM. The regimen combines Baricitinib (BAR), rituximab (RTX) and tacrolimus (TAC). In this study, we determine the differences in gene expression of peripheral blood between BRT- and conventional TC (TAC + cyclophosphamide)-Tx. [Methods] Differentially expressed genes (DEGs) were identified between pre- and 2-3 months after treatment. Clustering and Gene ontology (GO) analysis were performed. [Results] Two of three cases with TC died, while all four cases on BRT recovered. GO analysis showed that the immunoglobulin- and B-cell-mediated immune system was significantly suppressed in survivors; GO analysis of DEGs showed the expression of B-cell-related genes was significantly suppressed in BRT-Tx. In contrast, suppression of such pathways as cell proliferation was significant in TC-Tx. IFN scores showed an increase in type 2 and 3

in all deaths and an increase in type 1 in one death. [Conclusions] BRT-Tx significantly suppressed B-cell-related gene expression, whereas TC-Tx had less target specificity. It seems to suppress of the immune system via immunoglobulins and B cells is essential, and revealed the need for RTX combination. In the fatal cases, IFN scores increased after treatment, indicating a benefit of concomitant BAR.

## W54-6

**Randomized Placebo-Controlled Trial to Evaluate Efficacy and Safety of Subcutaneous Abatacept in Adults With Active Idiopathic Inflammatory Myopathy: Outcomes for Japanese Study Participants**

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Conflict of interest: Yes

[Objective] A randomized, placebo (PBO)-controlled trial of SC abatacept (ABA) and standard of care (SOC) was performed in pts with active, idiopathic inflammatory myopathy (IIM; NCT02971683). 52-wk results for the global population were reported (primary endpoint not met, trial terminated).[1] We present results from Japanese sites for the 76-wk treatment period (TP). [Methods] Adults with IIM received SC ABA+SOC or PBO+SOC in the 24-wk double-blind period. From wk 24-76 all pts received ABA+SOC. Primary endpoint: proportion meeting IMACS DOI. Safety and tolerability were assessed. [Results] Japanese sites enrolled 21 pts (ABA/PBO: 11/10; IIM subtypes: DM 7/7, PM 3/3, ANM [IMNM] 1/0); 19 completed the TP. Proportion of pts (ABA/PBO) achieving IMACS DOI at wk 24 was 72.7%/50%; at TP end 90%/87.5%. At TP end, mean MRC TIS was 47/55; MRC moderate/major responses were 70%/100%. Mean change from baseline at TP end for these outcomes: MMT8 (19.4/18.8), HAQ (-0.26/-0.52), PhGA VAS (-3.5/-3.8) and CDASI activity (-8.6/-8.6). The safety profile was consistent with the overall study population. [Conclusions] Throughout the 76-wk TP, pts in Japan with IIM tolerated ABA well and showed continued clinical responses to SC ABA therapy.

## W55-1

**Clinical Features and Prognostic Implications of Microscopic Polyangiitis in Cases of Clinically Indicated Yet Practically Unfeasible Renal Biopsy**

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Conflict of interest: None

[Objective] To study clinical characteristics and outcomes of microscopic polyangiitis (MPA) where renal biopsy was unfeasible despite the suspicion of nephritis. [Methods] We analyzed REVEAL cohort data from 2001-2023. Of 241 MPA cases fitting 2022 EULAR/ACR criteria, two groups were studied: renal biopsy-confirmed cases (RB group) and those suspected of renal involvement but for whom biopsy was deemed infeasible (non-RB group). Outcomes over 5 years after induction therapy were compared. Non-RB criteria: 1) new or worsened renal BVAS≧4 points (excluding hypertension) and 2) no biopsy-feasible sites except kidneys, but deemed infeasible due to high risk. Exclusion criteria: patients <18 years of age. [Results] 45 cases in RB group, and 22 in non-RB group were included. Non-RB group began treatment at older age (median 78.5 vs 68.0 years, $p=8.9\times10^{-4}$) and showed increased renal BVAS (12.0 vs 10.0, p=0.050). Total BVAS and eGFR showed no significant difference. Age-weighted Kaplan-Meier curves revealed non-RB group's poorer prognosis and higher 5-year mortality ($p=7.5\times10^{-6}$). Non-RB group had a higher trend of infection-related deaths than RB group (62.5% vs 0.0%, p=0.11). [Conclusions] MPA cases in non-RB group showed poorer outcomes and more infection-related deaths than RB group.

## W55-2

**Analysis of cardiac involvement in EGPA using cardiac MRI**

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Conflict of interest: Yes

[Objective] Eosinophilic granulomatosis with polyangiitis (EGPA) causes various organ complications, among which cardiac involvement, although relatively infrequent, is known as an important prognostic factor and may cause sudden death. We have been studying cardiac lesions in collagen disease by cardiac magnetic resonance imaging (CMR) for some time. In this study, we analyzed patients with suspected cardiac lesions by EGPA who underwent CMR and compared the results with other imaging tests and biomarkers. [Methods] This study is a retrospective observational study. In this study, 29 cases of EGPA diagnosed and treated at our clinic from 2015 to 2022 were selected. Of these, 16 cases were suspected to have cardiac involvement and CMR was performed. In these cases, we compared clinical symptoms, some biosummaries, echocardiography, and other test results between the groups with and without CMR findings. [Results] Of the 16 cases in which CMR was performed, 8 cases had findings and 8 cases had no findings. There were significant differences in troponin I and CK-MB between the two groups, but not in MPO-ANCA, NT-proBNP, peripheral blood eosinophil count, or EF on echocardiography. [Conclusions] The results suggest that CMR is useful in the early detection of cardiac lesions in EGPA.

## W55-3

**Pneumocephalus and cerebral abscess in Granulomatosis with Polyangiitis**

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Conflict of interest: None

A 33-year-old woman presented with a long history of headaches and nasal obstruction. Because she was pregnant at the time of onset, no further tests were performed. She was diagnosed with granulomatosis with polyangiitis (GPA) based on the saddle nose deformity, septal perforation, rhinitis, hearing loss, otorrhea, hypertrophic pachymeningitis, proteinase 3-anti-neutrophil cytoplasmic antibody positivity, and histopathological findings of nasal granulomatous lesions. The remission induction therapy with high-dose corticosteroids and intravenous cyclophosphamide ameliorated the GPA. A few months later, GPA relapsed with worsened headaches, and liquorrhea. Computed tomography revealed the enlargement of skull base bone defects and a continuous air image from the right olfactory fissure into the cranium. Contrast-enhanced magnetic resonance imaging revealed inflammation of the posterior ethmoid sinus, and a ring-shaped high-signal area at the base of the frontal lobe. She recovered with craniotomy to close the defects, long-term antibiotics therapy for cerebral ab-

scess, and remission induction therapy with high-dose corticosteroids and rituximab for GPA. We present this case to raise awareness of the risks of pneumocephalus and cerebral abscess in GPA.

## W55-4

**Predictors of immunosuppressive treatment in cutaneous arteritis: Analysis of clinical characteristics in 42 patients**

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Conflict of interest: None

Purpose: Cutaneous arteritis (CA) is necrotizing vasculitis of medium-sized vessels in the skin. We analyzed clinical features to identify predictors of immunosuppressive treatment in CA. Methods: Among 42 patients, 25 patients with pathologically confirmed and treated for more than 6 months were retrospectively analyzed. The cohort was divided into two groups: a steroid induction group (n=14) and a non-induction group (n=11). The induction group was further divided into a steroid-only group (n=4) and an immunosuppressive drug combination group (n=10). Results: The mean age was 41.2±18.0 years, and the male to female ratio was 1:4. Age at onset and platelet count (PLT) were significantly higher in the induction group than in the non-induction group, as was the percentage of patients with numbness and D-dimer > 1 μg/mL. The cut-off values were 43 years for age at onset and 340,000/μL for PLT. Comparison of the three groups showed that age at onset, PLT, neutrophil count (Neut), and CRP tended to be higher in the combination group. Conclusions: Numbness, D-dimer ≧1 μg/mL, age at onset ≧43 years, and PLT ≧340,000/μL are likely to be useful predictors of the need for systemic steroids. In addition, higher of age, PLT, Neut, and CRP are suggestive of additional immunosuppressant.

## W55-5

**Complication of Large-Vessel Vasculitis (LVV) in Medium and Small-Vessel Vasculitis (MVV and SVV)**

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Conflict of interest: None

[Object] To investigate complication of LVV in MVV and SVV. [Methods] We retrospectively collected clinical information from patients with MVV or SVV who had visited our department since April 2015. The clinical feature of MVV or SVV patients complicated with LVV was analyzed. [Results] 99 cases were enrolled; mean age was 66 y/o, female was 60%, MPA 45, EGPA 32, GPA 6, PAN 6, others 10. 3 cases (MPA 2, GPA 1) were complicated with LVV. One of the cases had been diagnosed with GCA 11 years before the diagnosis of MPA, but no recurrence of GCA was occurred at the time of diagnosis of MPA. In the other case, headache, jaw claudication, wall thickening of descending thoracic aorta, and stenosis of main branches of aorta were observed at the time of MPA diagnosis. In the last case, uneven wall thickening of the aorta and brachiocephalic artery was observed at the time of GPA diagnosis. All cases were treated with prednisolone as a monotherapy, with an average initial dose of 40 mg/day; however, in one case, remission induction was insufficient. There was one case of relapse and one case of death, and the cause of death was malignant tumor. [Conclusions] SVV and MVV vasculitis is rarely accompanied by LVV. However, as the clinical course is diverse, case series study is required.

## W55-6

**A rare case of Eosinophilic granulomatosis with polyangiitis with myositis**

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Conflict of interest: Yes

A 79-year-old man with bronchial asthma was admitted to our hospital due to muscle weakness, myalgia, and paresthesia of the lower extremity. His peripheral blood eosinophil count and CRP was elevated. The sinusitis, otitis media, pulmonary nodules and cavity were shown in CT scan, and multiple infarctions in brain MRI. Histologic examination of a rectal mucosa biopsy specimen revealed eosinophilic infiltration in perivascular and tears of vascular elastic fibers. He was diagnosed with Eosinophilic granulomatosis with polyangiitis (EGPA). In addition, we detected the elevation of CPK and myoglobin, diffuse hypersignal of STIR sequence in MRI of the extremity muscles, myogenic change in electromyogram, and numerous eosinophilic infiltrations in muscle fibers in muscle biopsy specimen. The measurable antibodies associated with myositis were negative. We concluded that it was myositis associated with EGPA. The eosinophil counts and CRP improved immediately after the treatment with glucocorticoid, 50 mg/day of prednisolone, and cyclophosphamide pulse therapy. Although myalgia is common in patients with EGPA, it is rare to be complicated with myositis.

## W56-1

**Imaging Characteristics and Pathological Features of Muscle MRI in ANCA-Associated Vasculitis Patients**

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Conflict of interest: None

[Objective] Muscle MRI scans in AAV patients often show abnormal muscle signals. While previous studies have mainly focused on muscle issues, we examined abnormalities in the blood vessels and perivascular regions. We specifically investigated perivascular signal abnormalities and their corresponding pathology on muscle MRI. [Methods] Out of the AAV patients admitted to our hospital between January 2016 and December 2022, we selected five individuals who had undergone lower extremity MRI and subsequently had muscle biopsies guided by their MRI findings. We conducted a retrospective analysis of the imaging characteristics and pathological results from these MRI scans. [Results] The study cohort comprised three males and two females, with an average age of 67.4 years at the time of diagnosis. Among them, three had GPA, and two had MPA, with all five individuals testing positive for MPO-ANCA. In all cases, STIR MRI showed high-signal perivascular areas around intramuscular vessels. Muscle biopsies consistently revealed vasculitis or perivasculitis in these areas. [Conclusions] Abnormal perivascular signals in MRI suggest active vasculitis, making MRI a potential alternative to biopsy in diagnosing AAV.

## W56-2

**Association of SERPINA1 with granulomatosis with polyangiitis and PR3-ANCA positive vasculitis in a Japanese population**

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Conflict of interest: None

[Objective] *SERPINA1* is known to be a susceptibility gene to granulomatosis with polyangiitis (GPA) and PR3-ANCA positive ANCA-associated vasculitis (PR3-AAV) in European populations. However, the *SERPINA1* Z allele (rs28929474A), which was associated with risk of GPA and PR3-AAV, was very rare in Japan. In this study, we examined whether *SERPINA1* is also associated with GPA and PR3-AAV in a Japanese population. [Methods] Resequencing of the coding region of *SERPINA1* was implemented in 125 GPA and 70 PR3-AAV patients. Detected variants were analyzed for their association with AAV. Allelic data of *SERPINA1* variants in about 54000 controls (54KJPN) were obtained from the Japanese Multi Omics Reference Panel (jMorp). [Results] The Z allele was not detected either in the AAV patients or in 54KJPN. Three missense variants detected by resequencing were not associated with AAV. On the other hand, synonymous variant, rs1049800, was significantly associated with GPA ($P=1.65x10^{-5}$, Odds ratio: 3.20) and PR3-AAV ($P=1.54x10^{-4}$, Odds Ratio: 3.63). [Conclusions] In a Japanese population, an association of *SERPINA1* synonymous variant with GPA and PR3-AAV was detected, which has not been previously reported.

## W56-3

**A case of polyarteritis nodosa in which testicular arteriography was useful for diagnosis**

Sairi Takahashi[1], Eisuke Takamasu[1], Keisuke Hirobe[1], Yuki Terashima[1], Kei Karakida[1], Issei Takahashi[1], Tomohiro Kato[1], Masahiro Iida[2], Nanase Honda[1], Yoshitaka Ueda[1], Kae Onishi[1], Yuji Miyoshi[1], Masako Utsunomiya[1], Yoshiki Nagai[1], Naoto Yokogawa[1], Kota Shimada[1]
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Conflict of interest: None

[Introduction] Scrotal pain is among the major symptoms listed in the American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa (PAN). Angiography of the celiac and renal arteries is often performed, while reports on the testicular arteries are scarce. [Case] A 76-year-old man was admitted to our hospital due to fever, general malaise, and left inguinal pain. There was no scrotal swelling or tenderness, but serum CRP level was elevated. The testicular artery was mildly dilated on CT. Blood and spinal fluid cultures showed no bacterial growth. MPO-ANCA, PR3-ANCA, antinuclear antibodies, and hepatitis B and C virus were also negative. In the course of fever, scrotal pain deteriorated, and erythema with infiltration on the abdomen and thighs appeared. Angiography revealed bilateral testicular arteries irregular in diameter and narrowed, and skin biopsy showed inflammatory cell infiltration in the medium-sized vessel of the subcutaneous tissue, leading to a definite diagnosis of PAN. [Clinical Significance] In this case, morphological changes in the testicular arteries were detected by angiography. When PAN is suspected, especially in patients with scrotal pain, angiography may detect testicular arteritis, which is relatively specific for PAN.

## W56-4

**Two cases of eosinophilic granulomatosis with polyangiitis with onset or exacerbation after administration of anti-IL-4/13 monoclonal antibody**

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Conflict of interest: None

The first case is a 38-year-old man. He developed bronchial asthma in X-2 years and gradually developed nasal obstruction, nasal polyps and motor neuropathy. He was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) in combination with the above symptoms, elevated eosinophils and positive MPO-ANCA. We used prednisolone (PSL) and intravenous cyclophosphamide as remission induction therapy, azathioprine as maintenance therapy, and intravenous immune globulin therapy. Although vasculitis symptoms improved, asthma were refractory and steroid-dependent, so dupilumab, an anti-IL-4/13 monoclonal antibody, was started on Y-1 month X year. Two weeks later, he showed worsening of cough and elevated eosinophils (7400/μL), which was exacerbation of EGPA. The second case is a 35-year-old man. He had asthma since childhood, which worsened in X-13 years. In year X, he had exacerbations of sinusitis and asthma, so dupilumab was started on Y-3 month. Cough developed that night, and the eosinophils were elevated to 3200/μL. PSL was increased, but eosinophils remained high and asthma attacks recurred. In Y-1 month, he developed shoulder and neck pain, headache and sensory neuropathy in the left lower leg. We diagnosed him with EGPA. We report these cases with some literature review.

## W56-5

**Relationship between the severity of systemic vasculitis with kidney involvement and serum sulfatides levels**

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Conflict of interest: None

[Objective] Sulfatides are the type of sulfated glycosphingolipids presenting with lipoproteins. Serum sulfatides (SS) are involved in the inflammatory pathway at the vessel, as well as coagulation and platelet aggregation, we analyzed the SS level of patients with various systemic vasculitis with kidney involvement (SVKI) diseases. [Methods] This retrospective cohort study compared the SS levels in control (kidney transplantation donors, n=23), IgA nephritis (IgAN, n=30), IgA vasculitis (IgAV, n=26), ANCA associated vasculitis (AAV, n=62), and anti-GBM diseases (GBM, n=10), which were admitted to our hospital between 2008 and 2021. Furthermore, we analyzed the relationship between SS level and kidney histological severity. [Results] The mean (± SD) SS level of donors, IgAN, IgAV, AAV, and GBM group was 8.30 (±1.72), 8.49 (±2.34), 6.01 (±1.72), 5.35 (±2.02), and 2.73 (±1.00) nmol/mL, respectively. Those with crescentic class-kidney biopsy finding showed significantly lower SS level than those with other class-kidney biopsy finding. [Conclusions] SS levels are associated with histological severity in patients with SVKI diseases. SS levels may serve as a new biomarker suggesting the presence of active glomerular lesions exhibiting crescent formation.

## W56-6

**Correlation between renal pathological classification and clinical course in patients with ANCA-associated vasculitis**

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Conflict of interest: None

[Background] ANCA-associated vasculitis is a systemic microangiitis disease. In particular, renal lesions occur at a high rate and greatly affect the prognosis. [Methods] We examined the renal histopathology and clinical course of 54 patients with ANCA-related vasculitis who underwent renal biopsy from 2007 to 2022. [Results] The mean age was 70.4±11.3 years old and female were 25 patients. Renal histopathology (international classification) was sclerotic, focal, crescentic, and mixed in 8, 31, 8, and 7 cases, respectively. Thirty-eight patients achieved remission and became ANCA negative, while 16 patients showed no response. The length of hospital stay, Cr, urine protein amount, mean initial steroid dose, and remission rate (%) by renal histopathology were 86.1: 60.0: 86.5: 61.5 days, and 2.4: 1.7: 2.7: 2.7 mg/dL, 2.9: 0.9: 2.7: 2.6 g/gCr, 35.0: 37.0: 46.2: 38.5 mg/day, and 37.5: 73.6: 50.0: 42.8%. for sclerotic, focal, crescentic, and

mixed, respectively. [Conclusion] In renal biopsy cases at our hospital, focal was the most frequent, mild disease, low Cr at initial admission, and good remission rate, and crescentic was poor even with the use of long and high doses of steroids. Renal histopathology was considered effective in predicting therapeutic effects.

## W57-1

**Investigation of the relationship between knee radiographs and disease activity and treatment background in rheumatoid arthritis patients who underwent artificial knee arthroplasty**

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Orthopaedic, KARIYA TOYOTA General Hospital, Aichi, Japan

Conflict of interest: None

[Objective] Pharmacologic therapy for rheumatoid arthritis (RA) is advancing, and knee joint replacement (TKA) due to RA joint destruction is declining. On the other hand, the incidence of knee osteoarthritis (OA) is increasing and the demand for TKA is rising; some reports indicate that RA patients also undergo TKA for OA. The purpose of this study is to investigate the background of RA patients who underwent TKA at our institution. [Methods] 24 RA patients who underwent TKA at our institution from January 2020 to December 2022 were selected. Preoperative patient background, presence of osteophytes on preoperative plain radiographs, Larsen's grade classification, and intraoperative synovial pathology were investigated. [Results] There were significant differences in DAS28CRP (3.0 vs 3.4, p=0.05) and SDAI (10.9 vs 14.7, p=0.03) between the groups with and without osteophytes. The presence or absence of synovitis on intraoperative synovial pathology was significantly associated with the presence or absence of prior DMARDs use. [Conclusions] High RA disease activity was associated with joint destruction with bone resorption and unlikely to cause OA changes including osteophyte formation, suggesting the presence of synovitis control by DMARDs.

## W57-2

**The Association Between Troughing in Scarf Osteotomy for Rheumatoid Hallux Valgus Deformity and the Alteration of the Foot Arch**

Takumi Matsumoto[1], Hiroyasu Mizuhara[1], Akihiro Uchio[1], Ryutaro Takeda[1], Kenta Makabe[1], Taro Kasai[1], Yasunori Omata[1], Toru Moro[2], Sakae Tanaka[1]
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Conflict of interest: None

[Objective] Troughing, a unique complication after a Scarf osteotomy for hallux valgus, concerns RA patients due to bone fragility. This study aimed to investigate the impact of postoperative troughing on the foot arch in RA patients and its relationship with osteoporosis [Methods] 27 RA patients post-Scarf osteotomy were studied. Pre-op and 1-year post-op weight-bearing X-rays measured Meary's angle, Calcaneal pitch, and troughing (T group ≧2 mm increase, C group <2 mm). Bone density was estimated using AI software developed by the University of Tokyo from preoperative chest X-rays. [Results] Post-op, Meary's angle increased (pre-op: 2.0° vs. post-op: 7.1°, $p < 0.01$), and Calcaneal pitch decreased (pre-op: 14.9° vs. post-op: 13.9°, $p = 0.04$). T group had more significant changes (T group vs. C group: [Meary's angle] 11.5° vs. 3.2°, $p = 0.02$; [Calcaneal pitch] 1.4° vs. -0.2°, $p = 0.04$) and lower femur bone density (T group vs. C group [%YAM]: 72.1 vs. 79.1, $p = 0.03$). [Conclusion] Troughing in Scarf osteotomy for RA patients is associated with a decrease in the foot arch. Troughing tends to occur in cases with low bone density, and caution is warranted, particularly in cases with osteoporosis.

## W57-3

**Comparison of joint-preserving surgery versus 1st MTP arthrodesis for rheumatoid forefoot deformity with high Larsen grade**

Soichiro Sakai[1,2], Toshifumi Fujiwara[2], Daisuke Hara[2], Yukio Akasaki[2], Yasuharu Nakashima[2]
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Conflict of interest: None

[Objective] Arthrodesis has been the gold standard of treatment for RA forefoot deformities, but recent drug therapies have led to more reports of the usefulness of joint-preserving surgery. We compared the effectiveness of joint-preserving with that of arthrodesis in RA patients with high Larsen grade. [Methods] Background, pre- and postoperative hallux valgus angle (HVA), M1M2 angle, and JSSF Hallux scale were analyzed for 74 feet in 57 RA patients (3 males and 54 females) who underwent joint-preserving or arithrodesis at the 1st MTP joint from 2008 to 2022. [Results] Methotrexate usage and duration of follow-up were higher in the arthrodesis group. The mean pre-op HVA was not different between the two groups (49°vs. 52°), and was corrected in the joint-preserving (JP) group immediately. (8° and 14°). The recurrence rate was not different between the two groups (14 and 8 cases), and the function was better in JP group (32 and 27 pts, p=0.01). In a study of 38 patients adjusted for background and pre-op function by propensity matching, post-op were better in JP group. (32 and 28 pts, p=0.04) [Conclusions] In RA patients with high Larsen grade, both showed similar symptomatic improvement. Joint-preserving surgery improved foot function, suggesting that may be effective even in severe RA.

## W57-4

**Outcome of joint-preserving surgery for rheumatoid forefoot deformity complicated by severe hallux valgus**

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Conflict of interest: None

[Objective] Good results of joint-preserving surgery for rheumatoid arthritis (RA) forefoot deformities have been reported. We report the results of modified Scarf and offset-osteotomy in RA forefoot deformity with severe metatarsophalangeal angle (HV angle) of 40° or more. [Methods] Fifteen patients who underwent surgery between 2018 and 2021 and could be followed up for at least 1 year were included in this study. Radiographic evaluation included the HV angle, M1M2 angle, M1M5 angle, and Hardy classification before surgery and final follow-up. Clinical outcomes were evaluated by the JSSF RA foot and ankle scale and SAFE-Q before surgery and final follow-up. The Wilcoxon test ($P<0.05$) was used for statistical analysis. [Results] The preoperative JSSF scale was 62.6, which significantly improved to 88.9 points at final follow-up. The preoperative HV angle improved significantly from 55.3 degrees to 11.7 degrees, the preoperative M1M2, M1M5 angle improved significantly from 17.8, 35.9degrees to 7.2, 15.9degrees. Hardy classification 5 to 7 was 22 preoperatively and 2 at the time of the study. The recurrence of hallux valgus was 13.6%. [Conclusions] The modified Scarf and offset-osteotomy are useful in RA forefoot deformity associated with severe hallux valgus.

## W57-5

**Possibility of joint preservation by modified scarf osteotomy for very severe hallux valgus**

Takaaki Noguchi[1], Makoto Hirao[2], Kosuke Ebina[1], Yuki Etani[1], Gensuke Okamura[2], Hideki Tsuboi[3], Atsushi Goshima[3], Yuki Tabuse[2], Jun Hashimoto[2]
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Conflict of interest: None

[Objective] The modified scarf osteotomy is generally used for moderate to severe hallux valgus (HV) deformities. Severe HV is defined as HVA greater than 40°, but this definition includes a wide range of HVA. In fact, HV with an HVA greater than 60° are often seen in patients with RA. However, it is currently unknown whether the modified scarf osteotomy

contributes to the maintenance of correction in such very severe HV deformities. [Methods] We studied 93 feet of 76 patients who underwent HV surgery and follow-up duration was an average of 50 months. The patients were divided into three groups according to the degree of HVA: 44 feet with 40° to 50° (α group), 30 feet with 50° to 60° (β group), and 19 feet with 60° or more (δ group). We evaluated X-ray, complications for surgery, JSSF, and SAFE-Q score. [Results] HVA improved significantly in 3 group at the final follow-up and there was no significant difference in recurrence of hallux valgus between the 3 groups. As for the score, all three groups showed significant improvement except for the SAFE-Q score for social function (P=0.08), but there were no significant differences between the groups. [Conclusions] The modified scarf osteotomy was suggested to be a safe and effective option for patients with very severe hallux valgus.

## W57-6

**Factors affecting delayed wound healing in forefoot surgery in patients with rheumatoid arthritis**

Atsuo Uefuji[1], Shunsuke Takahara[2], Yasushi Tanaka[1], Kazuko Shiozawa[1], Ryosuke Yoshihara[1], Miki Murata[1], Norihiko Amano[1], Miwa Nishida[1], Natsuko Nakagawa[1]

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Conflict of interest: None

[Objective] Delayed wound healing occurs relatively frequently during forefoot surgery in patients with rheumatoid arthritis (RA). Our hospital used carbon dioxide gas transdermal absorption therapy (CO2 therapy) to promote wound healing after forefoot surgery. [Methods] The subjects were 108 feet of 81 RA patients who underwent forefoot surgery, with an average age of 68.6 years. CO2 therapy was administered for 20 minutes every day from the second postoperative day until the day of discharge. We divided cases into the cured group and the delayed group. The factors considered were age, disease duration, preoperative CRP, glucocorticoid (PSL) usage, biological DMARDs usage, degree of preoperative forefoot deformity, and CO2 therapy. Regarding deformity, we investigated the hallux valgus angle (HV angle) and the maximum MTP dorsiflexion angle of lesser toes (MTP angle). [Results] The delayed group was in 21 feet of 20 patients (19.4%), and disease duration, PSL usage, MTP angle, and CO2 therapy showed a significant difference between the two groups. Logistic regression analysis showed that high doses of PSL, high MTP angle, and non-use of CO2 therapy influenced the occurrence of delay. [Conclusions] CO2 therapy seemed to be effective in preventing delay.

## W58-1

**Three-year safety of tofacitinib in patients with rheumatoid arthritis in Japan: final analysis of a post-marketing surveillance study**

Tsutomu Takeuchi[1], Masataka Kuwana[2], Naonobu Sugiyama[3], Shigeki Momohara[4], Tatsuya Atsumi[5], Syuji Takei[6], Naoto Tamura[7], Masayoshi Harigai[8], Takao Fujii[9], Hiroaki Matsuno[10], Kazuhiko Yamamoto[11], Yoshinari Takasaki[12], Nobunari Takahashi[13], Atsuo Nakajima[14], Ayako Nakajima[15], Miki Tanigawa[3], Yutaka Endo[3], Toshitaka Hirano[3], Masato Hoshi[3], Tsuneyo Mimori[16], Michiaki Takagi[17], Nami Okamoto[18], Sakae Tanaka[19], Yoshiya Tanaka[20]

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Conflict of interest: Yes

[Objective] Assess tofacitinib (TOF) long-term safety in Japanese patients (pts) with rheumatoid arthritis (RA) in a 3-year, all-case, post-marketing surveillance study. [Methods] TOF-treated and control (CTR; used methotrexate (MTX)/cs/bDMARDs/immunosuppressants) pts with poor RA control after over 8 mg/week MTX for more than 3 months were included. Serious infection (SI)/malignancy risk was compared by Cox proportional hazard models, each with certain covariates/weights. Propensity score weighting adjusted for pt characteristic imbalances. Observation periods: 1/3 years for SI/malignancy. [Results] At baseline (TOF: n=3731/CTR: n=2419): bDMARD (53.3%/12.2%) and MTX history (81.4%/98.6%), and RA stage (I-II: 45.3%/67.1%) and class (1-2: 76.5%/90.8%) were imbalanced. Incidence rates per 100 pt-years (pts with events/pt-years) for TOF/CTR: 6.86 (207/3016.2)/1.42 (32/2260.0) (adjusted hazard ratios (aHRs) across models: 3.3-3.8) for SI; 1.40 (138/9823.6)/0.88 (53/6023.1) (aHRs across models: 1.4-1.6) for malignancy. [Conclusions] TOF had more severe/refractory RA, a higher SI risk and slightly higher malignancy risk vs CTR. Unmeasured confounding factors may have affected results and should be interpreted cautiously.

## W58-2

**Upadacitinib (UPA) Monotherapy (Mono) in Methotrexate-Naïve Japanese (JPN) Patients (pts) With Rheumatoid Arthritis (RA): Results through 5 years (yrs) From SELECT-EARLY**

Tsutomu Takeuchi[1,2], Ronald Van Vollenhoven[3], Yukitaka Ueki[4], Tatsuya Atsumi[5], Nasser Khan[6], Yihan Li[6], Xianwei Bu[6], Sara K Penn[6], Yasutaka Okazaki[7], Vibeke Strand[8]

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Conflict of interest: Yes

Objectives To evaluate the safety and efficacy of UPA for MTX-naïve RA pts through 260wks (5yrs). Methods Pts were randomized to receive 48 weeks of double-blind UPA 7.5 (JPN only), 15, 30 mg, or MTX before entering an open-label, long term extension study. UPA 30 mg were switched to 15 mg prior to marketing approval. Data were analyzed for the overall and JPN pts. Results 314 (28JPN), 55 (all JPN), 314 (27JPN) and 317 pts (28JPN) were assigned to MTX, UPA 7.5, 15, and 30 mg. Of the 945 pts, 775 (82%) completed wk48 and entered the LTE, 690 (73%) completed 5yrs. Of the 138 Japanese pts, 123 (89%) completed wk48 and entered the LTE, 91 (77%) completed 5yrs. At 5 years, DAS28 CRP remission was 60%, 78%, and 81% for pts receiving continuous MTX, UPA 15, and 30 mg, in the overall pts, and 82%, 87%, 95%, and 94% for pts receiving continuous MTX, UPA 7.5, 15, and 30 mg in the JPN pts (As observed). In the overall pts, the rates of serious infections, HZ, CPK elevation, NMSC and neutropenia were numerically higher with UPA 15 and 30 mg than with MTX. The overall rates of MACE, VTE, and malignancy excluding NMSC were comparable across treatments. JPN data generally showed similar trends with global data. Conclusion UPA monotherapy sustained efficacy over 5yrs in RA pts, and no new safety signals were identified.

## W58-3

**Effects of JAK inhibitors on lipid and glucose metabolism in rheumatoid arthritis**

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Conflict of interest: None

[Objective] Although worsening of lipids has been reported with all

five JAK inhibitors for RA, the effect of JAK inhibitors on glucose metabolism is not clear. We investigated changes in serum lipid levels and HbA1c in RA patients treated with JAK inhibitors during 6 months. [Methods] We retrospectively analyzed changes in LDL-C, HDL-C, L/H ratio, TG, and HbA1c before and 1, 3 and 6 months after treatment with JAK inhibitors. [Results] There were 112 patients (37% male, mean age 65 years) who were treated with Baricitinib (BAR) in 39, Filgotinib (FIL) in 24, Upadacitinib (UPA) in 19, Peficitinib (PEF) in 16, and Tofacitinib (TOF) in 14 patients. Overall, LDL-C, HDL-C, and TG reached a maximum after 3 months. L/H ratio and HbA1c reached their minimum values after 1 month and 3 months, respectively. The drugs with the largest mean difference between peak values after JAK inhibitor treatment and pre-treatment values for LDL-C, HDL-C, L/H ratio, TG, and HbA1c were examined. LDL-C was 15.1 [1.2,29.0] mg/dL in UPA, HDL-C was 12.8 [6.3,19.3] mg/dL in FIL, TG was 33.6 [-16.3,83.5] mg/dL in TOF, L/H ratio was -0.3 [-0.6, -0.03] in PEF, HbA1c was -0.4 [-0.8, -0.03] % in TOF. [Conclusions] Serum lipid levels reach a maximum after 3 months and HbA1c reaches its minimum after 3 months with JAK inhibitors.

## W58-4

**The elevation of creatine kinase by JAK inhibitors in rheumatoid arthritis analyzed from PRESENT study**

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Conflict of interest: None

[Object] Creatine kinase (CK) was elevated by JAK inhibitors (JAKi) in RA. We investigated whether a similar elevation occur in multicenter prospective observational (MPO) study. [Methods] The data from 0 and 24 weeks (W) of "Effects of Biologics and JAKi on Sarcopenia in RA (PRESENT Study)" was used. Changes in CK and muscle mass were analyzed from three points: (1) csDMARDs vs b-/ts-DMARDs, (2) JAKi vs biologics, and (3) among five JAKi. Correlations were assessed in changes of CK and muscle mass. [Results] Age was 70 years, disease duration was 4.5 years, and DAS28-ESR was 4.77. 191 patients had data for 24W. There were no significant differences in CK or muscle mass at 0W. (1) CK change was significantly higher in b-/ts-DMARDs compared to csDMARDs (17.0 vs. 9.0 IU/L, p=0.001). (2) CK change was significantly higher in JAKi compared to biologics (46.0 vs 10.0 IU/L, p<0.001). (3) There was no significant difference among five JAKi (p=0.487). The change in muscle mass was not significantly different in all comparisons. No correlation was found between changes in CK and muscle mass (p=0.087). [Conclusions] In MPO study, CK changes were also significantly higher in the JAKi. The lack of correlation with changes in muscle mass is interesting and its mechanism remains to be elucidated.

## W58-5

**Examination of the efficacy and safety of reducing the dose of JAK inhibitors according to renal function -ANSWER cohort study-**

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Conflict of interest: None

[Purpose] Drug adjustments are often required due to comorbid renal dysfunction at RA patients. However, there are few reports regarding the effects and safety of drug reduction. In this study, we compared the effectiveness and safety of TOF, BAR, and FIL, which require dose adjustment depending on renal function for RA patients. [Method] Using data from the ANSWER Cohort, 274 patients were placed in a regular dose group with normal renal function (A: 183), a reduced drug group (B: 54), and a reduced drug group for renal dysfunction (C: 37), and compared their effectiveness and safety. [Results] There were significant differences in mean age between A (58.8) vs B (62.2), A vs C (75.1), and B vs C. The initial CDAI was A: 18.1, B: 18.0 and C: 17.6 with no significant difference. CDAI after treatment was no significant differences at 12,24 and 52 weeks. Regarding the CDAI remission rate, 12 weeks (A: 16.9%, B: 12.9%, C: 27.0%), 24 weeks (A: 20.22%, B: 14.8%, C: 21.6%),52 weeks (A: 24.6%, B: 22.2%, C: 18.9%), and the discontinuation rate due to adverse events from the start to 52 weeks (A: 75.8%, B: 81.7%, C: 85.3%) was a no significant difference. [Conclusion] There was no difference in efficacy and safety when reducing the dose of JAKi due to renal dysfunction compared with regular dose.

## W58-6

**Disease activity and treatment of rheumatoid arthritis associated with interstitial lung disease (RA-ILD) in real clinical practice -ANSWER cohort study -**

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Conflict of interest: None

[Objective] We evaluated the clinical characteristics of RA-ILD and its treatment using the ANSWER cohort. [Methods] RA patients enrolled in the ANSWER cohort from April 2013 to December 2022 were divided into two groups according to the presence of ILD at enrollment, and disease activity and treatment of the two groups were compared. [Results] Patients with ILD were older, more often male, had longer disease duration, and had significantly higher antibody titers for rheumatoid factor and anti-CCP antibodies, KL-6 levels, and use of bDMARDs and JAKi (11.2% vs. 23.8%) at the enrollment. There were no significant differences in smoking rates, HAQ, or disease activity (DAS28-CRP: 3.0±1.4 vs 2.9±1.5, DAS28-ESR: 3.7±1.5 vs 3.9±1.6). Disease activity after 6 months was significantly higher in the ILD group than in non-ILD group (DAS28-CRP: 2.2±1.0 vs 2.4±1.1, DAS28-ESR: 2.7±1.2 vs 3.1±1.2). The use of bDMARDs and JAKi in RA-ILD was 37.0%, and the rate of achievement of DAS28 remission was higher in JAKi-treated patients than in bDMARDs-treated patients (58.2% vs 84.2%). [Conclusions] RA-ILD was refractory to treatment compared to RA without ILD, and the use of JAKi for RA-ILD may increase the rate of remission, but future studies are needed to determine its safety.

## W59-1

**Peripheral Blood Mononuclear Cell Phenotype Analysis in a Successful Case of Resuming Tocilizumab After Prolonged Discontinuation for irAE Due to Atezolizumab Administration in Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] To elucidate the immunological dynamics during the administration of immune checkpoint inhibitors (ICI) complicated with rheumatoid arthritis (RA). [Methods] Peripheral blood mononuclear cells were collected from one case, and immunological cell populations were classified using Mass cytometry. Phenotypes with cell counts at 3 time points were identified. Case: 78-year-old male, ACPA/RF positive, in whom Tocilizumab (TCZ) had been administered long-term, maintaining clinical remission. Diagnosed with hepatocellular carcinoma, TCZ was discontinued and replaced with 10 mg/day of prednisone, but leading to disease exacerbation. Three weeks after starting combination therapy with atezolizumab and bevacizumab, he developed thrombocytopenia. worsened arthritis, and the patient resumed TCZ, resulting in total improvements. [Results] At three time points, ICI pre-administration, during irAE occurrence, and during irAE improvement, non-classical monocytes, naïve CD8 T cells, and dendritic cells exhibited “decrease, increase” changes. Conversely, classical monocytes, NK cells, ICOS-positive T cells, and plasma cells showed “increase, decrease”. [Conclusions] This suggests distinctive changes in the immunophenotype during ICI usage in the context of comorbid malignancy with RA.

## W59-2

**Clinical Factors Involved in the Efficacy and Occurrence of Adverse Events of Sarilumab in RA Patients**

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Conflict of interest: None

[Objective] We investigated the clinical factors involved in the efficacy and occurrence of AEs in RA patients treated with Sarilumab (SAR). [Methods] RA patients who started SAR at our hospital by July 2023 were divided into good response group, poor response group, and AE group. The Differences of clinical factors in each group were retrospectively investigated. [Results] Twenty-six patients were included in this study. Excluding one patient who was treated less than 3 months, 14 patients continued the treatment for more than 1 year, all achieved remission or low disease activity, and were considered as good response group. The treatment was discontinued due to poor response in 7 cases and minor AEs in 4 cases. Between good and poor response group, there were no significant difference in patients background, treatment history, blood test results or disease activity. However, the mean titer of autoantibody in poor response group tended to be higher. All AEs occurred due to the switch from other biologics than Tocilizumab (TCZ), whereas no AEs occurred in 13 patients who switched from TCZ. [Conclusions] SAR may be less effective in RA patients with very high autoantibody titers. When switching from b/ts DMARDs other than TCZ, we should be careful about the occurrence of AEs.

## W59-3

**Effectiveness and safety of Certolizumab Pegol for first-line biologic therapy in rheumatoid arthritis patients over 75 years old**

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Conflict of interest: None

[Objective] To examine the effectiveness and safety of Certolizumab Pegol (CZP) as first-line biologic therapy in rheumatoid arthritis (RA) patients over 75 years old. [Methods] A retrospective study was conducted in RA patients over 75 years old who received CZP as the first-line biologic therapy at our hospital from 2013 to 2023. Patients’ background, disease activities, and clinical course were investigated from the medical records. [Results] The 23 patients (17 women, 6 men) were a median 80 (77.5-83) years old at the start. The median disease duration was 5.4 (3.3-7.1) months. No patients received methotrexate, and 11 (47.8%) received prednisolone. The 21 patients able to be followed for more than 6 months showed a significant reduction in disease activity from early on (DAS28-ESR: 5.75 [4.93-6.61] vs. 3.49 [3.24-4.21); $p<0.001$). Eight adverse events (five infections, two skin rashes, and one case of itching) occurred. Five of the 21 patients discontinued treatment due to secondary ineffectiveness, including 2 due to decreased efficacy immediately after loading. [Conclusions] While the effect was attenuated after loading in some cases, CZP was considered useful as an early treatment for elderly RA patients.

## W59-4

**Tolerance of bDMARDs in Patients with Rheumatoid Arthritis Complicated by CKD Stage G4/G5**

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Conflict of interest: None

[Objective] The study aimed to evaluate the drug retention rates of first-line biological disease-modifying antirheumatic drugs (bDMARDs) in rheumatoid arthritis (RA) patients with chronic kidney disease (CKD) stage G4/G5, comparing hemodialysis (HD) and non-hemodialysis (non-HD) groups, and among different bDMARD modalities. [Methods] Bionaïve RA patients with CKD stage 4/5, newly introduced to bDMARDs between 2004-2022, were studied. The primary outcome was the 36-month drug retention rate. [Results] Of 68 patients, 39 were in the HD group and 29 in the non-HD group. The bDMARDs used were TNFα inhibitors (48 cases), IL-6 inhibitors (14 cases), and CTLA4-Ig (6 cases). The 36-month retention rate was 22.5% for HD and 43.7% for non-HD, with no significant difference (HR=1.33, 95% CI 0.65-2.72, $p$=0.44). By modality, IL-6 inhibitors had the highest retention rate at 61.1% compared to TNFα inhibitors (24.4%) and CTLA4-Ig (25.0%) (TNFα vs. IL-6: HR=0.23, 95% CI 0.07-0.77, $p$=0.02, TNFα vs. CTLA4-Ig: HR=0.91, 95% CI 0.28 - 3.01, $p$=0.88). [Conclusion] In RA patients with advanced CKD, HD status did not significantly impact bDMARD tolerance. IL-6 inhibitors demonstrated higher retention rates compared to other bDMARDs.

## W59-5

**The Safety of Biologics and JAK inhibitors in Patients with Rheumatoid Arthritis Complicated by Renal Dysfunction- the ANSWER cohort study-**

Yoichi Nakayama[1], Akira Onishi[2], Wataru Yamamoto[3], Ayaka Yoshikawa[4], Hideyuki Shiba[4], Naofumi Yoshida[5], Yonsu Son[5], Iku Shirasugi[6], Toshihisa Maeda[7], Masao Katsushima[8], Motomu Hashimoto[8], Yuki Etani[9], Tetsu Itami[10], Yuji Nozaki[10], Hideo Onizawa[2], Takayuki Fujii[2], Kosaku Murakami[11], Koichi Murata[2], Masao Tanaka[2], Shuichi Matsuda[2], Akio Morinobu[1]
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Conflict of interest: None

[Objective] Biologics (Bio) and JAK inhibitors (JAKi) can be used even for RA patients with chronic kidney disease (CKD). However, pharmacokinetics of some JAKi can be influenced by renal function. We aim to examine the drug tolerability of Bio and JAKi in RA patients with CKD. [Methods] RA patients treated with Bio or JAKi with renal excretion property were enrolled. Patients were stratified to 3 groups according to pre-treatment eGFR (Normal: eGFR ≧ 60, CKDa: 60 > eGFR ≧ 45, CKDb: 45 > eGFR). In each group, the drug discontinuation rates were compared between drugs using the Cox proportional-hazards model. [Results] In the normal group and the CKDa group, there were no differences in adverse events-defined discontinuation rate between Bio and JAKi. In the CKDb group, lower discontinuation rates were identified in TNFi use (HR: 0.24 [0.09-0.61]), IL-6Ri (0.37 [0.16-0.88]), CTLA4-Ig (0.38 [0.16-0.93]), compared to JAKi. Inefficacy-defined discontinuation rates were comparable between each Bio and JAKi. [Conclusions] Bio and JAKi were similarly tolerated from a safety perspective in RA patients with normal renal function or mild to moderate renal impairment (45 ≦ eGFR < 60). In patients with moderate to severe renal impairment (eGFR < 45), Bio showed better tolerability than JAKi.

## W59-6

**Comparison of continuation rates and efficacy of abatacept, IL-6 inhibitors, and JAK inhibitors for rheumatoid arthritis with interstitial lung disease**

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Conflict of interest: None

[Objective] To compare the continuation rate and efficacy of abatacept (ABT), IL-6 inhibitor (IL-6i) and JAK inhibitor (JAKi) in RA patients with interstitial lung disease (ILD). [Methods] Fifty-two patients with RA patients with ILD (ABT: 17, IL-6i: 24, JAKi: 11) between August 2011 and July 2020 were included. The changes in Pt-PainVAS, DAS28-ESR, and CDAI were compared among the 3 drugs. [Results] There were no significant differences in patient background at the start of treatment, DAS28-ESR was at least intermediate disease activity (ABT: 5.6, IL-6i: 5.2, JAKi: 4.8, p=0.39), 1 year continuation rate was not significantly different (ABT: 65%, IL-6i: 46%, JAKi: 55%, p=0.49). The most common reasons for discontinuation were inadequate response (ABT: 67%, IL-6i: 54%, JAKi: 40%). Pt-PainVAS change (ABT: -20.9, IL-6i; -19.4, JAKi: -20.7, p=0.99), DAS28-ESR change (ABT: -0.78, IL-6i; -1.95, JAKi: -1.92, p=0.15) and CDAI change (ABT; -8.67, IL-6i; -10.70, JAKi: -15.17, p=0.51) improved in patients who continued treatment for 1 year, and no significant difference was observed between the three drugs. [Conclusions] No significant differences were observed in the continuation rate and improvement in disease activity of ABT, IL-6i, and JAKi for RA patients with ILD.

## W60-1

**Effects on disease activity and relationship with PRO indicators up to 6 months from the start of administration of anifrolumab for SLE**

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Conflict of interest: None

[Objective] We analyzed data on anifrolumab (Ani) for SLE to examine its efficacy and its relationship to PRO indicators. [Methods] Of the 22 cases with Ani administration, 2 sets were created: 20 cases after 8w from the start of administration as a very short-term group (VST), and 16 cases after 24w in a short-term group (ST). We investigated the effects of Ani on laboratory data, SLEDAI, and correlation with PRO indicators. [Results] SLEDAI significantly decreased at 8w (4.65, p=0.04) in VST, at 24w (3.81, p=0.049) in ST compared to baseline (5.95, 5.94 respectively). The GC dosage significantly decreased at 8w (9.9 mg/dL, p=0.04) in VST, at 24w (7.0 mg/dL, p=0.03) in ST compared to baseline (15.7 mg/day, 10.3 mg/day respectively). PGA significantly decreased at 24w (0.75, p=0.02) compared to 12w (1.06). Both Fatigue VAS (fVAS) and Lupus Impact Tracker (LIT) decreased (but no significance vs baseline). There was no correlation between LIT, fVAS, and PGA with SLEDAI, GC dosage and laboratory data, but a strong correlation was observed between LIT and fVAS (r=0.908, p=0.002,95% C.I. (0.564-0.983)). [Conclusions] Anifrolumab has an early effect on disease activity for SLE and may be able to rapidly reduce GC. On the other hand, it was considered difficult to estimate PRO from test results and SLEDAI.

## W60-2

**Longitudinal analysis of clinical symptoms and immunocompetent cells in SLE patients receiving anifrolumab**

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Conflict of interest: None

**[Objective]** Blockade of type 1 interferon (T1-IFN) receptor with anifrolumab (ANI) shows clinical efficacy in SLE. Due to the pleiotropic effects of ANI, it remains unclear which cellular changes are associated with clinical efficacy. Therefore, we performed a longitudinal analysis of clinical symptoms and immunocompetent cells in SLE patients treated with ANI. **[Methods]** We analyzed clinical symptoms, laboratory findings, and changes in immunocompetent cells over time before and after induction of ANI in 7 patients with SLE. The obtained data were also compared with those of BLM-treated patients. **[Results]** Patients received PSL at a median dose of 10 (8-14) mg/day, with a median disease activity score (SLEDAI-2K) of 3 (2-9) at baseline. After ANI induction, an improvement in disease activity was observed in 5 of 7 patients. Cutaneous symptoms were markedly improved. PSL doses also declined. Immunocompetent cell analysis revealed a rapid decrease in Siglec-1 levels on monocytes, particularly in ANI responders, with modest effects on B and T cell subsets as well. **[Conclusions]** The clinical efficacy of ANI in patients with SLE was confirmed. These profiles also correlated with changes over time in several immunocompetent cells.

## W60-3

**Anifrolumab for Systemic Lupus Erythematosus: A Retrospective Evaluation of Efficacy and Safety**

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Conflict of interest: None

[Objective] To investigate the efficacy and safety of Anifrolumab (ANI) for SLE patients in our department. [Methods] A retrospective study

was conducted on 20 SLE patients who started ANI treatment in our department from February 2022 to August 2023. [Results] Average age was 44.7 ± 12.8 years. 2 males, 18 females. At the time of ANI initiation: prednisolone 6.8 ± 5.1 mg/day. Main therapeutic effects by 24 weeks were observed in rash (7/11, 63.9%), arthritis (4/8, 50.0%), and fatigue (5/10, 50%). The continuation rate up to 24 weeks was 45.0% (9/20). In the continuers, improvement in disease conditions was observed in all cases, with a significant reduction in average SLEDAI scores (4.2 ± 1.9 vs 0.2 ± 0.7, $p<0.01$). Comparing the 11 cases that showed improvement by 24 weeks to the 9 ineffective cases, there was a significant difference in average C3 at the time of ANI initiation (76.7 ± 16.4 mg/dL vs 108.1 ± 23.4 mg/dL, $p<0.01$). Adverse events included 1 case each of herpes zoster, bronchitis, and thrombocytopenia. [Conclusions] ANI proved useful for activity control under concomitant immunosuppressive therapy. The presence of low complement levels at the start of ANI suggested a potential association with its efficacy. No serious side effects were observed, indicating its safety.

## W60-4

**Effect of belimumab on clinical profiles in patients with systemic lupus erythematosus (SLE)-alterations of immunological activity, disease activity and daily living score-**

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Conflict of interest: None

[Objective] We have examined the effect of belimumab in patients with SLE. [Methods] We selected 45 cases (F/M 37/8) from 2018 to 2023 in patients with SLE treated with belimumab (BE) to clarify the effect of BE on immunological data, disease activities (SLEDAI), daily living score (DLS) and dose of PSL after treatment for 6 months (M), 12 M and 24M. [Results] Mean BMI and duration of disease were 20.7±3.7 kg/m2 and 12,4±13.4 years. After treatment with BE for 6M, 12M and 24M anti-dsDNA antibodies (AU/ml) were significantly decreased for 6M, 12 M and 24 M, respectively ($p<0.05$, before 50±91, 6M 20±46, 12M 14±28, 24M 11±21), and C3, C4 and CH50 (U/ml) were significantly increased. Levels of SLEDAI score were significantly decreased ($p<0.01$, before 12±7, 6M 5±3, 12 M 4±3, 24M 5.2±2.3 ($p<0.05$) and Doses of PSL (mg) were significantly decreased ($p<0.01$, before 11.6±10.0, 6 M 5.0±3.6, 12 M 4.7±3.1, 24M4.5±3.4). DLS scores were also significantly improved ($p<0.01$-0.05, before 26.1±13.6, 6M 18.6±12.3, 12M14.7±15.8, 24 M 13.1±11.9). Anti-SS-A and SS-B antibodies were tend to be decresed, but not anti-RNP antibody [Conclusions] Effects of BE on clinical results, and induction of clinical remission and maintenance treatment were useful without major adverse effects in patients with SLE.

## W60-5

**Safety and Efficacy of Belimumab (BLM) to Systemic Lupus Erythematosus in induction phase**

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Conflict of interest: None

[Objective] In EULAR 2023, suggested that GC use in the induction phase is a bridging therapy and the early use of immunosuppressive agents and biologics including BLM should be considered. However, the use of BLM in the induction phase has been reported only for active LN. In this study, we aim to evaluate the safety and efficacy of BLM in the induction phase. [Methods] Single-Center, retrospective cohort study. SLE patients with a history of BLM use during GC therapy were included. We analyzed after classifing into two groups: induction group (within 6 months from induction therapy) and non-induction group. [Results] All 40 patients included and 22 patients were classified as the induction group. They had shorter disease duration and significantly higher median SLEDAI-2K at the first visit. In addition, BLM was initiated with a significantly higher GC dose (median 25 mg vs. 5 mg, $p<0.001$). Median BLM exposure duration and the continuation rate was similar in both groups (77.3% vs. 77.8%). Discontinuation due to infection was not observed. In the induction group, 15 patients achieved both LLDAS and remission. 3 relapses occurred in each group at GC less than 5 mg. [Conclusions] The use of BLM for SLE in the induction phase was as safe and effective as in the non-induction phase.

## W60-6

**Long-term discontinuation of Belimumab in SLE after achieving low disease activity**

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Conflict of interest: None

[Purpose] We conducted a retrospective study of SLE patients who discontinued BEL long term at our hospital. [Methods] We retrospectively observed changes in disease activity and clinical background at 24, 48, and 96 weeks after discontinuation of BEL who had been on BEL for at least 24 weeks and who discontinued BEL after achieving SLEDAI 4 or less. The endpoints were prednisolone (PSL) dose and SLEDAI at the time of BEL discontinuation, 48 weeks and 96 weeks after BEL discontinuation. [Results] The number of evaluable SLE patients who met the above criteria was 8 patients at 48 weeks and 6 patiernts at 96 weeks. SLEDAI was 2.7±1.6 at discontinuation to 2.4±1.1 at 48 weeks to 1.0±1.1 at 96 weeks, maintaining a significant reduction when comparing BEL induction and 96 weeks ($p<0.05$, ANOVA). The PSL dose was 4.8±2.9 mg at discontinuation to 3.0±1.3 mg 48 weeks to 2.7±1.3 mg at 96 weeks. PSL use remained significantly lower when comparing BEL induction to 96 weeks ($p<0.05$, ANOVA). [Conclusion] SLE patients who achieved SLEDAI 4 or less after 24 or more weeks of BEL did not have flares of disease activity or increased PSL use at 48 or 96 weeks after discontinuation of BEL.

## W61-1

**How should we care for T-SPOT test positive patients in rheumatology? -Risk analysis and long-term prognosis of tuberculosis-**

Shinichi Nogi[1], Yusuke Yano[1], Mayuka Tanimura[1], Taro Kamemura[1], Ayaka Ito[1], Rikuo Hase[1], Hirotaka Tsuno[1], Akiko Komiya[2], Atsushi Hashimoto[3], Toshihiro Matsui[4]
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Conflict of interest: None

[Objective] T-SPOT is one of the tests for diagnosing of tuberculosis (Tb) infection. It is important exam to check about latent infection, especially to prevent reactivation during immunosuppressive treatment. From all T-SPOT data until 2022, we followed up the positive rate for 10 years and risk analysis of active Tb. [Methods] We retrospectively investigated all T-SPOT data and patients background from 2013 to 2022 and analyzed risk facfor of Tb. [Results] T-SPOT positive samples were 490 (4.9%) (in rheumatology; 179 (3.8%)) in 10103 all samples (in rheumatology; 4654) for 10 years in our hospital. The positive rate was decreasing year by year for 10 years. In 179 positive samples (157 patients) in rheumatology, 61% patients have rheumatoid arthritis, 56.7% patients (will) used DMARDs and 8 patients had active Tb. The other 149 positive patients were followed up for average 3.8 years (max 10.5 years), and no patient developed active Tb. CD64 were measured in 3 of the 8 patients with active Tb, and all of them were elevated very high levels. [Conclusions] After evaluation to be inactive Tb with T-SPOT positive, the risk of subsequent development to active Tb might be quite low. However, cases with DMARDs or elderly patients with lower ADL were the risk of developing to active Tb.

## W61-2

**Clinical Features of Pulmonary Fungal Infections in Patients with Rheumatic Diseases**

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Conflict of interest: None

[Objective] To clarify the clinical features of pulmonary invasive fungal diseases (IFD) in patients with rheumatic diseases under immunosuppressive therapy. [Methods] We conducted a retrospective observational study involving consecutive patients visited our hospital between June 2007 and July 2022. Inclusion criteria consisted of (1) a history of serum aspergillus antigen assay or detection of filamentous fungi in respiratory specimens, (2) immunosuppressive therapy for rheumatic diseases, and (3) testing prompted by suspicion of pulmonary IFD. [Results] A total of 368 patients met eligibility criteria. Final diagnoses were as follows; IFD (n=49), relapse of primary disease (n=86), bacterial infection (n=85), non-tuberculous mycobacteria infection (n=30), pneumocystis pneumonia (n=30), malignancy (n=25), and others (n=59). Risk factors of IFD were male (OR 3.2, p<0.001), smoking (OR 1.9, p=0.045), systemic vasculitis (OR 4.3, p<0.001), prednisolone intake >20 mg/day (OR 3.1, p=0.001), and interstitial lung diseases (OR 3.6, p<0.001). IFD had significant lower 5-year survival rate compared to non-IFD (54.7% vs 83.2%, p<0.001). [Conclusion] We should aware that IFD is not rare and has poor prognosis, especially in cases of systemic vasculitis or interstitial lung disease.

## W61-3

**Guideline compliance rates in HBV DNA monitoring in RA patients with resolved hepatitis B virus infection at our hospital**

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Conflict of interest: None

[Objective] This study aimed to investigate guideline (GL) compliance rates in HBV DNA monitoring in RA patients with resolved hepatitis B virus (HBV) infection at our hospital. [Methods] 438 patients receiving immunosuppressive drugs had been screened for HBV infection, and 73 patients with resolved HBV infection were included in this study. Medications used, number of HBV DNA tests, and GL compliance rates were examined. [Results] MTX was used in 53 cases, tacrolimus in 32 cases, biologic DMARDs in 22 cases, and JAK inhibitors in 4 cases, including those used in combination. Of the 65 patients who were treated regularly for one year, 19 had electronic medical records with the reminder measures (group A) and 46 without them (group B). The annual number of tests was 6.7±2.1 and 5.5±1.8 in group A and group B, respectively. Adherence to the HB treatment GL, which required testing every 1 to 3 months, was 94.7% in group A and 87.0% in group B. The compliance rate for 56 patients treated by RA specialists and 9 patients treated by non-specialists was 94.6% and 55.6%, respectively. [Conclusions] Monitoring was almost properly conducted according to the GL. Reminder measures on the records were effective. It is also necessary to make non-specialists aware of the importance of monitoring.

## W61-4

**The clinical characteristics of the patients with cytomegalovirus reactivation after induction therapy of rheumatic diseases**

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Conflict of interest: None

[Objective] To elucidate the clinical characteristics of patients (pts) with cytomegalovirus (CMV) reactivation after remission induction therapy (RIT) of rheumatic diseases, we investigated this study. [Methods] Among the pts admitted to our department from August 2022 to July 2023, those who were started the RIT for new-onset rheumatic diseases were included. [Results] Total 43 pts were analyzed (vasculitis, n=15; IgG4-related disease, n=9; PM/DM, n=7; SLE, n=3; RA, n=2; others, n=7). As induction therapy, methylprednisolone (mPSL) pulse therapy, high-dose glucocorticoids (GCs, 1.0 mg/kg), moderate-dose GCs (0.5-0.6 mg/kg), and low-dose or less GCs were used to 7%, 56%, 30% and 12% of pts, respectively. Other immunosuppressants (ISs) were used in 63% (IVCY, n=7; the others n=20). Comparing the clinical data of pts with CMV reactivation (n=10) and those without (n=33), i) older-age (75 vs 64 years old, p=0.007), ii) lower serum albumin level (2.6 vs 3.4 mg/dL, p=0.034), iii) higher dose of GCs (1.0 vs 0.6 mg/kg, p=0.003), and iv) IVCY (60 vs 3%, p<0.001) were the features of CMV reactivation. [Conclusion] CMV reactivation might be carefully considered after RIT of rheumatic disease in the elderly pts with hypoalbuminemia received intensive immunosuppressive therapy.

## W61-5

**Biomarkers aiding early diagnosis of septic arthritis in emergency medical practice**

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Conflict of interest: None

[Objective] To identify clinical inflammatory biomarkers in patients with septic and non-septic arthritis. [Methods] This retrospective chart review included 55 and 221 patients with septic and non-septic arthritis, respectively, treated between May 2018 and May 2023. [Results] Joints with arthritis included shoulder, elbow, wrist, hip, knee, and ankle. In the septic arthritis group, hematological examination showed higher white blood cell (WBC) count, neutrophil sequestration, C-reactive protein, and procalcitonin levels; joint fluid analysis revealed higher WBC count; and lower articular glucose concentration and the ratio of articular to hematic glucose concentrations, which showed the best potential as a diagnostic predictor of septic arthritis based on the receiver operating characteristic curve analysis. [Conclusions] The articular-hematic glucose concentration ratio, which showed the best potential as a diagnostic biomarker to distinguish between septic and non-septic arthritis, may aid effective estimation of the septic arthritis risk in emergency medical practice.

## W61-6

**Two cases of rheumatoid arthritis with pneumocystis pneumonia developed after discontinuation of sulfasalazine**

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Conflict of interest: None

[Case 1] A 73-year-old woman with rheumatoid arthritis (RA) being in remission on abatacept, methotrexate (MTX), and sulfasalazine (SSZ) discontinued SSZ 4 months prior. Sixteen days prior to her visit, she developed fever, and 6 days prior to her visit, she developed cough and dyspnea on exertion. She was diagnosed with pneumocystis pneumonia (PCP) based on low $SpO_2$, ground glass opacity on chest CT, elevated β-D glucan, and positive sputum PCR test for Pneumocystis. She was treated with sulfamethoxazole / trimethoprim (SMX/TMP) and prednisolone (PSL) and recovered. [Case 2] A 74-year-old woman with RA had been in remission on MTX, tacrolimus, and SSZ discontinued SSZ 3 months ago. Two days prior to her visit, fever, cough, and respiratory distress appeared. With ground glass opacity on chest CT, elevated β-D glucan and positive sputum PCR test for Pneumocystis, a diagnosis of PCP was made. Treatment with SMX/TMP and PSL improved her respiratory status and she was discharged. [Clinical Significance] A preventive effect of SSZ against PCP has been reported in patients with RA. Since SSZ has dual effect on RA and PCP, increased risk of PCP after stopping SSZ should be considered.

## W62-1

**Whether low nutritional status increase the surgical site infection in RA patients?**

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Conflict of interest: None

[Objective] We examined whether low nutritional status increase the risk of surgical site infection in RA patients or not. [Methods] We evaluated 1196 patients data who was performed orthopaedic surgery in 2017-2019 (Rheumatoid arthritis (RA): 248; others: 948). We evaluated weight, height, sex, duration of operation, implant use, type of surgery, total volume of bleeding, use of MTX, biologics, prednisolone, blood albumin, CRP, total protein, cholesterol, lymphocyte, and nutritional status using Geriatric nutritional risk index and Controlling Nutrition Status. [Results] Twenty two patients affect surgical site infection, 4 patients was RA and 18 patients were others. There was no statistical differences of rate of surgical site infection between RA patients and others. In all patients, male, longer duration of operation time, implant use, and higher volume of bleeding increased the rate of surgical site infection. Geriatric nutritional risk index showed that low nutritional status increased the rate of surgical site infection in RA patients. [Conclusions] Our findings showed that only in RA patients, low nutritional status increased the risk of SSI. Improvement of nutritional status is more important in RA patients before operation.

## W62-2

**Clinical significance of the polymerase chain reaction lateral flow method in the diagnosis of muscleskeletal infections in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To determine the clinical significance of the polymerase chain reaction lateral flow (PCR-LF) method for the detection of three staphylococcal species (methicillin-susceptible Staphylococcus aureus: MSSA, methicillin-resistant Staphylococcus aureus: MRSA, methicillin-resistant coagulase-negative Staphylococcus: MR-CNS) in the diagnosis of muscleskeletal infection patients with rheumatoid arthritis. [Methods] 22 episodes in 20 patients with suspected muscleskeletal infection underwent PCR-LF method. The background factors, final clinical diagnosis, and culture test results of these patients were investigated retrospectively and analyzed in relation to the results of the PCR-LF method. [Results] The number of episodes in which the final diagnosis was infection or non-infection was 15 and 7, respectively. Bacterial culture tests were positive in 5 episodes. Among the culture-negative episodes, the PCR-LR method was positive in 6 episodes (determined as MSSA: 2, MRSA: 0, MR-CNS: 4). The results of the PCR-LF method were consistent with the clinical course and antimicrobial reactivity in those episodes. [Conclusions] The PCR-LF method can provide useful information in culture-negative cases in the diagnosis of muscleskeletal infections in patients with rheumatoid arthritis.

## W62-3

**The Actual Condition of Pneumocystis Pneumonia in Patients with Rheumatoid Arthritis and the Preventive Effect of Salazosulfapyridine -Aichi Prefecture DPC Data**

Ryo Sato[1], Takahiro Imaizumi[2], Kenya Terabe[1], Junya Hasegawa[1], Masataka Maeda[3], Hironobu Kosugiyama[1], Mochihito Suzuki[1], Shuji Asai[1], Shiro Imagama[1]

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Conflict of interest: None

[Background] Pneumocystis pneumonia (PCP) in rheumatoid arthritis (RA) progresses rapidly, and prevention, early diagnosis, and treatment of PCP are essential. Previous case-control studies have suggested that salazosulfapyridine (SASP) is effective in the prevention of PCP. [Objective] To investigate the actual status of PCP in RA patients and the preventive effect of SASP on PCP. [Methods] Factors associated with PCP incidence and SASP involvement in PCP were examined using conditional logistic regression analysis using the Aichi Prefecture DPC database from 2015 to 2022. [Results] Univariate analysis of the control group (n=2989) and PCP group (n=151) adjusted for age and sex showed significant differences in MTX and b/tsDMARDs as factors associated with the development of PCP. In multivariate analysis, COPD (OR=1.65, P<0.05), PSL≦10 mg/day (OR=1.67, P<0.05), MTX (OR=5.15, P<0.001) and tsDMARDs (OR=2.67, P<0.05) were associated with PCP. Additional analysis by drug showed that SASP alone (OR=0.02, P<0.001) and SASP+b/tsDMARDs (OR=0.07, P<0.05). [Conclusions] The incidence of PCP was significantly increased in patients with pre-existing COPD, MTX, tsDMARDs, and use of PSL 10 mg/day or higher. Among them, the use of SASPs was associated with a reduced risk of PCP in RA patients.

## W62-4

**Study of 18-year trends in infectious disease hospitalizations of rheumatoid arthritis (RA) patients based on NinJa data registered by our department**

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Rheumatic Disease Center, Kurashiki Medical Center

Conflict of interest: None

[Objective] As the population of RA patients continues to age, there is concern that the number of hospitalizations for infectious diseases will increase. We investigated the trends in hospitalization for infectious diseases in RA patients at our hospital over an 18-year period. [Methods] Regarding the 11,449 patient-years of infectious disease hospitalizations registered from our department in the 18-year period from 2005-22 in the National Database of Rheumatic Diseases in Japan (***NinJa***), the first term (2005-10) and mid term (2011-16) and the latter half (2017-22), divided into 3 groups of 6 years and compared. [Results] 1,758 people were hospitalized, and the frequency decreased to 210,150,142 thousand person-years (tpy). Of these, 329 were infectious diseases, the frequency increased to 23,31,29 tpy. Pneumococcal pneumonia decreased by 2.0,0.6,0.6, and PCP by 4.9,1.8,1.2 tpy. NTM increased by 0,1.2,1.3 tpy. There were two cases of COVID-19 pneumonia, with an incidence of 1.1 tpy. [Conclusions] An 18-year study conducted at a single institution revealed that patients are aging and RA disease activity is decreasing due to increased use of MTX and Biologics, and hospitalizations of RA patients are decreasing, but hospitalizations for infectious diseases are increasing.

## W62-5

**Survey on Vaccination Practices Among Patients with Autoimmune Rheumatic Diseases (AIRD) and Rheumatologists (Kanagawa Study)**

Kenji Oku[1], Hidehiro Yamada[2], Masashi Akizuki[3], Haruko Ideguchi[4], Atsushi Ihata[5], Atsuhisa Ueda[6], Shigeru Ohno[7], Junichi Obata[8], Takuya Kakutani[9], Kimito Kawahata[10], Shinji Sato[11], Naoki Sawa[12], Akiko Suda[13], Hiroaki Taguchi[14], Mitsuhiro Takeno[15], Hiroyuki Hagiyama[16], Toshihiro Matsui[17], Masaomi Yamasaki[18], Kunihiro Yamaoka[1]

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Conflict of interest: None

[Objective] Investigating AIRD patient vaccination status in Kanagawa Prefecture [Methods] Online survey conducted from Jan. to May 2023 among 77 rheumatologists and 1673 AIRD patients in Kanagawa prefecture, gathering data on vaccination history, rates, awareness, and physician recommendations for available vaccines. [Results] Among patients (aged 58.6 (16-94) years, female 82.4%), 63.1% had rheumatoid arthritis, 14.8% had systemic lupus erythematosus (SLE), and 22.0% had other diseases. SLE patients had higher herpes zoster (HZ) occurrence in all age group (53.7% vs. 34.4%) including younger individuals (47.3% vs. 26.2%) with the rate of multiple recurrences (17.5% vs. 7.0%). Multifactorial analysis revealed that SLE and age 65+ were HZ risk factors. Low HPV (4.3%) and HZ (8.8%) vaccination rates due to concerns about side effects (62%) and lack of information (58.1%). Most patients (75.6-81.8%) were willing to vaccinate with adequate information. Rheumatologists reported giving suitable recommendations (72-100%). [Conclusions] High HZ rates in AIRD patients, especially those with SLE, highlight the need for early HZ vaccination. Low vaccination rates suggest a perception gap between rheumatologists and patients, necessitating changes in perspectives and better information dissemination.

## W62-6

**A Case of Progressive Multifocal Leukoencephalopathy (PML) in a Patient with Systemic Lupus Erythematosus (SLE) Improved by Immunosuppressant Dose Reduction**

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Conflict of interest: None

[Case] A 69-year-old female presented with dizziness. Four months ago, she was diagnosed with SLE and Lupus Nephritis Class V. She was initially treated with methylprednisolone and hydroxychloroquine and mycophenolate mofetil, which induced remission. One month ago, she developed dizziness and dysarthria upon physical exertion. An MRI scan revealed hyperintense lesions in the right cerebellar hemisphere and cerebellar peduncle, which were initially considered as cerebellar infarctions. Despite treatment, her neuroimaging findings and neurological symptoms worsened, suggesting cerebellar inflammation due to SLE. Therefore, she received steroid pulses, intravenous human immunoglobulin, and cyclophosphamide, but her condition continued to deteriorate. A CSF JC virus PCR test showed a high viral load of 803 copies/mL, confirming the diagnosis of PML. After the diagnosis, MMF was discontinued, and a gradual reduction in steroids led to a gradual improvement in her neurological symptoms. Three months after onset, the JC virus PCR load in the CSF decreased to 94 copies/mL, and there was no recurrence of SLE symptoms. [Discussion] This case is unique due to the early onset of PML during SLE treatment and the fact that improvement was achieved solely through a reduction of immunosuppression.

## W63-1

**Ankylosing Spondylitis Specified Medical Expense Certificate Holders Change (2015-2021)**

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Conflict of interest: Yes

[Objective] The current study aimed to estimate the number of patients based on the number of specific medical expense beneficiary card holders. [Methods] We investigated the number of holders of the certificate of recipients of specified medical expenses, which is published on the Intractable Disease Information Center's website every year, and the changes over the years from 2015 to 2021. [Results] The number of ankylosing spondylitis beneficiary certificate holders increased 4.5-fold from 2015 to 2021. However, the percentage of those in their 10s~30s, considered the age group with a favorable incidence of ankylosing spondylitis, decreased from 30% to 20%. On the other hand, the number of holders aged 70 and over increased 12-fold. The national average number of beneficiary certificate holders per 100,000 population was 3.34. By prefecture, Nagano Prefecture had the highest number of respondents (7.42) and Shimane Prefecture had the lowest (1.19). [Conclusions] The future direction might be in prefectures where the number of AS card holders per 100,000 population is above the national average and the rate of increase is also above the national average, there is a need to examine the appropriateness of AS diagnosis.

## W63-2

**Long-term outcome of Undifferentiated Peripheral Spondyloarthritis**

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Conflict of interest: None

[Objective] We aimed to investigate the long-term outcome of undifferentiated peripheral spondyloarthritis (upSpA) in clinical practice. [Methods] We observed 106 cases diagnosed with peripheral spondyloarthritis (pSpA) in our department between April 2015 and June 2022. We classified the group as upSpA if they met the ASAS pSpA classification criteria but did not belong to any other pSpA category. We retrospectively analyzed clinical findings, disease activity, and treatment outcomes, comparing them among groups within pSpA. [Results] Among the pSpA groups, there were 59 cases of upSpA (PsA: 23 cases, IBD-SpA: 6 cases, pSpA suspected: 18 cases). In comparisons between these groups, upSpA cases had a higher age of onset, higher frequency of dactylitis and arthritis, and a higher number of enthesitis on ultrasonography. At diagnosis, upSpA showed higher disease activity (DAPSA) and impaired physical function (HAQ), but these differences disappeared 12 months after treatment, and 15 cases (26%) achieved drug-free remission. [Conclusions] Our study suggests that upSpA exhibits high disease activity at diagnosis but tends to have favorable outcomes after treatment. Changes in diagnosis were observed, highlighting the importance of long-term observation in managing these patients.

## W63-3

**The effects of psoriatic arthritis on osteoporosis treatment**

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Conflict of interest: None

[objectives] The aim of this study was to investigate bone mineral density (BMD) change in patients with PsA. [Methods] We analyzed 35 PsA patients. BMD at the lumbar spine, proximal femoral and femoral neck were evaluated by DXA at baseline and 12 months after osteoporosis treatment. [Results] Mean age was 60.8±11.4 years, 21 patients were women. Osteoporosis was found in 40% of the patients. Mean BMD change during 12 months were 0.813 to 0.847 g/cm$^2$ at lumbar spine (p=0.03), 0.652 to 0.661 g/cm$^2$ at proximal femoral (p=0.35), 0.51 to 0.517 g/cm$^2$ at femoral neck (p=0.15) in 9 PsA patients with osteoporosis treatment, and were 0.914 to 0.917 g/cm$^2$ at lumbar spine (p=0.42), 0.826 to 0.8 g/cm$^2$ at proximal femoral (p=0.19), 0.655 to 0.656 g/cm$^2$ at femoral neck (p=0.48) in 9 PsA patients without osteoporosis treatment. BMD change at proximal femoral in PsA patients with osteoporosis treatment was higher than PsA patients without osteoporosis treatment (lumbar spine: p=0.14, proximal femoral: p=0.04, femoral neck: p=0.14). Multivariate liner regression analysis revealed that male (β=0.52, p=0.02) and no treatment for osteoporosis (β=0.58, p=0.02) inhibited the improvement of BMD at proximal femoral. [Conclusion] BMD in PsA patients improved by osteoporosis treatment.

## W63-4

**Usefulness of skin and joint assessment of psoriasis and palmoplantar pustulosis under the corporation between dermatologists and rheumatologists for the use of molecular target drugs**

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Conflict of interest: Yes

[Objective] This study examines the usefulness of skin and joint assessment of psoriasis and palmoplantar pustulosis under the corporation between dermatologists and rheumatologists. [Methods] In patients with psoriatic arthritis (PsA) or pustulotic arthro-osteitis (PAO) treated with molecular target drugs under the corporation between dermatologists and rheumatologists, the changes in PASI and DAPSA for PsA, and anterior chest pain for PAO were followed. The drug survival rate was also examined. [Results] Among 58 patients, there were 47 PsA, 3 PAO and 8 others. A total of 29 patients were newly treated with molecular target drugs. In PsA, 75% of patients achieved PASI90, and the ratio of low disease activity of DAPSA increased from 33% to 72% ($p<0.05$). In 2 patients with PAO, the average of anterior chest pain decreased by 3.5 scores. The drug continuation rate was 77.3% at 1 year. Three PsA patients changed the drugs to another one. The DAPSA scores improved in 2 patients after the change of the drugs. One patient diagnosed with frozen shoulder were treated by orthopedician. [Conclusions] The corporation between dermatologists and rheumatologists will enable the assessment of skin and joint lesions in parallel, thereby the improvement of PsA and PAO will be expected.

## W63-5

**Efficacy of Biologics in PsA Patients with Diabetes Mellitus**

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Conflict of interest: None

[Objective] Last year, we reported at this meeting that the efficacy of treatment response of PsA due to comorbidities was reduced in patients with DM comorbidities compared to those without comorbidities. On the other hand, proinflammatory cytokines such as TNFα are also implicated as a central etiologic factor in PsA and are also associated with insulin resistance (IR). To examine the therapeutic efficacy of biologics (bio.) in PsA patients with DM under real-world clinical conditions [Methods] The subjects were 127 PsA patients who were able to continue the same bio for more than 6 months. HbA1c in DM patients was examined for changes in 23 measured cases. [Results] PsA patients were age 60 years, PsA history 3 years, 56% male. The bio. used were TNFi 48%, IL17i 43%, IL12/23i 9%. HbA1c in DM was 6.5 at induction and 6.6 at 12M after induction. HbA1c worsened after bioinitiation in about half of the patients. There was no association between HbA1c level at induction and improvement in HbA1c and disease activity [Conclusions] There was no association between HbA1c or HbA1c change at the time of induction and disease activity of PsA. On the other hand, when using bio. for PsA with DM, care must be taken with glycemic control.

## W63-6

**HLA-B27 promotes transdifferentiation from fibroblasts to osteoblasts**

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Conflict of interest: None

[Objective] In spondyloarthritis, HLA-B27 alleles are well-recognized as contributors to disease susceptibility and activity. Nonetheless, their involvement in osteogenic pathology remains enigmatic. This study aimed to elucidate variations in conversion efficiency and functionality in fibroblast-to-osteoblast differentiation in the presence or absence of HLA-B27. [Methods] HLA-B27 (+) fibroblasts were generated through the introduction of the HLA-B27 gene into human dermal fibroblasts using a retroviral vector. HLA-B27-deficient fibroblasts served as controls and underwent cultivation in an osteoblast induction medium enriched with the ALK-5 inhibitor. Assessment of differentiability into osteoblasts involved qRT-PCR and quantification of calcified bone matrix through alizarin red staining. [Results] HLA-B27 (+) fibroblasts exhibited significantly elevated expression of ALPL and SPP1 genes compared to HLA-B27 (-) counterparts, leading to enhanced osteoblastic differentiation. Moreover, HLA-B27 (+) fibroblasts displayed robust staining even under ALK-5 inhibitor conditions at a lower concentration (1 μM) than the standard condition (5 μM). [Conclusions] The presence of HLA-B27 appears to facilitate the transdifferentiation from fibroblasts to osteoblasts.

## W64-1

**Clinical Features of Hypermobile Ehlers-Danlos Syndrome (hEDS) - A Survey Based on Patients Attending Our Hospital -**

Jun Hashimoto[1], Gensuke Okamura[1], Takaaki Noguchi[2], Shogo Ikeda[1], Shosuke Akita[1], Yuki Tabuse[1], Maiko Yoshimura[1], Akihiko Nakabayashi[1], Atsuko Tsujii[1], Yanakawee Siripongvutikorn[1], Akira Nishigaichi[1], Kurumi Yamamoto[1], Hyota Takamatsu[1], Shiro Ohshima[1], Makoto Hirao[1]
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Conflict of interest: None

[Objective] Ehlers-Danlos Syndrome (EDS) is divided into 13 types, with genetic abnormalities known for 12. Hypermobile EDS (hEDS) remains a mystery. Effective diagnosis and treatment demand interdisciplinary collaboration. Yet, many patients remain undiagnosed and suffer. This study examines the care of hEDS patients in our clinic. [Method] We studied 11 hEDS patients from our clinic, capturing symptom onset, diagnosis time, current complaints, and physical function. [Results] Of participants, 9 were female and 2 male, aged 10-53 (avg. 35). Symptom onset was 0-20 years (avg. 8). All sought medical attention at onset, but none were diagnosed then. Diagnosis age ranged 7-49 (avg. 30). Joints with dislocation history: shoulder (64%), knee (55%), elbow/ankle (45%), hand/hip (36%). Chronic pain was noted in 91%, with other symptoms like gastrointestinal issues (82%) and fatigue (73%). Many showed decreased physical function in adulthood; 38% needed electric wheelchairs post-21. [Conclusion] EDS symptoms vary widely. A marked feature is physical decline during adolescence and adulthood, more than childhood.

## W64-2

**Differentiation between polymyalgia rheumatica and elderly-onset rheumatoid arthritis based on serum MMP-3/CRP ratio**

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Conflict of interest: None

[Objective] We investigated whether the serum MMP-3/CRP ratio is useful for differentiating between EORA and PMR, even if it is not limited to polymyalgic (PM)-EORA. [Methods] We searched our hospital's med-

ical records to find patients whose onset was over 65 y.o., whose clinical diagnosis was EORA or PMR one year later, and whose serum MMP-3 and CRP levels were measured before treatment. EORA is classified as PM-EORA if there is swelling or severe stiffness in the shoulder, and NP (Non-PM)-EORA in other cases. [Results] We were able to analyze 25 PMR, 34 PM-EORA, and 32 NP-EORA. There was a significant difference in CRP (mg/dL) between each group with PMR 7.94±4.62 and EORA 2.84±3.31 (PM-EORA 4.18±3.89, NP-EORA 1.42±1.69). MMP-3 (ng/mL) were PMR 222±117, EORA 229±291 (PM-EORA 304±370, NP-EORA 149±138). The MMP-3/CRP ratio was significantly different between all groups with PMR 40.1±30.7 and EORA 204±240 (PM-EORA 127±133, NP-EORA 285±298). When the discrimination ability of the MMP-3/CRP ratio was examined using ROC analysis, AUC was 0.78 for PMR vs PM-EORA, but AUC 0.83 for PMR vs EORA, and the cut-off was 46.2 for both. [Conclusions] Even without distinguishing between PM-EORA and NP-EORA, the MMP-3/CRP ratio is lower in PMR than in EORA, which helps in differential diagnosis.

## W64-3

**The efficacy of sarilumab and steroid dose reduction effect for polymyalgia rheumatica at our hospital**

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Conflict of interest: None

[Objective] We investigated the clinical efficacy and dose reduction effect of Sarilumab. [Method] PMR patients who were able to evaluate ESR-PMR-activity score (AS) and clinical PMR-AS as disease activity indicators were included. We evaluated disease activity indicators from 4 to 52 weeks after the start of treatment for the SAR group that used SAR for remission induction and the control group that didn't use SAR. The amount of PSL at 24 and 52 weeks and the number of relapses up to 52 weeks were retrospectively evaluated. [Results] There was no significant difference in the background and the disease activity indicators between the SAR group (N=6) and the non-SAR group (N=12). The amount of PSL in the SAR group was significantly fewer (24 weeks: SAR vs non-SAR =1.88±1.64 mg/day vs 6.30±3.74 mg/day, P>0.01. 52 weeks: SAR vs non-SAR =0 mg/day vs 4.31±3.60 mg/day, P>0.01). The PSL-free achievement rate was significantly higher in the SAR group at both 24 and 52 weeks (Week 24: SAR vs non-SAR =50% vs 0%, P> 0.01. Week 52: SAR vs non-SAR =100 vs 8.33%, P>0.01). The number of relapses tended to be lower in the SAR group (SAR vs non-SAR =0.17±0.41vs 0.82±1.30, P =0.16). [Conclusions] SAR may significantly reduce the dose of PSL when used in combination during the induction period in PMR.

## W64-4

**Quantitative Evaluation of Activity in Relapsing Polychondritis**

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Conflict of interest: None

[Objective] Relapsing Polychondritis (RP) is a rare disease that causes inflammation of cartilage throughout the body, sometimes resulting in fatal respiratory deterioration. There are only a few markers of activity in RP, including CRP. The RP Disease Activity Index (RPDAI) is a method to evaluate disease activity, but it is a qualitative assessment of the presence or absence of symptoms, and a quantitative evaluation method needs to be established to deal with fatal conditions such as respiratory symptoms. [Methods] We retrospectively evaluated treatment interventions (e.g. biologic agents) among RP patients who visited our clinic October 2004 to April 2023. We compared the physician's evaluation, CRP, MMP3, imaging, respiratory function tests, steroid dosage, and VAS evaluation of overall and individual symptoms before and 3 months after the intervention. [Results] 56 patients and 106 interventions were studied. The mean age at intervention was 47.5. The amount of oral steroids, CRP, and overall VAS were significantly decreased in the treatment-effective group. [Conclusions] While CRP as an indicator of RP activity is useful, it is decreased by treatment itself, such as anti-IL6 antibody. The present analysis suggested that the overall VAS is important as an assessment of activity.

## W64-5

**Efficacy of over night CPAP for tracheobronchomalacia in biologics refractory relapsing polychondritis**

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Conflict of interest: None

A 31-year-old woman developed vertigo and hearing loss in X-10 and auricular swelling in X-9 and was diagnosed with recurrent polychondritis. Despite treatment with AZA and MTX, her auricular deformity and hearing loss worsened. The patient was treated with TCZ, IFX and ADA, but there was no improvement. PET-CT showed accumulation in the larynx, trachea and main bronchi. The patient was treated with IVCY and JAK inhibitor and was considered for SAR and stenting. The patient was admitted to hospital after resuscitation due to cardiopulmonary arrest caused by mucus accumulation in the subglottic stenosis at the time of outpatient treatment. A tracheotomy was performed for the subglottic stenosis. The patient developed atelectasis due to bronchial collapse. As sputum management was expected to be difficult with a stent, CPAP was started at night. The patient's atelectasis improved and he has been discharged from hospital for more than a year. [Clinical Significance] A patient with advanced hearing loss refractory to multiple biological agents developed fatal tracheal stenosis 9 years later. The patient developed fatal tracheobronchial stenosis after 9 years. Respiratory management with CPAP at night was effective and the patient was able to lead a normal life during the day.

## W64-6

**Arthritis associated with granulomatous mastitis shows reactive arthritis-like findings on ultrasound**

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Conflict of interest: None

[Case] A 28-year-old woman was admitted to the hospital because of polyarthralgia and painful erythema on her extremities during pregnancy. Blood tests showed WBC 10440/μL and CRP 16.7 mg/dL, but were negative for RF, ACPA, ANA, chlamydia, parvovirus B19, streptococci, and IGRA. However, *Corynebacterium kroppenstedtii* was detected in the pus. Biopsy of the breast induration revealed infiltration of neutrophils and lymphocytes, epithelial granuloma, and multinucleated giant cells, leading to the diagnosis of granulomatous mastitis. Ultrasonography showed no synovitis in the wrist joints, but inflammation at the quadriceps muscle and Achilles tendon attachments. [Clinical Significance] Granulomatous mastitis is a form of mastitis that occurs in women of childbearing potential. Although there have been no reports of detailed evaluation of joint lesions, in this case, tendon adhesion inflammation was found to be the predominant cause. Recently, *Corynebacterium spp.* have been reported to be involved in the pathogenesis of granulomatous mastitis, and the joint lesions associated with this disease were considered to be reactive arthritis-like based on ultrasound examination.

## W65-1

**Association between CD8 positive regulatory T cells (CD8+Treg) and clinical features in patients with primary Sjögren's syndrome (pSS), and inhibition of the pathogenesis by the induction of CD8+Treg differentiation**

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Conflict of interest: None

[Objective] To clarify pathogenic roles and therapeutic potential of $CD8^+$Treg in pSS. [Methods] 1) The population of peripheral $CD8^+$ and $CD4^+$Treg were compared by FCM between pSS patients and age gender-matched HC (each N=20). 2) In pSS, the association between $CD8^+$ and $CD4^+$Treg population and clinical features were examined. 3) We examined the effects of CDK 8/19 inhibitor (CDKi) against the induction of $CD8^+Foxp3^+$T cells differentiation from peripheral memory $CD8^+$T cells derived from HC and pSS by IL-2 and TGF-β. 4) The expression of molecules, suppressive ability for proliferation of responder T cells, and IL-10 production in the cells induced by method 3) were compared with those in memory $CD8^+$T cells. [Results] 1) $CD8^+$Treg population was significantly lower in pSS (0.27±0.14%) than in HC (0.68±0.48%), while $CD4^+$Treg population was comparable. 2) $CD8^+$Treg population correlated positively with age and negatively with dryness of ESSPRI. 3) The induction of $CD8^+Foxp3^+$T cells were enhanced by CDKi in HC (from 27.7±9.7% to 47.1±6.7%), as well as pSS. 4) The expression of CD25, GITR, CTLA4, and suppressive ability for proliferation were significantly enhanced, and IL-10 producing cells were tended to increase. [Conclusion] CDKi might restore $CD8^+$Treg which had suppressive function in pSS.

## W65-2

**progressive pulmonary fibrosis and management in patients with Sjogren's syndrome associated interstitial lung disease**

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Conflict of interest: None

[Objective] This study investigates the frequency of primary Sjögren's syndrome associated interstitial lung disease (pSjS-ILD) meeting the progressive pulmonary fibrosis (PPF) criteria and analyzes the specifics of recognition of disease progression. [Methods] The subjects were consecutive cases diagnosed with pSjS-ILD and the criteria for PPF were defined as an absolute decline of 5% or more in %FVC. [Results] The subjects included 62 cases of pSjS-ILD. The median age was 71 years, with 64.5% females and a median forced vital capacity (FVC) of 87.7%. Thirty cases (48.4%) met the PPF criteria, with a median time of 7.3 months to meet these criteria. Of the 30 cases that met the PPF criteria, attending physicians recognized disease progression in 23 cases (76.7%) at the time the PPF criteria were met, while they did not in 7 cases (23.3%). The group that did not recognize disease progression tended to have a longer duration since the initial evaluation and a lower annual rate of FVC decline. [Conclusions] About half of the pSjS-ILD cases met the PPF criteria, but one in four of them was not recognized. It tends to be challenging to recognize disease progression in groups with a longer duration since the initial evaluation and a lower annual rate of FVC decline.

## W65-3

**Prognostic evaluation using immunosuppressive therapy and salivary gland scintigraphy in Sjögren's syndrome**

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Division of Hematology and Rheumatology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan

Conflict of interest: None

[Objective] The purpose of this study was to determine the long-term prognosis of SS by salivary gland scintigraphy and to clarify factors that influence prognosis, such as extraglandular symptoms associated with SS and immunosuppressive drugs received for other collagen diseases. [Methods] The subjects were 47 patients, underwent salivary gland scintigraphy at the time of diagnosis, and were able to undergo salivary gland scintigraphy again one year later. [Results] 0% of cases with improvement in both parotid and submandibular glands without treatment, 26.2% of parotid gland with treatment, and 11.9% of submandibular gland with treatment. In the treatment group, the Cut Off value of each gland excretion rate, which predicts the presence or absence of treatment effects, was calculated from the ROC curve to be 17.85%. The effectiveness rate of this Cut Off value was 7.7% and 29.5% in cases with progressive and non-progressive glandular dysfunction, respectively, and the efficacy rate was significantly higher in cases with non-progressive disease. (P=0.0134) [Conclusions] In SS, if treatment is not started at an early stage of onset when some function remains, functional impairment will progress.

## W65-4

**Retrospective study of effectiveness of mizoribine in patients with Sjogren's disease, using disease activity score and salivary gland ultrasonography**

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Conflict of interest: None

Mizoribine (MZB), which is a purine metabolism antagonist, is reported to be useful to Sjogren's disease (SD). We analyzed the effectiveness of MZB for SD by disease activity and salivary gland ultrasonography (grey-scale and power Doppler signals (PD) scoring by OMERACT) annually to 3 years (only ESSPRI was followed in 1,3,6 months after starting additionally). Among 55 patients, 30 (54.5%) were effective group, 11 (20.0%) were invalid group, and 14 (25.5%) were discontinued group by adverse effect. In effective group, ESSDAI (fatigue) decreased, ESSDAI (glandular, articular) were on a declining trend 1 year later. ESSPRI (total, dryness, pain) decreased after 3 and 12 months, and ESSPRI (fatigue) decreased after 3 months. PD scores in salivary glands ultrasonography decreased 2 years later (1.44→0.94, p=0.041*), and in the decreasing patients, ESSPRI (haematological) and OHIP-14 decreased, and ESSPRI (fatigue) was on a declining trend. MZB has the ability to decrease the disease activity for various symptoms from the earlier stages and may suppress the inflammation in salivary glands. MZB may have the potential to extend the therapeutic options in SD.

## W65-5

**The long-term prognosis of childhood-onset primary Sjögren's syndrome**

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Conflict of interest: None

[Background] Childhood-onset primary Sjögren's syndrome (pSS) often shows fewer sicca and more extraglandular symptoms than adult pSS; its long-term prognosis is uncertain. [Objective] This study aims to understand the long-term clinical progression of childhood-onset pSS. [Methods] We studied pSS patients diagnosed before 16, with a disease duration of at least five years, continuing under our care. [Results] Eleven patients (9 females) were analyzed. Median age was 20.6 years, onset was 9.7 years, and symptom duration was 10.9 years. According to Japanese criteria, diagnoses were: Definite (3), Probable (5), and Possible (2). No sicca symptoms were seen at diagnosis. Six patients developed new autoantibodies over time, with a breakdown as follows; anti-DNA (3), anti-U1-RNP (2), antiphospholipid (2), and anti-Ku (1). One had thrombotic thrombocytopenic purpura, and another had antiphospholipid antibody syndrome and myositis. Four had extraglandular symptoms treated including prednisolone, mizoribine, hydroxychloroquine sulfate, and methotrexate. At the last visit, ESSDAI was 0-2. Three patients complained of sicca symptoms, and another three had parotid gland swelling within a year. [Conclusions] Additional autoimmune antibodies may be seen during follow-up in childhood-onset pSS.

## W65-6

**In-depth proteomic analysis reveals salivary protein signatures in childhood Sjögren's syndrome**

Hironori Sato, Takeshi Yamamoto
Department of Pediatrics, Graduate School of Medicine, Chiba University

Conflict of interest: None

[Objective] We performed protein analysis of saliva from childhood SS patients and investigated for useful molecules in the assessment of disease activity. [Methods] We collected eight saliva samples of differential disease activity from patients diagnosed with Definite or Possible SS and analyzed them using DIA-MS proteome analysis. We categorized into high disease (>14 points, n=4) and low disease (<5 points, n=4) activity groups in ESSDAI and evaluated proteins related to disease activity. [Results] A total of 7,421 proteins were identified from the salivary proteome analysis. The high disease activity group had many molecules related to the interferon-signaling pathway. We found 62 proteins with significantly different expressions as the result of Welch's t-test (25 upregulated, 37 downregulated). Among the upregulated 25 proteins included Mucin, HLA molecules, interferon regulatory proteins, and β2-microglobulin. Moreover, the expression intensity of these proteins tended to correlate with ESSDAI scores and salivary output. [Conclusions] Salivary protein signatures of childhood SS are similar to adult SS, and might be useful to evaluate disease activity.

## W66-1

**Investigation of the diagnostic and medical course of 9 cases of Familial Mediterranean fever (FMF: Familial Mediterranean fever) - A retrospective study at a single center -**

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Conflict of interest: None

METHODS: To examine the clinical characteristics of 9 cases of FMF diagnosed in our department from 2019 to 2023 from a retrospective perspective. RESULTS: Median age of onset was 29 (23-55), and cyclic fever was observed in all cases. Diarrhea was observed in 4/9 cases Arthritis was observed in 7/9, headache in 3/9, and skin rash in 2/9. Fever lasted less than 72h in 5 cases and longer than 72h in 4 cases. MEFV-related genes were searched, and mutations were found in 7/9 cases. 6/9 patients had been to more than 2 hospitals prior to our department, and 2 patients had been hospitalized. Despite the various prior diagnoses, none of the patients mentioned the possibility of autoinflammatory syndrome/periodic fever/familial Mediterranean fever in the course of their illnesses before coming to our department. None of the patients were instructed to measure their fever type regularly before coming to our clinic. Seven/nine patients had to take a leave of absence or leave their jobs by the time of diagnosis. Discussion: Many cases required leave of absence or separation from employment before diagnosis. A multifaceted approach. Furthermore It was considered necessary to educate patients about the approach of having a fever type recorded in cases of diagnostic difficulty.

## W66-2

**Status of diagnosis and treatment of familial Mediterranean fever patients in our division**

Hiroe Sato[1,2], Yoichi Kurosawa[1], Ayako Wakamatsu[1], Yukiko Nozawa[1,2], Daisuke Kobayashi[1], Takeshi Kuroda[1,2], Ichiei Narita[1]
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Conflict of interest: None

[Objectives] The number of patients with Familial Mediterranean fever (FMF) has been increasing due to increased awareness of the disease. The purpose of this study was to clarify the status of diagnosis and treatment of FMF patients in our division. [Methods] Patients who visited our department with FMF between April 2021 and March 2023 were investigated through medical records. [Results] Thirty-one patients were included and 14 of whom were male (45%). Age at onset was 31 (16-41) years, and it took 3.3 (0.7-11) years from onset to diagnosis. Genetic testing was performed in 20 cases (65%), and mutations in exon10 were found in 6 cases and mutations other than exon10 in 8 cases. Based on the diagnostic criteria of the Ministry of Health, Labor and Welfare research group, 25 cases (81%) were typical cases, and 3 cases (10%) were atypical cases. All patients had a history of using colchicine, and at the time of the investigation. Eight patients (26%) had a history of glucocorticoid use, one patient had a history of canakinumab use, and one patient was currently using tocilizumab. [Conclusions] Most of the FMF patients in our division were typical cases, but the genetic testing was performed in 65%. In many cases, the disease was well-controlled with colchicine.

## W66-3

**Clinical characteristics of Japanese patients with Familial Mediterranean Fever**

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Conflict of interest: None

[Objective] To investigate the clinical features of Japanese patients with Familial Mediterranean Fever (FMF), we evaluated clinical features in patients with FMF treated with colchicine or canakinumab. [Methods] We retrospectively reviewed 27 Japanese patients with FMF treated at our institute. We performed genetic analyses of the *MEFV* gene using targeted next-generation sequencing. [Results] The median follow-up period was 36.4 months. The median attack frequency was 1.0 times every 3 months before treatment initiation. All patients were treated with colchicine. Among the 27 patients, 20 (71.8%) showed a clinical response and 7 (25.9%) showed an incomplete response with sufficient doses of colchicine (n=5) and non-sufficient doses (n=2). These patients achieved a reduction in attack frequency after the initiation of canakinumab. In these seven patients with colchicine-resistant FMF (crFMF), the *MEFV* exon 10 variant was not detected, and the absence ratio of the *MEFV* variant was significantly higher compared to those without crFMF. [Conclusions] Colchicine was effective in 71.8% (20/27) of Japanese patients with FMF; however, the remaining patients (7/27) had crFMF. Canakinumab effectively controlled febrile attacks in crFMF, even in the absence of pathogenic *MEFV* exon 10 variant.

## W66-4

**Consideration of pathogenesis mechanisms through multiple pathways influenced by genetic rare variants in Japanese patients with palindromic rheumatism**

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Conflict of interest: None

[Objective] Palindromic rheumatism (PR) is a cryptogenic paroxysmal arthritis. Although multiple genes are suggested to be involved in the pathogenesis, it is difficult to identify frequent genetic mutations due to the small number of patients. Therefore, we aimed to identify disease-related genes with rare variants that have a high contribution to pathogenesis using whole genome sequencing (WGS). [Methods] The cases consisted of familial mother and daughter and one sporadic. The controls were 104 healthy WGS data from a public database. Rare variant analysis was performed by using SKAT-O, SKAT, and KBAC to search for disease-related genes. In addition, to determine disease-related variants, Japanese-specific variants and polymorphisms were removed from shared variants among cases. We also performed pathway analysis using Reactome. [Results] 74640 disease-related variants were detected, and 1884, 1036 and 875 genes were significant in SKAT-O, SKAT, and KBAC, respectively

($P$<0.05). Additionally, 540 disease-related genes including 1893 variants were significantly detected ($P$<0.05). We also detected significant 32 pathways ($P$<0.05). [Conclusion] It is suggested that multiple pathways affected by rare variants involve in the pathogenesis of PR.

## W66-5

**The involvement of TLR9-IL-12-IFN-gamma axis in the development of macrophage activation syndrome**

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Conflict of interest: None

[Objective] In mouse model of macrophage activation syndrome (MAS) like syndrome, IFN-γ is supposed to be a key cytokine. We investigated the involvement of toll-like receptor 9 (TLR9)-IL-12-IFN-γ axis in MAS-like syndrome. [Methods] The model of MAS was developed in C57BL/6 mice by repeated injection of CpG synthetic oligodeoxynucleotide which stimulates TLR9-mediated signals. Blood samples were collected on day 9 after 5 times of injection and analyzed by ELISA. Mouse Kupffer cell line and spleen cells were stimulated by CpG oligo, and cytokine levels of culture supernatants were measured by ELISA. [Results] In CpG oligo-injected mouse, serum IL-12 levels as well as IFN-γ-stimulated cytokines levels were significantly elevated. CpG oligo-induced IL-12 production from cultured Kupffer cells in a dose dependent manner. Furthermore, anti-IL-12 antibody completely inhibited CpG oligo-induced IFN-γ production from cultured spleen cells. Finally, anti-IL-12 treatment reduced disease severity of CpG oligo-induced MAS-like syndrome. [Conclusions] In TLR9-mediated MAS like syndrome, IL-12 was supposed to be candidate cytokine to induce IFN-γ and might be one of the therapeutic targets.

## W66-6

**Successful Recurrence Cytokine Storm Syndrome (CSS) Cases of Slow Plasma Exchange (PE) Combined with Immunosuppressants**

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Conflict of interest: None

We reported slow PE combined with immunosuppressants successfully contributed to two refractory cases of CSS. The first case had adult-onset Still's disease (AOSD) and the second had Ebstein-Barr virus Associated with Hemophagocytic Lymphohistiocytosis (EBV-HLH). [Case 1] A 50 years female. She got recurrence AOSD after receiving the Corona vaccination. Combination therapy of mPSL, IVCY and TCZ could not suppress her serum ferritin titer, 4038 ng/ml. Then, slow PE was introduced combining continuous iv of CyA. Consequently, her disease activity decreased despite tapering immunosuppressants due to infection. [Case 2] A 4 years girl. She was moved to our hospital because of a recurring high fever. Pulse therapy of mPSL did not control her disease activity; therefore, etoposide was given. She seemed to be in remission and her fever disappeared. Three days later, she showed disturbance of consciousness. Encephalitis with hypercytonemia was considered, then PE was performed. From the 2nd session, slow PE was performed. Her serum ferritin decreased from 60526 to 7669 ng/ml. After the 4th session, continuous iv of CyA and weekly etoposide induced remission. [Summary] Slow PE contributed the management of refractory CSS. It might suppress the rebound of cytokines without any side effects.

## W67-1

**Trend of outcomes in systemic lupus erythematosus**

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Conflict of interest: None

[Objective] This study aimed to investigate how outcomes in patients with SLE have changed since 2015, when hydroxychloroquine and mycophenolate mofetil became available in Japan and treatment strategies changed markedly. [Methods] We included 81 patients with SLE who were admitted to our department and treated with initial remission induction treatment from 2008 to 2012 and from 2016 to 2020. We compared the achievement of DORIS remission, flares, changes in SDI scores, and death between the groups using inverse probability weighting using the propensity score. [Results] Forty-nine patients in the Pre group and 32 patients in the Post group were analyzed. Patients in the Pre group had a higher nephritis and SLEDAI score than those in the Post group; initial use of immunosuppressive drugs increased in the Post group (31% vs. 94%), whereas cyclophosphamide use was similar. The Post group showed a remarkably higher percentage than the Pre group, with an adjusted hazard ratio of 2.42 (95% CI 1.18-4.96). The flares and SDI scores in the Pre group were lower than those in the Post group, and only one death occurred in the Pre group. [Conclusions] The implementation of treat-to-target strategies and the availability of effective therapeutic agents have led to improved outcomes in SLE.

## W67-2

**Longitudinal study of quality of care and relapse in SLE patients: the LUNA registry**

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Conflict of interest: None

[Objective] It is expected that relapse is less frequent in patients with SLE when high quality care is provided. The aim of this study was to investigate longitudinally whether patient-reported quality of care is associated with relapse in patients with SLE. [Methods] Patients with SLE enrolled in a multicentre SLE registry (LUNA) involving 20 centres in Japan were included. In the main analysis, factors were defined as the Satisfaction with Lupus Care (SLC) of Lupus PRO, a patient-reported measure of quality of care, and outcome as the presence or absence of disease relapse over one year, with the confounding factors in the model. Multiple assign-

ment was performed for missing confounding factors. [Results] There were 670 subjects, 574 (85.7%) women, age at study 45 [34-57] years, duration of illness 7.1 years [4.2-10.9]. SLC was 65.6 (61.7-69.8) and relapse occurred in 129 (12.2%) of 1054 patients. The main analysis showed an odds ratio of 1.23 (95% confidence interval 0.93-1.56, P=0.12). [Conclusions] In this study, there was no significant difference between patient-reported quality of care and relapse in patients with SLE. Quality of care in patients is a topic that deserves further attention in the future, not only in SLE.

## W67-3

**Prescription status of treatments for systemic lupus erythematosus by age group according to the National Database**

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Conflict of interest: None

Objective: To describe the prescribing status of treatments for systemic lupus erythematosus (SLE) by age group using the National Database (NDB). Methods: Patients with the diagnosis of SLE between April 2019 and March 2020 for which glucocorticoids (GC), immunosuppressive, immunomodulators or biological agents were prescribed at least once were enrolled. The overall prescription status of medications as well as that of oral GC, hydroxychloroquine (HCQ), mycophenolate mofetil (MMF), and tacrolimus (TAC) was analyzed by age. Results: A total of 74,277 patients were enrolled and who were aged 0-14, 15-24, 25-39, and 40 or older comprised 2.0%, 3.6%, 14.7%, and 79.7% respectively. The percentage of prescriptions of each drug was 89.1% for GC, 4.5% for GC pulse, 21.4% for HCQ, 12.0% for MMF, 22.9% for TAC. The percentage of prescription by age group was GC: 78.8% for patients aged < 15 and 89.2% for ≧ 15; HCQ: 24.5% for those aged between 6 and 14 and 21.4% for ≧ 15; MMF: 49.2% for patients aged 15 and 11.6% for ≧ 15; and TAC: 20.1% for patients aged <15 and 22.9% for ≧ 15. Conclusions: The present study, the first to use NDB to demonstrate the prescription percentage of SLE medications by age group, found that MMF was prescribed in a higher proportion of pediatric patients with SLE.

## W67-4

**Investigation of factors from achieved LLDAS to DORIS remission in systemic lupus erythematosus**

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Conflict of interest: None

[Objective] We aimed to identify the factors that differentiate patients who achieve DORIS remission and those who do not after achieving LLDAS. [Methods] The subjects were 126 patients with SLE at our hospital who achieved LLDAS at least once. We analyzed 50 patients, excluding those who had achieved LLDAS for less than 1 year, those who had relapsed, and those who met both the LLDAS and DORIS remission criteria. The primary endpoint was achieving DORIS remission 12 months after achieving LLDAS. Univariate and multivariate analyses were performed using sex, disease duration, affected organs and autoantibodies during the entire course, disease activity at the time of achieving LLDAS, and concomitant immunosuppressive drugs as background factors. [Results] Thirty-four patients achieved DORIS remission 12 months after achieving LLDAS. Univariate analysis suggested an association between DORIS remission and disease duration (p=0.0169) and SLEDAI-2K score (p=0.0345) at the time of LLDAS achievement. In the multivariate analysis, disease duration (p=0.0373) and SLEDAI-2K (p=0.0417) contributed to the achievement factor. [Conclusion] It became clear that the lower the SLEDAI-2K score and the shorter the disease duration, the easier it is to achieve DORIS remission after 12 months.

## W67-5

**Predictors for achieving and maintaining of Lupus Low Disease Activity State (LLDAS) in patients with systemic lupus erythematosus (SLE) on maintenance therapy**

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Conflict of interest: None

[Objective] To identify predictors for achieving and maintaining of LLDAS in patients with SLE on maintenance therapy. [Methods] 1) We evaluated clinical backgrounds and LLDAS achievement in patients diagnosed with SLE by Sep 2022, with available data at two time points (Mar and Sep 2023) retrospectively. 2) We divided cases into 4 groups (G) according to LLDAS achievement at two time point, such as G1: maintenance, G2: dropout, G3: newly achieved, and G4: not achieved, to identify predictors for LLDAS. [Results] 1) 291 patients were enrolled and 90.7% were female. Mean age was 48.6±14.9 years, with average disease duration of 204.2±137.4 months and mean SLEDAI-2K of 2.60±2.93. LLDAS was achieved in 160/291 cases (55.0%) at Mar 2023 and 179/291 (61.5%) at Sep 2023. 32 cases newly achieved LLDAS while 13 drop-outed. 2) Comparing G1 (n=147) with G2 (n=13) showed no significant differences in clinical backgrounds and treatment. In comparison between G3 (n=32) and G4 (n=99), G3 had significant male dominancy (28.1% vs 8.1%), shorter disease duration (129.7±114.2 vs 217.0±136.4 months), and lower prednisolone (PSL) dosage (7.64±2.41 vs 9.35±3.19 mg/day) (p<0.05). [Conclusion] Male, shorter disease duration, and lower PSL dosage could be predictors for achieving of LLDAS after six months.

## W67-6

**Sjögren's syndrome in patients with anti-SS-A antibody-positive systemic lupus erythematosus**

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Conflict of interest: None

Aim: Anti-SS-A antibodies (Abs) are frequently positive in systemic lupus erythematosus (SLE). We investigated the complication rate of secondary Sjögren's syndrome (SS) in patients (pts) with anti-SS-A Ab-positive SLE. Methods: Of 139 SLE pts (47.2 years old, female 89.9%, disease duration 13.8 years, SLEDAI 2.4) fulfilling ACR/EULAR classification criteria 2019 in our hospital between December 2022 and August 2023, 90 were positive for anti-SS-A Abs and 49 were negative. Saxon test, Schirmer test and fluorescent dye method, and lip biopsy were all performed on 53 of the 90 anti-SS-A Ab-positive pts. The primary endpoint was the complication rate of SS in anti-SS-A Ab-positive SLE pts. Results: The proportion of SS among anti-SS-A Ab-positive SLE pts was 43/53 (81.1%). The results was as following: Saxon test positive in 26 pts (49.1%), Schirmer test in 29 (54.7%), fluorescent dye test in 26 (49.1%), Schirmer test and fluorescent dye test in 20 (37.7%), and lip biopsy in 26 (64.2%). All three criteria except for anti-SS-A Ab were met in 9/53 (17.0%), 2/3 (25/53, 47.2%), 1/3 (9/53, 17.0%), and 0/3 (10/53, 18.9%) pts, respectively. Conclusion: SS are frequently observed in pts with SLE, although a detailed examination is rarely performed even when anti-SS-A Abs are positive.

## W68-1

**The study on antibody transfer rate to offsprings and incidence of congenital heart block and neonatal lupus erythematosus in pregnancies with positive anti-SS-A/Ro antibodies**

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Conflict of interest: None

[Objective] We investigated the neonatal antibody titers and the incidence of CHB and NLE in pregnancies with positive anti-SS-A/Ro antibodies. [Methods] The subjects were 55 offsprings from mothers with positive anti-SS-A/Ro antibodies. We retrospectively investigated maternal disease, medication, and obstetric outcomes. Anti-SS-A/Ro antibodies were measured, and all positive cases underwent electrocardiogram evaluation. Cytopenia and skin rash was evaluated during the neonatal period and at 4 months of age. [Results] Maternal age at delivery (median) was 33 (IQR 30-36) years, and anti-SS-A/Ro antibody titer was 64 (16-256) times. Maternal diseases included systemic lupus erythematosus in 23 cases (41.8%), rheumatoid arthritis in 16 cases (29%), and Sjögren's syndrome in 14 cases (25.4%). Prednisolone was administered in 50 cases (90.9%) and hydroxychloroquine in 8 cases (14.5%). The gestational age at delivery was 38 (37-39) weeks, and the birth weight was 2780 (2490-1984) g. There were 52 (94.5%) positive cases of anti-SS-A/Ro antibodies in the neonates. No cases of CHB and only one case of NLE were observed. [Conclusions] Maternal anti-SS-A/Ro antibodies were transferred to the offspring at a high rate. However, no cases of CHB and only one case of NLE were observed.

## W68-2

**The association between transient B cell depletion in infancy caused by maternal azathioprine administration and NUDT15 gene polymorphisms**

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Conflict of interest: None

[Introduction] Azathioprine (AZA) can be used to manage collagen disease during pregnancy. In this case, Maternal AZA usage during pregnancy lead to a disorder of B-cell maturation in fetus, possibly due to *NUDT15* gene polymorphism. [Case] A 22-day-old male infant was referred to at our department with suspicion of congenital B cell deficiency. His mother had SLE and took AZA during pregnancy. On the fourth day after birth, a KREC PCR test as screening test for congenital severe immunodeficiency was below the detection limit. The initial B cell count was low at 97 /μL but increased over time. The CD10 positivity rate in B cells was initially high at 98.7% and decreased over time, suggesting a disorder of B cell maturation during the fetal period. Analysis of the *NUDT15* gene polymorphism revealed the mother had Arg/Arg homozygosity, while the father and the infant had Arg/Cys heterozygosity. The Paternal heterozygosity of *NUDT15* gene may have reduced AZA metabolism in fetus, resulting in B cell differentiation disorder. [Clinical Significance] This case suggests that gene polymorphisms related to drug metabolism in both parents may influence the effects of thiopurine drugs on the fetus in pregnant women.

## W68-3

**Pregnancy Outcome in Systemic Lupus Erythematosus Patients with Serological Activity**

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Conflict of interest: None

[Objective] Pregnancy outcome is poor in systemic lupus erythematosus (SLE) patients with high disease activity. Attitudes regarding pregnancy in SLE patients with serological activity differs among rheumatologists according to a recent survey, and we herein examined the outcome of pregnancy in SLE patients with serological activity. [Methods] We retrospectively analyzed the charts of SLE patients who became pregnant between 2012 and 2022 at our hospital. Seventeen singleton pregnancies with no active symptoms at conception and with serological activity were compared with seven pregnancies with no active symptoms and without serological activity. [Results] There were no significant differences in the age of the mothers or the proportion of patients with anti-phospholipid antibody syndrome (3/17 (17.6%) vs 2/7 (28.6%)). The proportion of patients with pregnancy induced hypertension was 4/1 7 (23.6%) in the serologically active group and 2/7 (28.6%) in remission group. There were no significant differences in preterm births (3/17 (17.8%) vs 0/7) or low birth weight babies (6/17 (35.3%) vs 3/7 (42.9%)). [Conclusions] Pregnancy outcomes are acceptable in SLE patients with serological activity without active symptoms.

## W68-4

**A study on the actual situation of pregnancy in patients with systemic lupus erythematosus in Kyoto university hospital**

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) occurs more frequently in young women and have difficulty getting pregnant. We aimed to report on the conditions leading up to pregnancy. [Methods] The results of questionnaire for SLE patients attending our hospital and their medical records were examined. Comparison was made between women who developed SLE before their first pregnancy (early group) and those who developed SLE after their first pregnancy (late group). [Results] Of the 369 SLE patients who consented to the questionnaire, 277 (75%) responded, of which 262 (94.6%) were female. The mean number of children was 0.49 in the early group (139 patients, mean age 45.5 years) and 1.67 in the late (107 patients, 57.6 years). The mean age of first pregnancy was 29.6 years in early group and 25.9 in the late. Among the early group, 44 patients (73%) had pregnancy permission from their doctor, and 28 (46%) had on schedule. Among 58 patients who avoided pregnancy, 25 (43%), 21 (36%), and 34 (59%) patients answered as the result of discussions with their doctor, partner, or concern about the drug effects on the fetus. [Conclusion] It has been suggested that age at pregnancy and circumstances that discourage pregnancy may contribute to the lower family size among early group patients.

## W68-5

**The importance of planned pregnancy in systemic lupus erythematosus**

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Conflict of interest: None

[Purpose] Systemic lupus erythematosus (SLE) is affected in young women, who often experience pregnancy. This study examined the pregnancy outcomes of patients (pts) with SLE. [Methods] We analyzed 46 pregnancies in 34 pts with SLE, who visited our department from April 2011 to September 2023. [Results] The mean age at SLE onset was 23.1 years old, and at pregnancy was 32.0. The mean SLEDAI at conception was 1.54. 12 pts were positive for antiphospholipid antibodies and 17 had a history of lupus nephritis. There were 4 unplanned pregnancies. Glucocorticoid (GC) was administered at conception in 44 cases, with immuno-

suppressant (IS) in 26. Low-dose aspirin was given in 10 cases. The mean SLEDAI was 1.68 in the 2nd trimester and 1.83 in the postpartum. 6 had relapse of SLE in the 2nd trimester and 4 in the postpartum. There were 2 preeclampsias, 2 fetal deaths, 6 preterm births, and 14 low birth weight (LBW) infants. There were no significant differences between preterm birth or LBW and GC dose at conception, use of IS, SLEDAI at conception, or relapse. However, unplanned pregnancies were associated with significantly more preterm births. [Conclusion] Because unplanned pregnancies have poor outcome, it is advisable to consider a planned pregnancy with preconception care.

## W68-6

**Effectiveness of Low-dose aspirin in pregnancy with Systemic Lupus Erythematosus**

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Conflict of interest: None

Objective: Low-dose aspirin (LDA) is recommended for preventing pregnancy complications in pregnancies with systemic lupus erythematosus (SLE), but its effectiveness remains unclear. We conducted this study to evaluate the usefulness of LDA in pregnancies with SLE. Methods: We retrospectively collected data on the underlying disease, treatments, complications, and pregnancy outcomes for pregnancies with SLE delivered at our hospital from December 2002 to September 2023, and analyzed the association between LDA and pregnancy outcomes. Results: Among 150 pregnancies, there were 22 cases of hypertensive syndrome of pregnancy (HDP), 52 of preterm birth, 4 of stillbirth, and 42 of small for gestational age (SGA). SGA was higher in the LDA group (OR 2.43, 95%CI 1.11-5.33), but the difference disappeared when antiphospholipid antibody syndrome (APS) was excluded. When we divided the population without APS into those with antiphospholipid antibody positivity, hypertension, or chronic kidney disease, and those without, HDP was significantly lower in the LDA group (OR0.17, 95%CI 0.04-0.78) in the former, and there were no cases of HDP in the LDA group in the latter. Conclusion: Our results suggest that LDA may be useful in preventing HDP in pregnancies with SLE, excluding APS.

## W69-1

**Safety and efficacy of the adjuvanted recombinant zoster vaccine in patients with autoimmune diseases: a prospective cohort study**

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Conflict of interest: None

**Object**: We investigated prospectively the safety and efficacy of the recombinant zoster vaccine (RZV). **Methods**: Participants were evaluated either vaccinated or unvaccinated based on shared decision making from July 2020. Adverse reactions collected for 30 days after each two doses and disease flare compared with and without vaccine during 6 months. Vaccine efficacy against herpes zoster (HZ) was evaluated after completing 2 doses. Selection bias was adjusted by propensity score-based inverse probability of treatment weighting (IPTW). **Results**: Patients were 106 vaccinated (GCs: 22.6%, MTX: 50.0%, bio: 30.2%, JAKi: 64.2%) and 68 unvaccinated (GCs: 20.6%, MTX: 50.0%, bio: 44.1%, JAKi: 55.9%) in median follow-up 356 days. In 83 patients vaccinated, local adverse reactions occurred in 89.2% in median 4 days. Systemic adverse reactions occurred in 72.3% in median 2 days. Disease flare was reported by 7.5% in vaccinated group and 10.3% in unvaccinated group (p=0.529). HZ incidence rate was 2.9/100PY in vaccinated group and 9.7/100PY in unvaccinated group (p=0.072). Hazard ratio was 0.29 (95%CI, 0.078-1.120; p=0.073) before IPTW and 0.24 (95%CI, 0.064-0.909; p=0.036) after IPTW. **Conclusions**: Our study did not identify any safety concerns of RZV and usage of RZV tended to reduce the incidence of HZ.

## W69-2

**Experience with recombinant zoster vaccine (RZV) in systemic autoimmune disease patients**

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Conflict of interest: None

[Objective] To evaluate the clinical characteristics of Japanese patients with systemic autoimmune disease who received RZV. [Methods] We retrospectively analyzed the clinical characteristics of 70 patients who had received RZV during April 2020 to May 2023 in Oita Red Cross Hospital. [Results] The 70 (15 M, 55 F) patients comprised 53 with RA and 5 with SLE and 12 with other cases. The mean age at the time of the initial vaccination was 72 ± 10 years. Twenty-nine patients had a past history of herpes zoster (HZ). The use of JAK inhibitors at the time of first RZV vaccination was observed in 39 patients. In 18 patients with RA, anti-varicella zoster virus IgG antibodies were measured before and after vaccination, and in 16 cases antibody titers were increased. The average observation period was 602 days. Three cases of HZ after vaccination were observed, but no postherpetic neuralgia was observed. Adverse events were observed in 42 patients (injection site pain in 29, fever in 17, fatigue in 7, nausea in 5, headache in 4, skin rash in 2, dizziness in 1, chills in 1, diarrhea in 1, and RA flares in 1). [Conclusions] There were no cases with serious adverse reactions. Three cases of HZ were observed after vaccination, but they were not severe.

## W69-3

**Effects of recombinant herpes zoster vaccine (RZV) on disease activity in rheumatoid arthritis -The ANSWER cohort study-**

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Conflict of interest: None

[Objective] While rheumatoid arthritis patients are at high risk of developing herpes zoster (HZ), there is concern that recombinant herpes zoster vaccine (RZV) can relapse rheumatoid arthritis. We investigated the effect of RZV on disease activity of rheumatoid arthritis. [Methods] We analyzed 86 patients who received RZV in the ANSWER cohort database retrospectively. Using the date of the first RZV vaccination as the reference date, the control window was defined as 9 months to 3 months prior, the lag window as 3 months to the reference date, and the risk window as 12 months from the reference date. Disease activity relapse was defined as worsening of DAS28ESR of 0.6 or greater, or a 50% or greater increase in the tender or swollen joints counts. [Results] There was no significant difference in incidence between the control and risk periods. The swollen joints counts and DAS28ESR on the reference date were significantly increased in the group with relapse during the risk period compared to the group without relapse. [Conclusions] No significant increase in the incidence of relapse with RZV was observed during the observation period. The cases of arthritis relapse after RZV administration had higher disease activity at the time of the first vaccination.

## W69-4

**Anti-rheumatic medication and risk of herpes zoster in patients with rheumatoid arthritis: A case-crossover study from the NinJa registry**

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Conflict of interest: Yes

Objective: The aim of this study is to investigate the relationship between anti-rheumatic drug use and helps zoster development by using a large database of rheumatoid arthritis (RA). Method: We obtained data from the National Database of Rheumatic Diseases by iR-net in Japan (*NinJa*). We adopted the case-crossover design in which only data from cases are used, and data of cases at the time of event and those at time points before the event are compared. We identified patients with RA who developed herpes zoster between from 2018 to 2021. Use of anti-rheumatic drug at the time of herpes zoster development and those at time points before the disease development were compared. Results: A total of 601 subjects were identified. Janus kinase inhibitor use had an increased risk of herpes zoster (crude odds ratio 7.6, 95% confidence interval 3.4- 17.0). Conclusion: Janus kinase inhibitor use was identified as a risk factor of herpes zoster in real world data. Vaccination for the disease should be encouraged.

## W69-5

**Analysis of the effect of recombinant subunit herpes zoster vaccine on joint symptoms of rheumatoid arthritis in clinical practice**

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Conflict of interest: None

[Objective] We analyzed the effects of a recombinant subunit herpes zoster vaccine on joint symptoms of rheumatoid arthritis in a clinical setting. [Methods] 71 cases that met the ACR/EULAR RA classification criteria and were vaccinated with RZV were included. Characteristics of cases where disease activity worsened after vaccin were analyzed. [Results] Seventy-one patients vaccinated with RZV were observed for 6 months after vaccination. A total of 71 patients completed two doses of RZV vaccination. The DMARDs being administered were MTX (70.4% in 50 cases), TNF inhibitors (1.4% in 1 case), IL-6 inhibitors (4.2% in 3 cases), abatacept (7.0% in 5 cases), and JAK inhibitors (22.5% in 16 cases). Oral steroids (GC) were used in 2 cases, 2.8%, with an average dose of 2.5+/0.7-mg/day. Among these, there were 2 cases, 2.8%, of relapsed disease activity (10≦CDAI) after vaccination. (7.5+/-2.1 increase compared to pre-RZV CDAI, average 14.5+/-6.2 weeks after first RZV vaccination). In both cases, CDAI improved in an average of 4.0 weeks without intensification of treatment. [Conclusions] In this analysis, the recurrence of joint symptoms in RA after RZV vaccination was 2.8%, and no need to strengthen treatment such as changing/adding DMARD.

## W69-6

**Epidemiological study of herpes zoster Incidence and vaccine awareness in patients with rheumatic diseases**

Mitsuru Watanabe[1], Sho Higuchi[1], Mirai Hozumi[1], Yui Amari[1], Yukina Yokoyama[1], Takanori Ito[1], Mizuki Kato[1], Tatsuo Watanabe[2], Yoichiro Haji[1]
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Conflict of interest: None

[Background] Despite high incidence of herpes zoster (HZ) infection associated with JAK inhibitors (JAKi) in Asian population, epidemiologuc data is still lacking and the effect of vaccination is uncertain in clinical practice. [Objective] To evaluate the epidemiology of HZ by assessing the patient's backgrounds and vaccination status. [Methods] We conducted descriptive questionnaires to our patients from June to September 2023. [Results] We evaluated 621 patients, mean age was 63.7 years, 72.4% was female, 51.0% had RA, and 7.6% had SLE. Twenty eight % (175/621) experienced HZ, 23.4% (41/175) was after diagnosis, SLE patients tended to experience before diagnosis. (42.6%, 20/47) HZ vaccine was administered to 79 patients. (RA 59.4%, 47/79). Only one patient had HZ after starting JAKi. The proportion of patients who could recognize HZ from the picture was significantly lower, even though they were aware of existance of vaccine. (Pearson chi2 = 38.5385, $p<0.01$) The most common reason for non-vaccination was lack of information. (31%) [Conclusion] Recognition of HZ remains low, we need appropreate patient education. Vaccination could reduce the incidence of herpes zoster even after the use of JAKi.

## W70-1

**Does stopping of molecular target drugs increase postoperative complications after orthopaedic surgeries in patients with rheumatoid arthritis ?**

Hiromu Ito[1,2], Hajime Ishikawa[3], Shigeyoshi Tsuji[4], Masanori Nakayama[5], Keiichiro Nishida[6], Takeshi Mochizuki[7], Kosuke Ebina[8], Toshihisa Kojima[9], Takumi Matsumoto[10], Ayako Kubota[11], Arata Nakajima[11], Atsushi Kaneko[12], Isao Matsushita[13], Ryota Hara[14], Koji Sakuraba[15], Yukio Akasaki[16], Tsukasa Matsubara[17], Yuichi Mochida[18], Katsuaki Kanbe[19], Shigeki Momohara[20]
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Conflict of interest: Yes

[Objective] We aimed to investigate whether stopping of molecular target drugs before operations increase postoperative complications after orthopaedic surgeries in patients with rheumatoid arthritis (RA). [Methods] We collected cases of orthopaedic surgeries for patients with RA undergone in specialized institutions in Japan. Demographic data, types of operations, drugs used for RA, stopping time periods of them, and postoperative complications within a year were recorded. We compared the incidence ratios of postoperative complications between stopping and no-stopping groups. [Results] A total of 1953 cases were eligible for analyses. The averages of age, duration of the disease, and DAS28-CRP at the time of operation were 71.8 years, 18.6 years and 2.84, respectively. There were no statistical differences in incidence ratios of delayed wound healing, SSI and death, but that of flare-up was statistically higher in the stopping group. The incidence ratio of flare up was higher in IL-6 inhibitor group, and that of delayed wound healing was higher in major surgery group. [Conclusions] T he perioperative stopping of molecular target drugs may increase the incidence ratio of flare up in orthopaedic surgeries in patients with RA but does not influence those of other complications.

## W70-2

**Perioperative discontinuance of janus kinase inhibitors in patients with rheumatoid arthritis who underwent orthopaedic joint surgery**

Kengo Harigane[1], Yuichi Mochida[1], Ayako Nomura[1], Akiko Nagaoka[1], Naomi Kobayashi[2], Ken Kumagai[3], Hyonmin Choe[3], Shunsuke Yamada[3], Yutaka Inaba[3]

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the influence of perioperative discontinuance of janus kinase inhibitors (JAKi) in patients with rheumatoid arthritis (RA) who underwent joint surgery. [Methods] Twenty-six surgeries in 22 patients (female: 21 surgeries in 17 patients, male: 5 surgeries in 5 patients) were involved in this study. The incidences of perioperative RA flare-up symptoms were retrospectively investigated. [Results] The averaged age at the time of surgery was 67.6 years. RA flare-up were observed in 8 surgeries (30.7%) during the discontinuance of JAKi. In 8 surgeries with flare-up, preoperative DAS28-ESR was significantly higher than 18 surgeries without flare-up of RA (3.78 vs. 2.53, p<0.01). The discontinuance period in cases with flare-up was also significantly longer than the cases without flare-up (6.9 days vs. 4.8 days, p=0.03). [Conclusions] RA flare-up were observed in 30% of the cases during the discontinuation of JAKi. In the cases with flare-up, preoperative DAS28-ESR was higher, and the discontinuance period of JAKi was longer than the cases without flare-up. From these results, preoperative disease activity should be well controlled to prevent RA flare-up. The appropriate perioperative discontinuation period of JAKi will be continuously discussed.

## W70-3

**What are the risk factors for periprosthetic fractures in total hip arthroplasty for hips with rheumatoid arthritis?**

Reina Miyafusa[1,2], Daisuke Hara[1], Koji Sakuraba[2], Hidetoshi Tsushima[3], Satoshi Ikemura[4], Yukio Akasaki[1], Toshifumi Fujiwara[1], Hisaaki Miyahara[2], Junichi Fukushi[2], Yasuharu Nakashima[1]

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Conflict of interest: None

(Introduction) Advances in DMARDs have reduced the number of rheumatoid arthritis (RA) hips indicated for total hip arthroplasty (THA) that present with severe preoperative joint destruction. Therefore we hypothesize that the incidence of perioperative periprosthetic fractures (PPF) after initial THA for RA hips is on the decline. The purpose of this study is to compare before and after the widespread use of bDMARDs to determine if the incidence of PPF has changed and what factors are associated with fracture occurrence. (Methods) Primary THA cases performed from 1998 to 2019, 158 cases from 1998-2003 (early period) and 125 cases from 2012-2019 (late period) were included in the study. The cases from these two periods were compared in terms of PPF and patient background. (Results) The incidence of PPF was 3.8% in the earlier period and 4.8% in the later, showing no significant difference. PPF patients had significantly poorer CONUT, and more previous joint surgery, which were also significantly associated with PPF in multivariate analysis. (Conclusions]) Despite the widespread use of DMARDs, THA in RA hips remains a risk factor for PPF. THA in RA patients with poor preoperative nutritional status and a history of frequent arthroplasty should be especially watched for PPF.

## W70-4

**Risk factors for dislocation after total hip arthroplasty in patients with rheumatoid arthritis**

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Conflict of interest: None

Purpose: The incidence of dislocation after total hip arthroplasty (THA) in rheumatoid arthritis (RA) patients is higher than that in osteoarthritis patients. Methods: Of 113 RA patients who underwent primary THA at our facility from January 2006 to December 2022, 67 patients who had standing whole spine X-rays were included, and the risk factors for dislocation was evaluated. Results: Eight patients (11.9%) were found to have dislocation. There were no significant differences in cup inclination, cup anteversion, percentage within the Lewinnek safe zone, stem anteversion, combined anteversion, leg length difference, head diameter, pelvic incidence (PI), and sacral slope between the dislocated and non-dislocated groups. The dislocation group had larger PI-LL and smaller postoperative hip offset. ROC curves showed that PI-LL > 30°, postoperative hip offset < 30 mm, and leg extension or shortening > 25 mm were significant risk factors for dislocation. Discussion: The estimated cup anteversion in the standing position did not differ between the dislocated and non-dislocated groups. The strategy of cup placement should be carefully considered. Conclusion: PI-LL >30°, postoperative hip offset <30 mm, and leg extension or shortening of >25 mm are risk factors for dislocation in RA patients.

## W70-5

**Examination of synovial histopathological characteristics in rheumatoid arthritis patients treated with biological disease-modifying antirheumatic drugs**

Masanori Sudo[1,2], Asami Abe[1], Nariaki Hao[1], Sayuri Takamura[1,2], Satoshi Ito[1], Daisuke Kobayashi[2], Hiroshi Otani[1], Kiyoshi Nakazono[1], Akira Murasawa[1], Ichiei Narita[2], Hajime Ishikawa[1]

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Conflict of interest: None

[Objective] To investigate the histopathological characteristics of the synovium of rheumatoid arthritis (RA) patients. [Methods] 1617 synovial histopathological specimens were evaluated using Rooney's synovial inflammation score (RS). The specimens were divided into two groups whether bDMARDs treatment was not used (bDMARDs-naive group, n=1069) or used (bDMARDs group, n=548), and compared. [Results] The proportion of ultrasound power doppler (PD) grade 1 or higher was 81% vs 72% (p<0.001), ACPA 229±321 vs 240±330 (p=0.513), DAS28-ESR 3.6±1.1 vs 3.3±3.0 (p=0.005), CRP 0.4±0.7 vs 0.3±1.1 (p=0.887), and MMP-3 108±50 vs 179±248 (p=0.16). The mean RS was Total score 27 (20-36) vs 21 (19-28) (p<0.001), Synoviocyte hyperplasia 2 (1-2) vs 1 (0-2) (p<0.001), Fibrosis 10 (9-10) vs 10 (10-10) (p<0.001), Perivascular infiltrates of lymphocytes 3 (0-7) vs 0 (0-3) (p<0.001), Focal aggregates of lymphocytes 3 (0-6) vs 0 (0-3) (p<0.001), Diffuse infiltrates of lymphocytes 1 (0-4) vs 0 (0-1) (p<0.001), and Proliferating blood vessels 9 (7-10) vs 9 (7-10) (p=0.325). [Conclusion] bDMARDs treatment has an inhibitory effect on pathological synovial cell proliferation, lymphocyte infiltration, and fibrosis.

## W70-6

**Elderly onset rheumatoid arthritis: diagnosed before artificial joint surgery**

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Conflict of interest: None

[Introduction] We report a case of osteoarthritis that was referred to our hospital for surgery and diagnosed as EORA at the time of joint surgery. [Case] The cases are 5 cases that were referred to our hospital for artificial joint replacement, and were diagnosed with EORA before sur-

gery. All patients were female, the average age was 67.2 years, and the diagnosis in all cases at the time of referral was osteoarthritis of the hip in 1 case and knee joint in 4 cases. Hip cases had an acute onset and joint destruction progressed over a short period of time, but no acute onset cases were observed in knees. RA was suspected in 4 cases of knee joints based on preoperative plain X-ray images. In addition, preoperative testing showed high levels of CRP in all cases. ACPA was positive in 3 patients, and RA was diagnosed in 4 patients in the knee. The hip joint case was monoarthritis, and a preoperative biopsy was performednd. Joint replacement was performed in all cases, and the course was uneventful with no complications. RA treatment was favorable in all cases. [Discussion] The prevalence of knee pain and osteoarthritis is high in the elderly. Early diagnosis is required before joint destruction progresses, and this must be kept in mind during outpatient treatment.

## W71-1

**Controlling disease activity with molecular targeting drugs prevent the progression and new development of interstitial lung disease in rheumatoid arthritis**

Ayae Tanaka[1], Kazuhiro Kurasawa[1], Yuki Aizawa[1], Yuhi Yoshida[1], Tomoka Hiyama[1], Anna Hasegawa[1], Tomoyuki Miyao[1], Satoko Arai[1], Takayoshi Owada[2], Reika Maezawa[1], Masafumi Arima[1], Kei Ikeda[1]
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Conflict of interest: None

Object: We previously reported that the progression of interstitial lung disease (ILD) as well as disease activity was suppressed by switching from biologics to JAK inhibitors (JAKis) in patients with rheumatoid arthritis (RA). To examine whether this inhibition of ILD is JAKi-specific or not, we analyzed the association between the disease activity and the progression of ILD in patients treated with biologics. Methods: Participants were 180 patients with RA under biologics therapy for more than six months and received chest CT scans before and during the treatment. Change of ILD was compared between patients who achieved low disease activity (LDA group) by DAS28-ESR and those who did not (non-LDA group). Results: In 180 participants, 38 patients achieved LDA by biologics, and ILD was observed in 67 patients at the start of the therapy. Progression of ILD was found in 2 of 18 patients in the LDA group and 18 of 40 in the non-LDA group (p=0.06). ILD developed newly in 1 of 20 patients in the LDA group and 22 of 93 in the non-LDA group (p=0.07). New or progressive ILD was found in 3/38 in the LDA group and 40/142 patients in the non-LDA group (p=0.009). Conclusion: Controlling disease activity with molecular-targeting drugs prevents the progression and new development of ILD in RA.

## W71-2

**Significant impact of disease activity on the radiological and physiological severity of interstitial lung disease in rheumatoid arthritis**

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Center for Rheumatic Diseases, Mie University Hospital

Conflict of interest: None

[Objective] To investigate the association between the disease activity of rheumatoid arthritis (RA) and the severity of interstitial lung disease (ILD). [Methods] Consecutive RA patients who visited our Hospital between December 2020 to December 2023 were included. The presence of ILD was clinically defined. The severity of ILD was semi-quantified based on high-resolution computed tomography (HRCT). Patients without ILD were scored as zero. Associations between the severity of ILD and baseline covariates were investigated. [Results] We included 134 patients. The extent of ILD was 0% in 114, 0 - 10% in 13, and >10% in 7 patients. Disease activity score 28 with C reactive protein (DAS28-CRP), DAS28 with erythrocyte sedimentation rate (DAS28-ESR), clinical disease activity index (CDAI), simplified disease activity index (SDAI), methotrexate usage, positive rheumatoid factor and anti-citrullinated protein antibody were significant covariates affecting the extent of ILD. DAS28-CRP, DAS28-ESR, CDAI and SDAI indices were significant predictors for ILD extent > 10% (odds ratio 2.25, 2.83, 1.10 and 1.09). DAS28-CRP and DAS28-ESR significantly affected the values of forced vital capacity percent predicted. [Conclusions] Disease activity of RA have a significant impact on the severity of ILD.

## W71-3

**Long-term follow-up of rheumatoid arthritis treated with biologic agents while treating MAC pulmonary disease**

Shogo Banno[1], Nobata Hironobu[1], Makoto Yamaguchi[1], Satoru Ito[2], Akimasa Asai[1], Keisuke Kamiya[1], Fumiya Kitamura[1], Hirokazu Sugiyama[1], Yasuhiko Ito[1], Takuji Ishimoto[1]
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Conflict of interest: None

[Objective] RA airway involvement with bronchiectasis (BE) and cellular bronchiolitis (CB) is associated with ACPA and RF and exacerbated by MAC infection. We aimed to evaluate the long-term follow-up of RA patients who received biologics after treatment for MAC-PD. [Methods] 30 of 1123 RA patients were diagnosed with MAC-PD. 8 patients who received biologics after RECAM (CAM, EB, RFP) were retrospectively evaluated by chest CT. 3 were diagnosed with MAC-PD while receiving Bio, 5 had MAC-PD before receiving Bio. [Results] Median observation of MAC-PD 105 months (49-131), all was detected M. avium, and nodular and bronchiectatic (NB) type, 3 shown for cavitary NB; age at MAC diagnosis 66 years, RA duration 16 years, BMI 18.4; all positive for ACPA 256 U/mL, RF 242 U/mL; 2 RECAM patients failed to continue, 6 continued for more than 13 months (median 31 months); Bio was started and resumed (5 ABT, 3 TNFi) at RA high disease activity. Bio was continued for 49 months after MAC treatment. All became negative for bacteria, but 3 became re-positive, 2 had CT exacerbation, 4 were treated for the second MAC regimen. [Conclusion] Patients with high ACPA and RF levels can be treated with Biologics during pulmonary MAC therapy, and Biologics can be administered with careful monitoring of MAC.

## W71-4

**Clinical features of bronchiectasis with rheumatoid arthritis resulting in progressive destructive lesions of the airway**

Kenji Ishiguro[1], Takahiro Yagi[1], Moeko Ochiai[1], Akiko Kobayashi[1], Akio Mimori[1], Hitoshi Tokuda[2], Shunta Kaneko[1]
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Conflict of interest: None

[Objective] We investigated the long-term clinical characteristics of patients with RA-BE in our hospital. [Methods] Patients with RA-BE who were admitted to our hospital at least one time from April 2013 to October 2023 and had been attending our hospital for more than 3 years were extracted. Then we divided the group into destructive BE group and non-destructive BE group based on continuous CT findings. Each clinical course was analyzed retrospectively. [Results] Eighteen patients were enrolled in this study. Duration of RA was 11.5 years and BE was 3.0 years. Titer of anti-CCP antibody was 94.9 U/mL. Bronchiectasis Severity Index was 9.5 points. 7 patients (39%) were classified in the destructive BE group. Compared to the non-destructive BE group, the percentage of cystic bronchiectasis was significantly higher (57% in the destructive BE group and 0% in the non-destructive BE group, $P = 0.01$). During the study period (median 6.0 years), the annual number of hospitalizations due to worsening airway symptoms was significantly higher in the destructive BE group (1.25 times per year, non-destructive BE group: 0.42 times per year, $P = 0.02$). [Conclusion] We revealed that there was a subgroup of RA-BE patients with a phenotype of chronic inflammation and progressive airway destruction.

## W71-5

**Risk analysis for acute exacerbation of interstitial pneumonia in patients with rheumatoid arthritis**

Tomoyuki Miyao[1], Kazuhiro Kurasawa[1], Rika Sato[1], Ryota Koike[1], Yuki Aizawa[1], Yuhi Yoshida[1], Tomoka Hiyama[1], Anna Hasegawa[1], Ayae Tanaka[1], Satoko Arai[1], Takayoshi Owada[2], Reika Maezawa[1], Masafumi Arima[1], Kei Ikeda[1]
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Conflict of interest: None

Objective: To identify risk factors for acute exacerbation of interstitial pneumonia (IP-AE) in patients with rheumatoid arthritis (RA). Methods: We analyzed 74 RA patients with IP who were receiving treatment in our department at Apr 2010. We reviewed charts for up to 10 years and determined the incidence rate of IP-AE by using Kaplan-Meier method and identified risk factors by using a Cox proportional hazard model. Results: 43 patients were women with mean age of 67.1 year-old. MTX was used in 32 patients at baseline and in 39 during the study period, biologics in 28 at baseline and in 39 during the study period, and glucocorticoids (GCs) in 54 at baseline and in 57 during the study period. Cumulative incidence rate over 10 years was 12%. Neither sex, age, RA disease duration, CT-based severity of IP, nor RF/ACPA positivity was a significant risk factor. Use of GC (HR 0.81, p=0.78) at baseline was not a significant risk factor. Although use of MTX (HR 0.31, p=0.11) and biologics (HR 0.17, p=0.10) at baseline was not a significant risk factor, both ware a factor that tended to suppress IP-AE. Use of MTX (HR 0.38, p=0.16) and biologics (HR 0.54, p=0.37) was not a significant risk factor. Conclusions: No significant risk factors for IP-AE were identified including MTX and biologic use.

## W71-6

**The study of determinants influencing the life expectancy in rheumatoid arthritis patients afflicted by pulmonary non-tuberculous mycobacterial disease in our hospital**

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Conflict of interest: None

Background: Several patients afflicted by rheumatoid arthritis (RA) manifest bronchiectasis, a condition characterized by central or peripheral airway lesions, as an extra-articular symptom. Furthermore, this cohort demonstrates a heightened propensity for the development of pulmonary non-tuberculous mycobacterial disease (NTM-PD) relative to the general populace. Objective: To assess the clinical trajectory of RA patients afflicted with NTM-PD, we investigated the life expectancy and the associated contributing factors. Methods: We conducted a retrospective analysis of the clinical progression of RA patients suffering from NTM-PD who received treatment at our hospital from April 2011 to March 2023. Results: Out of the 69 RA patients diagnosed with NTM-PD at our hospital, 11 patients succumbed during the observation period. Disparities emerged in the survival curves based on age at NTM diagnosis (70 years or older), with notably diminished prognosis noted in the group with interstitial pneumonia. Conclusion: These results suggest that the presence of interstitial pneumonia associated with RA influences the prognosis of RA patients with NTM-PD.

## W72-1

**Usefulness of Serum S100 Protein Measurement in SLE**

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Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, Kagawa University

Conflict of interest: None

[Objective] To determine the utility of S100 protein measurement as a therapeutic indicator for SLE. [Methods] SLE patients who received additional treatment from 2016 to 2023 were included. SLEDAI-2K, SLEDAS, and CLASI scores were used to assess disease activity, and serum S100A8 and S100A9 were measured by ELISA to analyze the association between these indicators and treatment details before and after treatment. [Results] One hundred SLE patients were included; median SLEDAI was 4. It was higher in patients with lupus nephritis and in skin lesion, S100 protein was higher in patients with higher CLASI scores. After 3 months (3M), all disease activity scores and S100 protein decreased significantly. Next, the all subjects were divided into 5 groups (A: HCQ, B: small dose of glucocorticoid (GC), C: moderate or higher dose of GC, D: belimumab, and E: anifrolumab) according to treatment. After 3M, S100 protein in A, B, and C decreased significantly, while D showed no decrease; in E, S100 protein were low at baseline, but decreased further in E. [Conclusions] S100 protein decreases with declining activity in SLE and could be an indicator of disease activity. It is suggested that the effect on S100 protein in SLE may differ depending on the treatment.

## W72-2

**Study on the clinical significance of anti-lipoprotein lipase antibodies in patients with systemic lupus erythematosus**

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Conflict of interest: None

[Objective] Arteriosclerosis is known to be a problem in patients with systemic lupus erythematosus (SLE). However, it is not clear to what extent immunological mechanisms are involved in arteriosclerosis. Here, we investigated the frequency and clinical significance of anti-LPL antibody positivity in SLE patients. [Methods] The presence or absence of anti-LPL antibodies in the serum of 80 SLE patients who visited our hospital from 2013 to 2020 was determined using Western blotting. We investigated the correlation between anti-LPL antibody positivity and blood test data. [Results] The mean age was 50.9 years, 90.0% were female. A high rate of anti-LPL antibody positivity was observed in 52 patients (65.0%). In anti-LPL antibody positive subjects compared to negative subjects, the levels of Sm antibodies and IgM were significantly higher. Triglyceride levels tended to be higher in anti-LPL antibody positive subjects. Cardiovascular events were significantly higher in anti-LPL antibody positive subjects. [Conclusions] In our study, anti-LPL antibodies were found to be positive at a high rate in SLE patients. We suspect that the presence of anti-LPL antibodies may cause cardiovascular events through a mechanism that induces hypertriglyceridemia and other immunological mechanisms.

## W72-3

**Clinical features of anti-interferon alpha antibody high titer-positive systemic lupus erythematosus**

Hirokazu Taguchi[1], Shuji Sumitomo[1], Shion Kachi[1], Ryo Takeuchi[1], Hideki Oka[1], Hayato Shimizu[1,2], Maki Kanamori[2], Hiroaki Nishioka[2], Koichiro Ohmura[1]
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Conflict of interest: None

[Objective] SLE patients with high anti-interferon alpha (aIFN-α) antibody titers have been reported to have more severe infections and less active disease, but the number of reports is limited. We tried to elucidate the clinical characteristics of aIFN-α antibody high-titer SLE. [Methods] Antibody titers of anti-human IFN-α2 antibodies were measured using commercially available ELISA kit in plasma from 124 SLE patients in our hospital. Clinical characteristics of patients with aIFN-α antibody titers of 310 ng/mL or higher, which is considered a guide to neutralizing antibodies, were searched for in the medical records. [Results] Three patients (2.4%) were positive for high titer of aIFN-α antibody with antibody titers of 84750, 535000, and 1035 ng/mL, respectively. All three patients achieved DORIS remission with a low dose of cyclosporine. None of the patients had a history of severe infection. In all cases, aIFN-α antibody ti-

ters were measured for about one year before and after the disease and did not show significant fluctuations. [Conclusions] Three SLE patients with high aIFN-α titer-positive SLE had low disease activity, but no severe infections were observed during an average of 33 years of illness.

## W72-4

**Clinical features of secondary thrombocytopenia in systemic lupus erythematosus: the importance of proton pump inhibitors as causes**

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Conflict of interest: None

[Objective] We investigated the causes and clinical characteristics of patients with systemic lupus erythematosus (SLE) who developed secondary thrombocytopenia. [Methods] Patients who were admitted to our hospital for treatment of new-onset or relapse of SLE between January 2014 and September 2023 were extracted. Then we investigated secondary thrombocytopenia occurred during the course of hospitalization. We analyzed the clinical characteristics of patients retrospectively. [Results] 152 patients (78% female) were enrolled. 38 patients had secondary thrombocytopenia. The causes were due to SLE-related immune thrombocytopenia in 4 cases, cytomegalovirus infection in 14 cases, and drug-related or other factors in 24 cases. Among the drug-related factors, the most common were considered to proton pump inhibitors (PPIs), which were observed in 7 cases. Compared to the group of patients who used PPIs but never experienced thrombocytopenia during the course of hospitalization (59 cases), the rate of low complement levels on admission was statistically significantly higher in the group with secondary thrombocytopenia due to PPIs (100% vs 59%, $P = 0.04$). [Conclusion] We suggested the possible existence of a subgroup of PPI-induced secondary thrombocytopenia in the management of SLE.

## W72-5

**The association between periodontitis and relapse of systemic lupus erythematosus: a prospective observational study**

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) is reported to have a high prevalence of periodontitis, suggesting an association with disease activity. However, the association between periodontitis and disease relapse has not been studied. [Methods] The study design was a prospective observational study. The subjects were SLE patients younger than 65 years who visited our department. The primary outcome was SLE relapse. The primary analysis included periodontitis as the outcome variable, and the following confounding variables: age, gender, current smoking, current prednisolone dose, maximum PSL dose after SLE diagnosis, and current immunosuppressive drugs. [Results] The primary analysis included 120 patients with a mean age of 40.2 years and 88.3% women. The mean follow-up period was 4.5 years. The prevalence of periodontitis by severity was 31.4% for no periodontal disease, 1.7% for mild disease, 59.3% for moderate disease, and 7.6% for severe disease. SLE relapse was observed in 35.6%. Logistic regression adjusted for confounding factors showed that relapse for the no periodontitis group was significantly higher than for the mild OR 1.2 moderate OR 0.6, and severe OR 2.6. [Conclusions] We found no significant association between the severity of periodontitis and SLE relapse.

## W72-6

**Clinical features of systemic lupus erythematosus without complement reduction**

Ryo Takeuchi[1], Shuji Sumitomo[1], Hideki Oka[1], Shion Kachi[1], Hirokazu Taguchi[1], Hayato Shimizu[2], Maki Kanamori[2], Hiroaki Nishioka[2], Koichiro Ohmura[1]

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Conflict of interest: None

**Objective**: About 20% of patients with systemic lupus erythematosus (SLE) do not have low complement at the onset of the disease, but the clinical characteristics of these patients are not fully understood. **Methods**: 62 SLE patients who were diagnosed at our hospital and for whom complement (C3 and C4) data at onset were available were included. We compared the patients with and without low complement at the onset of the disease by extracting clinical information from the medical record. **Results**: 12 of 62 patients (19%) did not show complement reduction at disease onset. There was no significant difference by organ involvement except for slightly more arthritis (50% vs. 36%), slightly less fever (17% vs. 38%), and slightly less leukopenia (36% vs. 68%) in the non-hypocomplement group. Anti-DNA antibody titers were significantly lower in the non-hypocomplement group (median 5.0 vs. 94.5 IU/mL). Anti-SS-A antibody positivity was slightly lower (33% vs. 67%), but anti-Sm antibodies were not different between the two groups. CRP values did not differ between the two groups. **Conclusions**: The characteristics of SLE patients without complement reduction are low anti-DNA antibodies, and possibly more arthritis, less fever and leukopenia, and fewer anti-SS-A antibody positivity.

## W73-1

**The difference between Late-Onset Rheumatoid Arthritis and Rheumatoid Arthritis in the Elderly in terms of their characteristics from the T-FLAG study**

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Conflict of interest: None

[Objective] The number of late-onset RA patients (LORA) is increasing, and it is important to understand how their characteristics differ from those of young-onset RA (YORA). The aim of this study was to identify the characteristics of elderly RA. [Methods] Of 595 patients enrolled, 445 patients who were available for 3-year follow-up were included; patients who developed RA at age 65 years or older were defined as LORA, and those younger than 65 years were defined as YORA. After PS, patient background and clinical outcomes were compared (LORA: 84 patients vs. YORA: 84 patients). [Results] There were 121 LORA patients (27.2%). After PS, both groups were 75 years old and SDAI (6.4 vs. 5.9) with low disease activity. LORA vs. YORA showed significant differences in women (62 vs. 86%), disease duration (6 vs. 22 years), seropositivity (79 vs. 94%), and grip strength (21.2 vs. 16.5 kg). No significant differences were found in the physical assessment, HAQ-DI (0.42 vs. 0.62), or in the Kihon checklist for frailty assessment (7.3 vs. 7.1). Regarding the amount of change over 3 years, a significant difference was found in grip strength (-0.9 vs. -2.9 kg). [Conclusion] The differences in gender and seropositivity between LORA and YORA suggest that immunological differences may exist.

## W73-2

**Clinical Characteristics of Patients Enrolled in the Multicenter Registry Study of Late-Onset Rheumatoid Arthritis (LORIS Study)**

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Keizo Maeda[8], Akio Morinobu[9], Akira Onishi[9], Takahiko Sugihara[10], Isao Matsushita[11], Toshihiko Hidaka[12], Toshihiro Matsui[13], Toshihisa Kojima[14], Shuji Asai[15], Keiichiro Nishida[16], Ryozo Harada[17], Motomu Hashimoto[18], Hiromu Ito[19], Takumi Matsumoto[20], Mikako Yasuoka[1], Masayoshi Harigai[7]
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Conflict of interest: None

[Objectives] A nationwide multicenter registry study was initiated with the aim of establishing evidence for the treatment of elderly-onset rheumatoid arthritis (RA). [Methods] RA patients aged 65 years or older, within 2 years of onset, and newly starting treatment with one of the csDMARDs or starting treatment with a molecular-targeted agent were included. In addition to usual clinical information, extensive background information including grip strength, cognitive function, and psychosocial factors using a questionnaire was collected for comprehensive frailty assessment. [Results] From January 13, 2022, to October 20, 2023, 201 patients (112 MTX, 54 other csDMARDs, and 35 molecular-targeted drugs) were enrolled from 21 centers. The mean age of the 195 patients with complete baseline data was 75.7 ± 6.0 (65-93) years, 30% were male, and 75% of cases were enrolled and started treatment within 10 days of confirmed diagnosis. Based on the Kihon Checklist (KCL) ≧8, 62.7% of all patients were frailty. There was no difference in treatment initiating agents by frailty status, although Glucocorticoid prescriptions were significantly more common. [Conclusions] The frequency of frailty in late-onset RA was high, suggesting the influence of social factors.

## W73-3

**Relationship between adverse event occurrence and frailty in the treatment of elderly rheumatoid arthritis patients**

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Conflict of interest: None

[Objective] We investigated the relationship between frailty and adverse events in the elderly rheumatoid arthritis patients. [Methods] We included 1525 patients who attended the Kyoto University Rheumatology Center between January 2011 and July 2022, who were follow-up-eligible for 5 years from the age of 70, 75, 80, or 85 years. Frailty was scored using the 5-item modified frailty index. [Results] At age 70 (n=656), 75 (n=505), 80 (n=259), and 85 (n=105) years, 21%, 32%, 42%, and 44% had frailty; death within 5 years occurred in 1.8%, 4.6%, 7.7%, and 10.5%; the odds ratio for age and frailty was 3.2 (p<0.001,95%CI: 1.7-6.0) and 2.0 (p=0.008,95%CI: 1.2-3.2). Adverse events requiring hospitalization within 5 years, excluding death, occurred in 3.5%, 2.6%, 5.4%, and 4.8% of patients, with odds ratios for age and frailty of 0.9 (p=0.64,95%CI: 0.5-1.5) and 2.8 (p<0.001,95%CI: 1.6-4.9). Furthermore, odds ratios for age and frailty for adverse events with or without hospitalization were 0.9 (p=0.39,95%CI: 0.6-1.2) and 2.3 (p<0.001,95%CI: 1.6-3.2). [Conclusions] Frailty and age were significant risk factors for the occurrence of death; the presence of frailty was a significant risk factor for the occurrence of adverse events within 5 years and for adverse events requiring hospitalization.

## W73-4

**Evaluation of physical function in rheumatoid arthritis patients by locomotive syndrome stage**

Hiroto Yamamoto[1], Mochihito Suzuki[1], Takaya Sugiura[1], Yuki Saito[1], Kenya Terabe[1], Yoshifumi Ohashi[3], Ryo Sato[1], Hironobu Kosugiyama[1], Junya Hasegawa[1], Yusuke Ono[1], Toshihisa Kojima[2], Shuji Asai[1], Shiro Imagama[1]
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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a trigger for the decline of physical function. The aim of this study was to investigate the association between locomotive syndrome stage and physical function in RA patients. [Methods] A total of 324 patients who participated in a prospective cohort study on frailty in RA patients (Fairy study) were included. The bioelectrical impedance (BIA) method was used to measure total muscle mass. Patient background, disease activity (DAS-CRP), physical function (walking speed, Timed Up and Go Test (TUG)), and total muscle mass were compared according to the degree of locomotion at case entry. [Results] Of the 324 patients, the patient background for each locomotive syndrome stage (0/1/2/3) was 61 / 63 / 66 / 66 years old (P=0.22) and DAS-CRP was 1.58 / 1.85 / 2.12 / 2.32 (P<0.01). Regarding physical function, walking speed was 1.44 / 1.29 / 1.22 / 1.08 m/sec (P<0.01) and TUG was 8.25 / 8.50 / 8.98 / 11.0 seconds (P<0.01). Total muscle mass was 40 / 35 / 35 / 33 (P=0.229). [Conclusions] The progression of locomotive syndrome stage was related to various physical function assessments, but the involvement of muscle mass was not clear. Patients with RA showed a decline in physical function with progression of locomotive syndrome stage.

## W73-5

**Validity of evaluation mixed with Joint Index Vector and pain score for fragility fracture prediction in patient with rheumatoid arthritis**

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Conflict of interest: None

Objective: The validity of mixed evaluation with the Joint Index Vector method (JIV) and pain score (PS) for the prediction of fragility fracture (FF) in patients with rheumatoid arthritis (RA) was evaluated. Methods: RA patients monitored JIV and PS from baseline were picked up. The primary endpoint is an incident of the first FF. Associations of Vxy and Vz in the JIV and PS were statistically evaluated. Results: A total of 278, with 39 males and 239 females, were picked up. Mean age at baseline; 74.1-year-old, 7.6 years; RA length, 51.4 months; the observation period, 140; prevalent FF, 44; incident FF (inc-FF), 4.35; mean SDAI, 0.545; mHAQ, PS; 25.5, Vxy; 0.13, and Vz; 0.06 during follow-up. There was no significant correlation of Vxy; however, significant correlations of Vz and PS with inc-FF were shown. Risk ratios (RR), the cut-off index (COI), and the Hazard ratios (HR) were 5.21 and 1.02, 0.01 and 26.47, and 3.54 and 3.36 for Vz and PS, respectively. When COI for each factor is fulfilled, add 1 point, and the two are summed. Then the RR was 3.18, the AUC was 0.727, the HR was 10.32 with 2/0, the specificity when 0 was 96.1%, and the sensitivity when 2 was 35.7%. Conclusions: It is suggested that the index mixed with JIV and PS is a powerful indicator for predicting inc-FF.

## W73-6

**Associated factors of frailty and diagnosis of sarcopenia using SARC-F in patients with rheumatoid arthritis patients: ~multicenter observational study T-FLAG~**

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Conflict of interest: None

[Objective] To investigate the relationship between frailty and sarcopenia in patients with rheumatoid arthritis (RA). [Methods] 682 patients who could record the Japanese version of the Physical Frailty Diagnostic Criteria (J-CHS) and the simplified sarcopenia assessment tool SARC-F (sarcopenia score of 4 or more out of 10) were analyzed. Patients were divided into the groups of non-frailty (n =508) and frailty (n =178). Factors associated with frailty were examined by multiple logistic regression analysis. The relationship between J-CHS and SARC-F was examined by the Pearson correlation coefficient. [Results] Compared to the non-frail group, the frail group was older (mean, 73.4 vs. 67.1 years), had a longer disease duration (15.5 s. 11.9 years), and had a higher DAS28-ESR (3.49 vs. 2.55), HAQ-DI (1.16 vs. 0.29, and SARC-F score (4.6 vs. 1.7). Factors associated with frailty (adjusted odds ratio) were age 1.02, DAS28-ESR 1.48, HAQ-DI 2.07, and SARC-F 1.39. The correlation coefficient between J-CHS and SARC-F was 0.59. [Conclusions] Improving DAS28-ESR, HAQ-DI, and SARC-F is necessary to overcome frailty. The diagnosis of sarcopenia by SARC-F correlates with the diagnosis of frailty by J-CHS, making it a useful diagnostic tool for RA patients.

## W74-1

**Baricitinib dose reduction in patients with rheumatoid arthritis achieving sustained disease control: final results of the RA-BEYOND study**

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Conflict of interest: Yes

[Objective] To investigate the efficacy and safety of baricitinib (Bari) dose reduction in patients (pts) with rheumatoid arthritis achieving sustained disease control. [Methods] In a long-term extension study, pts who received Bari 4-mg for ≧15 months and achieved sustained low disease activity (LDA-Clinical Disease Activity Index [CDAI] ≦10 for pts from prior Phase 3 studies [RA-BUILD/BEAM/BEACON/BALANCE]) for the last ≧3 months were randomized in a blinded manner to continue 4-mg or step down to 2-mg. Efficacy and safety were assessed through 96 weeks after randomization. [Results] Both 2-mg and 4-mg arms were assigned 498 pts each. CDAI in 2-mg and 4-mg were 35.5 and 35.8 at the start of the prior study, and 4.30 and 4.19 at randomization, respectively. CDAI mean change from randomization to Week 96 was significantly larger in 2-mg (3.41) vs. 4-mg (1.90) (p=0.001); significantly fewer pts in 2-mg (59.9%) vs. 4-mg (70.2%) achieved LDA at Week 96 (p=0.001). Incidence of step-down emergent adverse events (AEs), serious AEs, and serious infections were significantly lower with 2-mg vs. 4-mg. [Conclusions] In pts who sustained disease control with Bari 4-mg, even after dose taper, about 60% in the 2-mg arm maintained efficacy even though it was significantly lower than 4-mg arm.

## W74-2

**Long-term efficacy of baricitinib in patients with rheumatoid arthritis who have had inadequate response to csDMARDs or bDMARDs: results from RA-BEYOND up to 7 years of treatment**

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Conflict of interest: Yes

**Objective:** To disclose the long-term efficacy of Baricitinib (BARI) in patients with rheumatoid arthritis. **Methods:** Data up to 7 years (yrs) from three phase 3 studies, RA-BUILD (csDMARD-IR), RA-BEAM (MTX-IR) and RA-BEACON (TNF-IR), followed by a long-term extension (LTE) study was analyzed. **Results:** 583, 1091, and 448 patients from RA-BUILD, RA-BEAM, and RA-BEACON participated in LTE, respectively. The percentage of patients who remained in LTE at yr 3/7 was 56%/25% in BARI 4 mg group and 80%/31% in BARI 2 mg from RA-BUILD; 54%/16% in BARI 4 mg from RA-BEAM; 50%/17% in BARI 4 mg and 65%/26% in BARI 2 mg from BEACON. The main reason for patient withdrawal at yr 7 was sponsor decision based on the fulfilment of the study objectives. For SDAI measure, low disease activity response rates (RRs) were achieved by 70-80% in most of the BARI treatment groups and ranged 47-88% at yr 3 and 7 across the studies. The remission (REM) RRs ranged 15-32% at yr 3 and 7. These RRs for SDAI, CDAI and DAS28-CRP were comparable except that the REM RRs approximately doubled in DAS28-CRP ranging 33-66%. HAQ-DI ≦ 0.5 RR was achieved by 15-29% of BARI-treated patients at yr 3 and 7. **Conclusions:** In observed data, BARI maintained efficacy in csDMARD-IR and bDMARD-IR populations up to 7 yrs.

## W74-3

**Safety of baricitinib in patients with rheumatoid arthritis: 3-year data from an all-case post-marketing study in Japan**

Atsuo Nakajima[1], Masataka Kuwana[2], Tatsuya Atsumi[3], Michiaki Takagi[4], Nobunori Takahashi[5], Tsutomu Takeuchi[6,7], Naoto Tamura[8], Ayako Nakajima[9], Takao Fujii[10], Hiroaki Matsuno[11], Taeko Ishii[12], Naoto Tsujimoto[12], Atsushi Nishikawa[12], Machiko Minatoya[12], Yoshiya Tanaka[13], Nami Okamoto[14]
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Conflict of interest: None

[Objective] To assess the real-world safety of baricitinib (Bari) in patients (pts) with rheumatoid arthritis (RA). [Methods] Bari's all-case post-marketing study enrolled pts (Sep 2017-Feb 2023) and followed each pt for up to 3 yrs. Demographics, serious adverse events (SAEs), and AEs of special interest (AESI) were collected. [Results] Of 4794 pts, 4720 (total follow-up: 9066.2 pt-yrs) were included in the analysis set (mean age 64 yrs, 80% female, mean RA duration 12 yrs, 53% received MTX when Bari treatment started). The persistence rate of 3 yrs of Bari treatment was 45%. Incidence rates (IR) (/100 pt-yrs) of SAEs and deaths were 10.42 and 0.43, respectively. The most common cause of deaths was pneumonia. IR of AESI were: herpes zoster (HZ) 4.68, serious infection (SI) 3.05, malignancy 1.09, interstitial pneumonia 0.48, major adverse cardiovascular events 0.35, venous thromboembolism 0.25, gastrointestinal perforation 0.11, and hepatitis B virus reactivation 0.04. Among AESIs, the highest incidence of HZ (7.80) and SI (5.56) occurred ≦6 months after treatment initiation; no clear trend for other AESIs was observed. [Conclusions] The Bari safety profile in pts with RA with up to 3 yrs' observation was similar to previous reports; no new safety concerns were identified.

## W74-4

**Baricitinib therapy targeting cytokine secretions in rheumatoid arthritis: A multicenter prospective stud y**

Teppei Hashimoto[1], Kazuyuki Tsuboi[2], Kazuteru Noguchi[1], Takeo Abe[1],

Tetsuya Furukawa[1], Takahiro Yoshikawa[3], Koji Tateishi[4], Yasuhiro Terashima[4], Takashi Yamane[5], Nao Shibanuma[6], Naoto Azuma[1], Kiyoshi Matsui[1], Akira Hashiramoto[7]
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Conflict of interest: None

[Objective] Cytokines, such as TNF-α and IL-6, peaks from midnight to early morning in RA. Baricitinib (BAR) therapy targeted cytokine secretion improved CIA mice. Therefore, we also evaluated in RA patients. [Methods] This 24-week trial included patients who received DMARDs or bDMARDs and had not reached remission. A total of 120 patients were assigned to one of four doses: BAR2 mg morning, 2 mg evening, 4 mg morning, or 4 mg evening. We evaluated ACR response rate and the change in CDAI. [Results] The participants, who were followed up to 12 weeks, included 29, 27, 26, and 28 patients from 2 mg morning, 2 mg evening, 4 mg morning, and 4 mg evening groups, respectively. Disease duration was shorter in 2 mg groups. There were no other differences in patient background in all groups. The average reduction in CDAI at week 12 was 5.6±10.6 and 13.5±7.4, and the ACR20 response rate at week 12 was 52% and 80% in the 2 mg morning and evening, respectively ($P<0.05$). In the 4 mg groups, the ACR20 response rate at week 12 was 62.5% and 86.4% in the morning and evening, respectively ($P=0.09$). The average reduction in CDAI at week 12 was comparable, but CDAI improved in the evening group at weeks 4 and 8 ($P<0.05$). [Conclusions] BAR therapy targeting cytokine secretion was effective in treating RA.

## W74-5

**Comparison of the clinical efficacy and safety of baricitinib and sarilumab in rheumatoid arthritis patients**

Toshitaka Yukishima[1], Toshiaki Miyamoto[1], Yukio Nakamura[2], Haruka Yonezawa[1], Shin-ichiro Omura[1], Tomonori Kobayakawa[3]
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Conflict of interest: None

[Objective] To compare the clinical efficacy and safety in rheumatoid arthritis (RA) patients treated with baricitinib (BARI) and sarilumab (SAR) for 52 weeks. [Methods] We enrolled 98 RA patients who received either BARI or SAR therapy and could be followed for 52 weeks from our hospital. Patients in the BARI group (n=67) and SAR group (n=122) were compared for outcomes including DAS28-CRP, SDAI, and CDAI. Adverse events were also assessed for safety evaluation. [Results] Average age at treatment initiation was 69.2±13.0 years and 65.7±14.1 years, and the mean disease duration was 163.6±174.1 months and 85.2±94.9 months, respectively. Efficacy has improved significantly in both groups at 52 weeks, but there was no significant difference in the rate of change between the two groups. The continuation rates were 64.2% and 58.2%, respectively, which were statistically significantly higher in the BARI group. The rates of inadequate response at 52 weeks were 10.4% and 18.0%, respectively. The incidence of herpes zoster was 3.0% and 1.6%, respectively, and was statistically significantly higher in the BARI group. [Conclusions] Comparable results were observed for the clinical efficacy of BARI and SAR in RA patients over a 52-week treatment period. Future studies are expected.

## W74-6

**Comparative study of the clinical efficacy of baricitinib and filgocitinib in rheumatoid arthritis patients in a real-world setting**

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Conflict of interest: None

[Objective] To compare the clinical efficacy of baricitinib (BAR) and filgotinib (FIL) in rheumatoid arthritis (RA) patients. [Methods] The study utilized data from a multicenter registry and included 214 RA patients treated with BAR and 180 patients treated with FIL. Patients were followed for at least 24 weeks were included. Drug persistence rates and SDAI scores were compared between the two groups. [Results] Patient backgrounds (BAR group vs. FIL group) were as follows: age (63.6 vs. 63.0 years), disease duration (12.7 vs. 13.1 years), b/tsDMARD use (67.7 vs. 69.0%), MTX use (59.3 vs. 47.9%), glucocorticoid use (33.1 vs. 43.6%), and SDAI score (33.1 vs. 43.6%). The cumulative discontinuation rate due to inadequate response was (9% vs. 7%) at 24 weeks in, and the cumulative discontinuation rate due to adverse events was (9% vs. 10%) at 24 weeks, with no significant difference between the two groups. In the BAR vs. FIL group, SDAI scores were (17.8±1.6 vs. 18.8±3.3) at baseline, (10.3±1.3 vs. 9.7±2.2) at 4 weeks, (8.7±1.2 vs. 8.5±2.0) at 12 weeks, and (7.9±1.2 vs. 8.7±2.2) at 24 weeks. There was no significant difference between the two groups. [Conclusions] In a 24-week observational study, BAR and FIL had similar clinical efficacy as assessed by drug persistence rate and SDAI.

## W75-1

**Retrospective Investigation into Use of the Glucocorticoid in Treatment of Rheumatoid Arthritis in Our Hospital**

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Conflict of interest: None

[Objective] The actual administration of glucocorticoid (GC) in the treatment of rheumatoid arthritis (RA) remains unclear, we conducted a retrospective investigation into the use of GC in RA patients at our hospital. [Methods] 446 RA patients continuously treated at our hospital from January 1, 2020 to March 31, 2023 were included in this study. We investigated the administration of GC in the first quarter of 2020 (P1) and in the first quarter of 2023 (P2). [Results] The mean age at diagnosis on RA of 446 patients was 54.2±15.2. At P1, the mean age was 64.8±15.2, and the average of DAS28 was 2.2±0.9. 344 patients were GS-free, while 122 patients were administrated GC. At P2, DAS28 was 2.01±0.84. Patients treated with JAK inhibitors increased from 51 to 80 patients, and treated biologics increased from 155 to 170 patients. Patients administrated GC decreased from 122 (26.2%) to 89 (19.1%) patients, their mean dosage of PSL decreased from 4.6±3.3 mg to 2.3±2.7 mg. 377 GC-free patients tended to include patients who could share goals for reducing GC, and/or active use of anti-rheumatic drugs. [Conclusions] We were able to reduce the GC administration rate. In sequentially updated RA treatment, it is important to share treatment goals with patients and use anti-rheumatic drugs proactively.

## W75-2

**Ginger-derived Extracellular Vesicles suppress arthritis**

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Conflict of interest: None

[Objective] Rheumatoid Arthritis (RA) is associated with epigenetic changes, and the involvement of miRNA has been reported. However, synthetic miRNA is unstable within the body. On the other hand, extracellular vesicle (EV) containing plant-derived miRNA are stable and have gained attention. In this study, we investigated the anti-arthritic effects of ginger-derived EV containing miRNA. [Methods] EV were extracted from ginger by ultracentrifugation. In vitro, ginger-derived EV were added to human rheumatoid synovial fibroblasts. Anti-inflammatory effects, cell proliferation and cell migration were evaluated. In vivo, CAIA model was created in DBA/1J mice. Control group and EV group were orally administered PBS or EV daily, anti-arthritic effects were evaluated. Furthermore, microarray of ginger was conducted. [Results] In vitro, EV group showed inhibition of MMP3 and IL-6. Moreover, proliferation and migration abilities were significantly inhibited in the EV group. In vivo, arthritis and histological evaluation were significantly suppressed in the EV group. The microarray confirmed the presence of miRNA in ginger that is identical to those in human. [Conclusions] Our study suggests that ginger-derived EV can suppress arthritis. Ginger-derived EV may be considered as new treatment for RA.

## W75-3

**Efficacy of add-on iguratimod in patients with rheumatoid arthritis who inadequately respond to tumor necrosis factor, tocilizumab, or adalizumab**

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Ichinomiya Municipal Hospital

Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) practice guidelines do not include a statement against the use of additional concomitant therapy with biologic agents (Bio). Therefore, we evaluated the efficacy and safety of iguratimod (IGU) in addition to TNFα inhibitors (TNFi), tocilizumab (TCZ), and abatacept (ABT). [Methods] From January 2014 to August 2022, 53 RA patients who were eligible for analysis of additional concomitant use of IGU in cases of inadequate Bio response at our hospital were included (TNFi group: 19 patients, TCZ group: 15 patients, ABT group: 19 patients). CDAI and mHAQ at 0, 4, 12, and 24 weeks after the start of IGU were observed retrospectively, and adverse events were also investigated. [Results] The mean CDAI and mHAQ scores for the TNFi, TCZ, and ABT groups, respectively, showed improvement at week 24 from the start of IGU. The overall CDAI remission rate improved from 9.4% at week 0 to 28.3% at week 24. Adverse events through week 24 were elevated liver enzymes (4 patients), rash (1 patient), gastric discomfort (1 patient), stomatitis (1 patient), and decreased eGFR (1 patient), each of which resulted in IGU discontinuation. [Conclusions] Add-on IGU was an effective treatment option for patients in inadequate responders to biological agent.

## W75-4

**Treatment Outcomes of Rheumatoid Arthritis: Evaluation of 10-Year Data from the KURAMA Cohort**

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Conflict of interest: Yes

[Objective] Advances in rheumatoid arthritis (RA) treatment, highlighted by biological disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs), have altered the paradigm of RA treatment in the last decade. Therefore, real-world clinical evidence is needed to understand how treatment strategies and outcomes have changed. [Methods] Using an observational cohort of RA from 2012 to 2021, we collected cross-sectional data of RA patients annually to analyze a trend in RA management. Mixed-effect models were applied to examine the statistical implications of changes over time in treatment outcomes with a background adjustment. [Results] We analyzed a cumulative total of 5,070 RA patients between 2012 and 2021. b/tsDMARD use increased, whereas glucocorticoid use decreased from 2012 to 2021. Disease activity and functional disability measures improved over time. The percentage of tsDMARD prescriptions considerably increased. After adjustment for patient characteristics using mixed-effect model, the annual change of RA disease activity and functional disability fared significantly better from 2012 to 2021. [Conclusions] Overall treatment outcomes advanced in the past decade.

## W75-5

**Clinical features and treatments of monoarticular rheumatoid arthritis**

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Conflict of interest: None

[Objective] We conducted this study to clarify clinical features and treatment for monoarthritis type rheumatoid arthritis (RA). [Methods] Patients with monoarthritic RA who visited our outpatient clinic were evaluated for gender, age, autoantibodies, imaging findings, and treatment. Polyarthritic RA was used as a control group. [Results] Seventy-nine patients with monoarthritis (60 female), with a median age of 51 years at the first visit. The median time from onset to first visit was 6 months for monoarthritis and 2 months for polyarthritis (p=0.002). Among seronegative cases, 36.7% had monoarthritis and 15.8% had polyarthritis (p=0.004). Bone destruction in images (X-rays) at the initial examination showed that 40.4% were monoarthritis and 18.6% were polyarthritis (p=0.006). Surgery was performed in 11 patients with monoarthritis. Medication was performed at diagnosis in 67 (90.5%) patients with monoarthritis and 79 (100%) patients with polyarthritis. For initial treatment, methotrexate was used in 43 (64.2%) patients with monoarthritis and 49 (62.0%) patients with polyarthritis. [Conclusions] This study revealed even monoarticular RA requires the same drug therapy as polyarthritis. It is necessary to diagnose monoarthritis-type RA early and perform therapeutic intervention.

## W75-6

**Development of a treatment for rheumatoid sarcopenia using skeletal muscle electrical stimulation: A preliminary report**

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Conflict of interest: None

Introduction Sarcopenia in rheumatoid arthritis (RA) is complex and involves aging and disease effects. It is prevalent, but has no effective treatment. We focused on electrical stimulation and treated outpatients. This report shows the short-term results. Methods We enrolled 8 RA patients who completed 6 months of rehabilitation. They received 1-2 units of electrical stimulation for 20 minutes per unit, 1-2 times per week. We

evaluated RA-related, physical function, and body composition parameters at baseline, 3 months, and 6 months. Results The mean age was 73.9 years, and the mean disease duration was 4.6 years. There were no adverse events due to stimulation. The SDAI was 6.5 at baseline and 5.3 at 6 months. Sarcopenia was in 3 cases at baseline and 2 cases at 6 months. The HAQ did not change from 0.375, and the EQ-5D decreased from 0.837 to 0.804. The locomotive syndrome score decreased from 12.6 to 11.0. There was improvement in function and composition, but no difference. Conclusion This study had few cases, but was feasible without adverse events. However, the visit frequency was optional, and some cases paused due to COVID-19, which made it closer to the real situation than previous reports. We want to increase cases and report more details on training and effect.

## W76-1

**Study on the Prognosis and the Continuation or Discontinuation of Immunosuppressive Therapy in CTD Coexisting with Malignant Tumors**

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Conflict of interest: None

[Objective] To examine the prognosis and immunosuppressive therapy of patients with connective tissue diseases (CTD) coexisting malignancies. [Methods] From the medical database of our hospital from April 2019 to August 2023, 77 patients were extracted and analyzed, who received CTD and tumor treatment and whose outcomes were clearly documented. [Results] Among these patients, 28 (36%) did not require adjuvant therapy after resection and experience recurrence until 2023. Among the 49 patients who received chemotherapy, 13 (16%) died during the follow-up period; lung cancer in 7 patients, pancreatic cancer in 2, hematological malignancies in 2, gastric cancer in 1, and distal bile duct cancer in 1. There were 12 cancer-related fatalities. The mean follow-up period from the detection of the tumor was 44.3 months ± 34.5 months. 24 patients (31%) discontinued all or some of their immunosuppressive agents; methotrexate (MTX) in 12 patients and tacrolimus (TAC) in 6 patients. Among these 24 patients, 12 experienced CTD exacerbation within 1 year, and tocilizumab was introduced in 4 patients of rheumatoid arthritis. [Conclusions] Management of CTD in the context of coexisting malignancies requires individualized adjustments based on tumor prognosis and performance status.

## W76-2

**Treatment in patients with rheumatoid arthritis and malignancies in our hospital**

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Conflict of interest: None

[Objective] The treatment of patients with rheumatoid arthritis (RA) and pre-existing cancer can be challenging. The purpose of this study was to investigate the treatment of RA with pre-existing cancer. [Methods] Of the 385 RA patients who visited our hospital between May and August 2023, 47 patients with a confirmed history of cancer were included, and their cancer type, duration of disease, RA treatment, and disease activity were investigated. In addition, 15 patients who had been attending the hospital before the onset of cancer were compared with the changes in treatment and disease activity. [Results] The mean age was 73.6 years. Malignancies included 9 breast, stomach, lung, liver, 5 lymphomas, 4 uterus, 3 bladder, 2 thyroid, KIT-positive GST, gallbladder, ureter, MPNST, prostate, brain, kidney, colon, esophagus, choroid melanoma, and leukemia in 1. BIO was used in 10 patients, CDAI 3.6, and no cancer recurrence was observed. Of the 15 patients, disease activity did not worsen from pre-cancer CDAI of 4 and CRP of 0.24 to CDAI of 3.3 and CRP of 0.38 at the last observation (p=0.73). [Conclusions] It was thought that patients with a history of malignancies and who developed malignancies during RA treatment could have a good course of disease activity with DMARDs.

## W76-3

**Biological DMARDs (bDMARDs) therapy for RA after regression of LPD or achieving complete remission with chemotherapy**

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Conflict of interest: None

[Background] There is a scarcity of reports about RA treatment with bDMARDs after remission of LPD. The relapse risk of LPD with bDMARDs therapy for RA after remission of LPD is not well known. [Methods] 24 RA patients diagnosed with LPD between April 2003 and March 2021 were included in this study. We analyzed a correlation between LPD relapse and DMARD therapy after regression of LPD or achieving complete remission with chemotherapy. [Results] clinical features at diagnosis of LPD <mean age: 70.8 years, female: 75%. RA treatment (MTX: n=18, TAC: n=4, csDMARDs (non-immunosuppressants): n=10, bDMARDs: n=8). median LDH: 310.5U/L, median sIL-2R: 3093.5U/ml. regression LPD: n=5, persistent LPD: n=19. histology (diffuse large B cell lymphoma: n=14, classic Hodgkin lymphoma: n=6) >. RA treatment after remission of LPD <TAC: n=7, csDMARDs (non-immunosuppressants): n=16, bDMARDs: n=12 >. LPD relapse after the resumption of RA treatment: n=5. The relapse rate of LPD was significantly lower in the group with bDMARDs than the group without bDMARDs after remission of LPD ($P<0.05$). [Conclusions] For RA treatment after remission of LPD, the use of bDMARDs was not associated with LPD relapse. Further accumulation of data and studies on the safety of bDMARDs with RA after remission of LPD are needed.

## W76-4

**Clinicopathological analysis of recurrent methotrexate-related lymphoproliferative disorders of patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To analysis of recurrent methotrexate-related lymphoproliferative disorders (MTX-LPD) of patients with rheumatoid arthritis (RA). [Methods] We performed an analysis of the RA patient characteristics, clinicopathological features, treatment and outcomes of cases with recurrent MTX-LPD who were treated from 2008 to 2023 in our hospital. MTX-LPD was diagnosed based on the clinical and/or radiographic findings and histological examinations in some cases. [Results] There were 31 RA patients with MTX-LPD. Spontaneous regression occurred in 61% (19/31) after MTX discontinuation. 26% (8/31) required additional chemotherapy and/or supportive care for persistent LPD. 13% (4/31) relapsed. Details of recurrent cases, 2 cases were pathologically diagnosed as Hodgkin lymphoma. 1 case showed high soluble IL-2 receptor at the diagnosis of LPD. 1 case received readministration of MTX because no diagnosis of LPD at first onset. [Conclusions] Hodgkin lymphoma and high soluble IL-2 receptor at LPD onset have been identified as the risk factors of recurrent MTX-LPD. When MTX-LPD is suspected it is recommended to perform pathological examinations whenever possible. Even after regression has achieved, careful consideration of administration of immnosuppressants is needed for RA.

## W76-5

**Actual condition of lymphoproliferative disorders in rheumatoid arthritis patients using Aichi Prefecture DPC data**

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Conflict of interest: None

[Background] The risk of developing lymphoproliferative disorders (LPD) in rheumatoid arthritis (RA) patients is higher than in healthy controls, and it is important to understand the risk factors for LPD in RA pa-

tients. [Methods] Using Aichi Prefecture DPC data from April 2012 to March 2023, we selected LPD patients (n=133) out of probable RA patients (n=22850) by matching age and sex in a nested case-control design. The factors associated with the development of LPD were examined by conditional logistic regression analysis. [Results] The mean age was 70 years, and univariate analysis showed significant differences in factors associated with the development of LPD, such as Sjögren's syndrome, MTX, and tsDMARDs. In multivariate analysis, patients with Sjogren's syndrome were significantly at risk for developing LPD (OR=2.82, P<0.05). The results of classification by drug showed that MTX (OR=2.37, P<0.05), MTX+TAC (OR=4.49, P<0.001), bio+MTX (OR=2.61, P<0.05), and tsDMARDs+TAC (OR=1.45, P<0.05) were factors associated with the development of LPD. [Conclusions] In this study, MTX was a risk factor associated with the development of LPD. In addition, concomitant use of TAC and tsDMARDs, as well as the presence of Sjögren's syndrome, may increase the risk of developing LPD.

## W76-6

**Incidence, predictive factors, and clinical features of lung cancer in patients with rheumatoid arthritis**

Shunsuke Mori
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Conflict of interest: None

[Objective] Lung cancer is one of the most common malignancies in patients with rheumatoid arthritis (RA). The aim of this study was to evaluate the incidence, predictive factors, and clinical features of lung cancer in RA patients. [Methods] Between April 2001 and December 2022, 770 patients (198 males and 572 females) were registered. They were followed until an occurrence of lung cancer or the end of June 2023. All patients received high-resolution computed tomography (HRCT) examination at the start of RA treatment. [Results] Twenty-one patients (16 males and 5 females) developed lung cancer. The crude incidence rates were 946 per 10,000 patient-years for males and 90 per 10,000 patient-years for females. The standardized incidence ratio in males was 2.87 (95% CI, 1.46-4.27). Squamous cell carcinoma was the most prevalent histological type. Fifteen male patients showed interstitial lung disease (ILD), emphysema, or both on HRCT scans. One was a heavy smoker. The presence of these complications was the strongest predictor for lung cancer in male RA patients (hazard ratio18.5, 95% CI 2.4-145, $p = 0.005$). [Conclusion] Regular imaging examination is important for early diagnosis of lung cancer in male RA patients with ILD and emphysema.

## W77-1

**Analysis of 165 cases suspected of pseudogout in our hospital**

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Conflict of interest: None

[Objective] Pseudogout is a popular arthritis caused by calcium pyrophosphate dehydrate deposition (CPPD). It is occasionally accompanied with high fever and important disease to discriminate others. [Methods] We extracted 221 cases suspected of pseudogout from 2018 to 2022. We analyzed 165 cases presenting arthritis. [Results] 67 cases proved CPPD (men: 24 cases women: 43). Mean age was 84. Concurrent diseases were systemic infection (9 urinary tract infections, 3 pneumonia, 1 bacteremia), 9 DM, 4 bronchial asthma, stroke and CKD. Mean age in non-CPPD cases was 76 (men: 51 cases, women: 103 cases). Concurrent diseases were 9 CKD, 8 HT and stroke, and 6 DM. Final diagnosis of arthritis in non-CPPD cases were 15 autoimmune diseases (RA 10, PMR 4 GCA 1), 12 local infection and 6 gout. Mean value of CRP was 9.49 mg/dl (SD 7.16) and significantly higher than the value of no-CPPD, 7.00 mg/dl (SD6.96). There was no significant difference in MMP3 values. [Conclusions] Systemic infections are often accompanied with CPPD. Many cases in non-CPPD were diagnosed as autoimmune disease, local infection or gout.

## W77-2

**Long-term low-dose Colchicine therapy for patients with difficult-treated Crystal-induced arthritis**

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Conflict of interest: None

[Objective] This study aimed to examine the clinical outcomes of long-term low-dose colchicine therapy in patients with difficult-treated Crystal-induced arthritis. [Methods] The study included 11 cases of gouty arthritis and 5 cases of pseudo-gout arthritis. In the gouty arthritis group, colchicine was administered for an average of 14.5 months (range: 2-48 months) with concomitant use of febuxostat in 10 cases and dotinurad in 1 case. No oral steroids or NSAIDs were used. In the pseudo-gout arthritis group, colchicine was administered for an average of 9.2 months (range: 3-22 months) with concomitant use of oral NSAIDs in 3 cases, acetaminophen in 1 case, and rectal NSAIDs in 1 case. No oral steroids were used. [Results] In gouty arthritis cases, after initiating 0.5 mg/day colchicine, no new acute attacks were observed during the follow-up, regardless of serum uric acid levels. Similarly, in pseudo-gout arthritis cases, colchicine prevented acute attacks in all cases. [Conclusions] Long-term low-dose colchicine therapy effectively prevents acute attacks in patients with difficult-treated Crystal-induced arthritis. This study indicates the utility of long-term low-dose colchicine therapy for preventing recurrent acute attacks in crystal-induced arthritis.

## W77-3

**Comparative study of overlapping arthritis in cases of 1st MTP joint gout and ankle joint gout**

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Conflict of interest: None

[Objective] In this study, we compared the characteristics of arthritis in patients with gout in the 1st MTP and gout in the ankle joint. [Methods] In 156 gout patients, joint US was performed on all inflamed joints and the 1st MTP. The other arthritic sites were examined by dividing into groups with and without 1st MTP arthritis (1st (+)G or 1st (-)G), and with and without ankle arthritis (Ank (+)G or Ank (-)G). [Results] There were 102 cases (65%) in 1st (+)G and 54 cases (35%) in 1st (-)G). Overlapping arthritis were no significant difference between the two groups in the wrist joints, in the finger joints, in the elbow joints, in the knee joint. s Ankle joints were significantly higher in 1st (-)G ($p<0.0001$). There were 49 patients (31%) in Ank (+)G and 107 patients (69%) in Ank (-)G. Overlapping arithritis in Ank (+)G were significantly higher in the wrist joint s ($p<0.05$), the finger joints ($p=0.09$), the elbow joints ($p<0.05$) and in the knee joints ($p<0.01$) than Ank (-)G. There was a lot of inflammation in the Achilles tendon, triceps tendon, quadriceps tendon, and patellar ligament, and there were gout nodules on the tendon. [Conclusions] There was more simultaneous overlapping other arthritis in Ank (+)G, and the site of inflammation was similar to that of peripheral SpA enthesitis.

## W77-4

**Relationship between Calcium pyrophosphate dehydrate deposition in Knee Joint Fluid and Calcification on Radiographic Images**

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Conflict of interest: None

[Purpose] We investigated the relationship between the presence of calcification on radiographs and the presence of CPPD in joint fluid using knee joint fluid. [Methods] We examined the relationship between the presence or absence of calcification on X-ray images and the presence of CPPD in joint fluid aspirated at the time of treatment using polarized light microscopy in patients with knee joint fluids. [Results] There were 56 patients, including 17 males and 39 females, ranging in age from 21 to 96 years, with an average of 73.7 years. 4 patients had bilateral knee edema, resulting in 60 joints. 32 of the 60 joints were right-sided and 28 were left-sided. The volume of aspirated joint fluid ranged from 5 ml to 70 ml, with an average volume of 19.7 ml. 20 joints were radiographically calcified, and CPPD was found in the fluid of 13 joints. All of the 40 joints without radiographic calcification were negative for CPPD in the joint fluid. [Conclusion] In the present study, CPPD was negative in the joint fluid of all cases in which calcification could not be confirmed on radiographs. This may be due to the older age of the patients. It is interesting to note that there were cases in which the presence or absence of CPPD differed between the left and right sides of the joint.

## W77-5

**Study of fatty liver and steatohepatitis in patients with gout by the Japan Society of Hepatology "Nara Declaration" and Fib -4 Index**

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Conflict of interest: None

[Objective and Methods] Gout patients are often associated with fatty liver. In June 2023, Jpn Society of Hepatology issued the Nara Declaration stating that if serum ALT exceeds 30 U/L, chronic liver disease (CLD) is suspected, and liver fibrosis is evaluated with the Fib-4 Index (Fib4: age x AST/(platelet counts xRADALT)). We compared Fib4 with the Liver Fibrosis Index (LFI) on echo elastography in 122 gout patients with ALT 31 or higher (CLD group). In addition, 83 non-drinkers and 39 drinkers were compared. [Results] Fib4 correlated positively with age and AST and negatively with platelet counts but not with ALT in the CLD group. LFI correlated positively with AST and ALT, but not with age or platelet counts. Fib4 and LFI showed no correlation. Fib4 and LFI were positively correlated in the non-drinkers, but not in the drinkers. There were no significant differences in age, platelets, ALT, BMI, LFI, or degree of fatty liver between the two groups, but AST and Fib4 were significantly higher in the drinkers. [Conclusions] These results suggest that Fib4 may be overestimated in patients with alcoholic liver disease because of its increased AST dominance. Fib4 is useful for the screening of liver fibrosis in CLD in gout nondrinkers.

## W77-6

**Metabolomics analysis identifies differential diagnostic serum biomarker for pseudogout and rheumatoid arthritis**

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Conflict of interest: None

[Objective] To identify the serum differential diagnostic biomarkers for pseudogout and rheumatoid arthritis (RA) using metabolomic analysis. [Methods] We collected the serum of 18 pseudogout and 12 RA patients. We also collected the serum of five pseudogout patients after improving their arthritis. We performed metabolomic analysis using GC-MS. For detecting the metabolites which characterizing pseudogout, we performed univariate and multivariate statistical analysis. Next, for assessment the utility of the detecting metabolites, we performed validation study using additional serum of 11 pseudogout and 13 RA patients. [Results] A total of 101 metabolites were identified. Nineteen metabolites were different between pseudogout and RA, and 9 metabolites were different between pseudogout with arthritis and not with arthritis. As results from analysis, we identified hydroxyl butyrate and 2,3-bisphospho-glycerate, which elevating in pseudogout with arthritis. Furthermore, as results from validation study, hydroxy butyrate in pseudogout was significantly higher than RA. ROC analysis revealed AUC of 0.748, with a sensitivity of 90.9% and specificity of 69.2%. [Conclusions] We identified hydroxy butyrate as the potential differential diagnostic biomarker for pseudogout and RA.

## W78-1

**Rapidly destructive coxopathy caused by primary hyperparathyroidism; a case report. Co-management may be effective**

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Conflict of interest: None

64-years-old woman suffer from her left hip pain. Three months later, she was diagnosed as RDC due to SIF. YAM of L-spine was 61% and YAM of hip was 70%. Four months later, THA was performed. Next day of operataion, a hospitalist started to treat her. A hospitalist gave her the final diagnosis. It was primary hyperparathyroidism and she needed surgery of tumor. When a doctor treat RDC or SIF, the radiograph of hip grabs his attension. He thinks of nothing but THA but he should consider the background of RDC. It is important to pay attention to different diagnosis of secondary osteoporosis. The doctor who works well may be not a orthopedic serugion but a hospitalist.

## W78-2

**Short to middle-term outcomes of surgical treatment for Progressive collapsing foot deformity with inflammatory arthritis (4 cases)**

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Conflict of interest: None

[Objective] There is few report to describe the possibility of joint-preserving surgery for flexible progressive collapsing foot deformity (PCFD) in patients with inflammatory arthritis (IA). In this report, IA with flexible PCFD underwent flexor digitorum longus transfer (FDLT), spring ligament reconstruction, and calcaneocuboid distraction arthrodesis (CCDA). Feasibility of the possible joint-preserving surgery in IA was evaluated. [Methods] 3 patients [1 RA, 1 systemic lupus erythematosus, and 1 ongoing juvenile idiopathic arthritis] with 4 feet were included. Every foot had almost no destruction in talonavicular and subtalar joints. Radiographic parameters [Meary's angle, calcaneal pitch angle (CPA), Pronated foot index (PFI), tibiocalcaneal angle (TCA)] and clinical scores (JSSF-scale, SAFE-Q) were evaluated at preoperative and final follow-up. [Results] The average postoperative observation period was 24 months. All radiographic parameters were improved (Meary's angle 22.3°→3.0°, CPA 6.0→16.5°, PFI 46.0→79.8°, TCA 9.8→2.8°). All clinical scores were also improved (JSSF-scale 48.3→81.8, SAFE-Q 296.0→370.9). [Conclusions] Even in IA, joint-preserving surgery could have a possibility to be indicated against PCFD, as long as disease activity could be well controlled by drug therapy.

## W78-3

**Assessment of Clinical Outcomes Following Debridement, Antibiotics, and Implant Retention with Locally Administered High-Concentration Antimicrobial Therapy in the Management of Periprosthetic Joint Infections After Total Knee Arthroplasty**

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Conflict of interest: None

[Objective] Periprosthetic joint infection (PJI) is a serious complica-

tion in total knee arthroplasty (TKA). In our institution, DAIR combined with local high-concentration antimicrobial therapy via a Hickman catheter is the first choice for PJI treatment after TKA. This study aims at assessing the clinical outcomes with PJI after TKA by this method. [Methods] A cohort of 13 knees with PJI after TKA underwent DAIR and local high-concentration antimicrobials agents. The mean age at DAIR was 76 years, and the mean follow-up periods was 4.4 years. This study investigated the incidence of PJI after TKA at our hospital, treatment details, and the success rate of implant retention. [Results] The incidence of PJI after TKA in our institute was 0.6%. The mean duration from the onset of infection to the DAIR was 17.5 days, accompanied by a concurrent period of local antimicrobial treatment period of 22 days. The antimicrobial agents employed aminoglycosides in six knees, vancomycin in six knees, and penicillin in one knee. Three knees exhibited recurrent infections, with one knee requiring a two-stage revision. The rate of implant retention culminated at 92%. [Conclusions] DAIR with local high-concentration antimicrobial administration demonstrates its effectiveness in managing PJI.

## W78-4

**Long-Term Outcome of Cementless PS Type Total Knee Arthroplasty in Rheumatoid**

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Conflict of interest: None

[Objective] In the case of PS-type Total Knee Arthroplasty (TKA), cemented fixation is the most common method. In our department, we have experienced a small number of long-term cases of cementless PS-type TKA for rheumatoid arthritis patients. [Methods] Between 2000 and 2008, four cases and five knees were operated with cementless Hi-tech Knee PS-type TKA for rheumatoid arthritis patients. The follow-up periods ranged from 5 to 23 years. Age at surgery ranged from 42 to 52 years. Cementless TKA was performed in patients with good bone quality intraoperatively. [Results] At the last follow-up, 3 knees in 3 patients were able to walk independently, and 2 knees in 1 patient were at the level of a supported gait due mainly to back pain. All implants did not have loosening on XP at the last follow-up. They did not complain of pain in the operated knee. [Conclusions] In the long-term results, there were no failures, and the TKAs were functional at the last observation. We believe that the good long-term durability was due to the following factors: the patient was young at the time of surgery and had good bone quality, the patient had rheumatoid arthritis and was relatively inactive, and the Hi-tech knee was all made of titanium, including the femur, and adhered well to the bone.

## W78-5

**Contact styles of Zweymüller-type implant MIRFY with shortened stem length**

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Orthopaedic Surgery, Chiba University

Conflict of interest: None

INTRODUCTION: We have developed and use the MIRFY (Mizuho), which has a shortened stem length and a round bag shape on the outer wing of the stem. The aim of this study is to compare the implant-femur contact state, bone reaction, and stem alignment between MIRFY and conventional Zweymüller-type implant Profemur Z (MicroPort). METHODS: A total of 102 cases per group were selected, propensity score-matched for age, gender, BMI, and Canal Flare Index (CFI). Contact status was evaluated according to Gruen's zone classification using the ZedHip (LEXI). The incidence of varus and flexion insertion of the stem more than 2°, and the presence of more than 2degrees of stress shielding, radiolucent line (more than 2 mm), and subsidence (more than 2 mm) were determined by X-ray. RESULTS: The contact status was higher in the P group in zones 2 and 6, and in the M group in zones 3 and 5. The results were varus insertion (15%, 28%, respectively), flexion insertion (15%, 48%, respectively), and radiolucent line (47%, 29%, respectively). And no significant differences were observed in stress shielding and subsidence. DISCUSSION: MIRFY contact state was slightly more distal. DAA also achieved the intended implant insertion. Further long-term study is needed to evaluate the biomechanical fixation.

## W79-1

**Survey of Anti-SSA Antibody-Positive Patients in Our clinic Based on Oral Problems Questionnaire and the Usefulness of Nursing Care**

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Hikari Chuo Clinic

Conflict of interest: None

[Objective] Oral problems are common in patients with rheumatoid arthritis (RA) and collagen diseases. We report a survey of oral problems in our clinic and the usefulness of nursing care. [Methods] The patients who visited our clinic during the month of September 2023 were surveyed using the questionnaire on dry mouth. [Results] 416 patients (female 367 (88.2%)) responded to the questionnaire. There were 50 cases (49 female) with suspected Sjögren's syndrome (SS), including those who were positive for anti-SSA antibodies and had extraglandular symptoms such as arthritis in addition to dry symptoms but had not yet been histologically diagnosed. Questionnaire results were rated on a 4-point scale from 0 to 3 for 7 items: dry mouth, viscosity of saliva, oral burning, craving for drinking water, oral pain at night, taste disorder, and food intake difficulty. The mean total score was 2.4 for RA without SS suspected and 7.9 for suspected SS cases. [Conclusions] This questionnaire revealed that many patients were unaware that the cause of their problems was due to decreased salivary secretion. We recommend and instruct patients to gargle with Sodium hydrogen carbonate (NaHO3) as a part of total care related QOL by nurses and have observed improvement in oral candidiasis, oral fever, and pain.

## W79-2

**Examination of Assessment Indices for Foot Problems in Patients with Rheumatoid Arthritis**

Haruki Kobayashi[1], Takanori Azuma[1], Yumiko Arai[1], Masakazu Shimizu[1], Yuji Moriyama[1], Takumi Umeno[1], Takaki Ura[1], Yasuhisa Ueda[2]
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Conflict of interest: None

[Objective] The importance of foot care in patients with Rheumatoid Arthritis (RA) has been reported. However, DAS28 does not include foot assessment, and HAQ has limited items related to foot evaluation. In this study, we used an assessment index for disease activity in the foot and examined its relationship with other assessment indices. [Methods] We included 153 RA patients (age 65.8±12.8 years) who visited our clinic and provided responses to questionnaires from September 14, 2023, to September 30, 2023. Disease activity in the foot was assessed using RADAI-F5. We used DAS28-CRP, mHAQ, and RAPID3 as evaluation criteria and examined their correlation with RADAI-F5 using Spearman's rank correlation coefficient. [Results] The RADAI-F5 score was 1.47±1.60, and 52% of patients had foot problems. DAS28-CRP, mHAQ, RAPID3 showed remission in 79%, 88%, 44% of cases respectively. RADAI-F5 had a weak positive correlation with DAS28-CRP and mHAQ (r=0.40, r=0.42). RADAI-F5 had a strong positive correlation with RAPID3 (r=0.67). [Conclusions] DAS28-CRP and mHAQ alone may not adequately capture foot disease activity in RA patients. To assess foot disease activity from an early stage, the use of the straightforward RADAI-F5 assessment is considered effective.

## W79-3

**Attempts to Improve Treatment Satisfaction of Rheumatoid Arthritis Patients by Registered Rheumatoid Arthritis Pharmacists**

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Conflict of interest: None

[Objective] To compare treatment satisfaction among patients through continuous intervention by rheumatoid arthritis registered pharmacists. [Methods] We conducted face-to-face assessments from March 2020 to September 2023 with 48 rheumatoid arthritis patients in our rheumatology department. Assessment criteria included patient demographics (age, gender, disease duration, comorbidities), disease activity, medication regimens, intervention frequency, medication adherence (AD), and shared decision-making (SDM). [Results] When comparing the group with decreased treatment satisfaction (n=21) to the group with stable or increased satisfaction (n=27), there were no significant differences in age (65.0, 64.7 years), gender female (76%, 89%), or pharmacist intervention frequency (3.0, 3.6). There were no significant differences in disease activity. However, the group with increased treatment satisfaction had higher pharmacist intervention satisfaction. [Conclusions] A correlation was observed between increased treatment satisfaction and pharmacist intervention satisfaction. To enhance pharmacist intervention satisfaction, a novel approach is needed, focusing not only on medication counseling and medication adjustment but also on patient guidance leading to SDM in medication selection.

## W79-4

**Results of Patient Satisfaction Survey of Clinical Path Admission for Induction of Biologic Agents for Patients with Rheumatoid Arthritis**

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[1]Nursing Department, Kitsato University Hospital, [2]Department of General Medicen, Kitasato University School of Medicine, Kitasato University Hospital, Kanagawa, Japan, [3]Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kitasato University Hospital, Kanagawa, Japan

Conflict of interest: None

[Objective] To identify the Impact of Patient Background on Patient Satisfaction with Clinical Path Admission [Methods] The satisfaction of Twenty five patients who cooperated with a questionnaire after admission to the path was scored out of Eighty points on a twenty-item and the relationship with patient background was analyzed. [Results] Overall (N equal Twenty five) satisfaction with the path was Seventy fiveplus or minus Nine. Six (N equal Eleven) in Two Thousand Twenty Two and decreased to Seventy one point eight plus or minus six point nine (N equal Fourteen) in two thousand twenty three mainly due to the “length of hospital stay” item The satisfaction level of those under sixty four years old was Six point two points lower in two thousand twenty three at Seventy two point nine plus or minus eight point three compared to Seventy nine point oneplus or minus zero point eight five in Two Thousand Twenty Two but patients from sixty five to seventy four years and over seventy five years old groups increased, indicating a decrease in intergenerational differences. In addition, the item for ‘ease of asking questions increased in all age categories. [Conclusions] Regarding the length of hospitalization, there is no specific number of days requested, so the survey will be continued. (1290)

## W79-5

**Long-term safety of rheumatoid arthritis patients receiving biologic DMARDs under our multi-disciplinary collaborative care**

Megumi Kobayashi[1], Nami Usuda[1], Yoshioki Yamasaki[1,2], Yoshiki Ishizaki[1,2], Youjiro Minegishi[3], Hidehiro Yamada[1,4]
[1]Department of Rheumatology, Yokohama General Hospital, [2]Department of Rheumatology, Collagen Disease and Allergy, St. Marianna University School of Medicine, [3]Department of Orthopedics, Yokohama General Hospital, [4]Medical Center for Rheumatic Diseases, Seirei Yokohama Hospital

Conflict of interest: None

[Objective] We previously presented lower incidence of severe infection among rheumatoid arthritis (RA) patients receiving biologic DMARDs under our multidisciplinary collaborative care. We further investigated their long-term safety. [Methods] A survey was retrospectively conducted in 226 patients with RA who received etanercept (n = 62), abatacept (n = 137), or tocilizumab (n = 27) from July 2012 to June 2020. [Results] Of 226 patients, 125 (55.3%) had two or more risk factors of infection (age ≧ 65, pulmonary involvement, diabetes, corticosteroid use, and history of cerebrovascular diseases). The mean observation period was 43 months, the treatment retention rate, the cumulative adverse event rate, and the cumulative ineffective rate were 50%, 32%, and 30%, respectively. Hospitalization was required in 16 patients due to infections (mean age 75 years, 2.01/100 person-years). Other serious adverse events included malignancies (n = 16), acute exacerbation of interstitial lung disease (n = 4), psoriasis-like skin rash (n = 4). Three patients died. [Conclusion] Severe infections could not be completely abolished. It is important to provide more extensive guidance to elderly patients having multiple risk factors.

## W79-6

**The birth of a new academic field, Onco-Rheumatology, and the knowledge/skills required for rheumatologists**

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Conflict of interest: Yes

[Objective] The field of Onco-rheumatology, in which oncologists and rheumatologists collaborate in cancer treatment, is becoming increasingly important. This study aimed to clarify what kind of knowledge is required in this emerging academic field. [Methods] A retrospective observational study using the consultation database of the Department of Onco-Rhematology established in a cancer hospital. [Results] A total of 370 consultations were conducted between January 2020 and October 2023. The consultation contents were as follows: management of known rheumatic diseases: 41 (11%), consultation on possible rheumatic diseases for undiagnosed conditions: 121 (32.7%), consultation on irAE (immune-related adverse events): 194 (52.4%). Only 14% of irAE-related consultations were about rheumatic irAE, and most of the consultations were related to non-rheumatic irAE, such as hepatitis and diarrhea/colitis. [Conclusions] The knowledge of rheumatologists regarding the approach to systemic/multi-organ inflammatory conditions and the use of steroids/immunosuppressive drugs/biologic agents are required in the field of Onco-Rheumatology, especially in the management of irAEs.

## W80-1

**Factors affecting skeletal muscle quality in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] We have reported that rheumatoid arthritis (RA) patients with normal SMI and locomotive syndrome (LS) have reduced skeletal muscle quality. The aim of this study was to investigate factors associated with skeletal muscle quality in patients with RA. [Methods] A total of 160 RA patients attending rheumatology outpatient clinics were included in this study. Phase angle (PhA), calculated by the bioelectrical impedance method, was used to assess skeletal muscle quality and patients were divided into two groups according to median PhA and compared between the two groups in terms of age, sex, disease duration, medication, DAS-28 (CRP), SMI, and prevalence of LS. Logistic regression analysis was performed to identify PhA-related factors using the various test results as independent variables. [Results] The low-PhA group had significantly higher age, DAS-28 (CRP) and prevalence of LS and lower SMI than the High-PhA group. Age and SMI were identified as factors associated with low-PhA. [Conclusions] It is suggested that RA patients with older age and lower SMI are associated with an increased risk of lower PhA. In addition to muscle strength and SMI, the assessment of PhA is considered important for the early detection of LS and LS reserve.

## W80-2

**Comparison of exercise function and body composition in elderly women with rheumatoid arthritis and elderly women in general**

Takaya Sugiura[1], Mochihito Suzuki[1], Hiroto Yamamoto[1], Yuki Saito[1], Chinami Ohnishi[1,2], Kenya Terabe[1], Yoshifumi Ohashi[1], Ryo Sato[1], Hironobu Kosugiyama[1], Junya Hasegawa[1], Yusuke Ono[1], Toshihisa Kojima[3], Shuji Asai[1], Shiro Imagama[1]

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Conflict of interest: None

[Objective] We investigated the differences in physical function and body composition between RA patients and healthy subjects by comparing the results of a general health examination [Methods] Between 2021 and 2022, a total of 904 subjects, 328 of RA patients (RA group) and 576 of health examination group, were included in the study. The degree of muscle mass was measured using BIA. Grip strength, which reflects upper limb muscle strength, and 10m walking speed and standing test, which reflect lower limb muscle strength, were measured for motor function. [Results] A total of 463 elderly women aged 65 years or older were eligible for all the tests, and the RA group had low disease activity with SDAI of 5.46 and HAQ-DI of 0.45. The age of patients in the health checkup group was 76/73 years ($p<0.01$), and the locomotor 25 was 9.7/17.0 ($p<0.01$), which was higher in the RA group. All physical functions were lower in the RA group. There were significant differences in trunk muscle mass (19.1/18.3 kg, $p<0.01$), upper limb muscle mass (3.0/2.9, $p<0.01$), and lower limb muscle mass (11.0/10.8, $p=0.13$), but no significant differences in lower limb muscle mass. [Conclusions] Elderly female RA patients showed a decrease in general motor function compared to healthy subjects.

## W80-3

**The novel criteria for diagnosing Rheumatoid Sarcopenia using musculoskeletal ultrasound**

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Conflict of interest: None

[Objective] The aim of this study is to establish criteria for musculoskeletal ultrasound in the diagnosis of sarcopenia. [Methods] This is a cross-sectional study enrolling, 30 female patients with rheumatoid arthritis from August 2022 to April 2023 and 6 healthy female controls. Data were obtained by measuring the skeletal muscle mass index (SMI) using dual X-ray absorptiometry and muscle thickness at the anterior thigh level determined by a standardized ultrasound protocol. Two rheumatologists performed ultrasound examinations and analyzed the relationship between muscle thickness, physical function assessment, and ultrasound muscle echogenicity. [Results] Maximum muscle thickness of either the left or right thigh was the strongest correlation with SMI ($r=0.813$, $p<0.001$). The most sensitive cutoff value for diagnosing sarcopenia based on muscle thickness was “maximum muscle thickness at the anterior thigh < 24 mm on either side “ (Sensitivity: 91.67%, Specificity: 83.33%). Muscle thickness was significantly correlated with grip strength ($r=0.535$, $p<0.05$) and stand-up test ($r=0.553$, $p<0.05$), as well as ultrasound muscle echogenicity ($r=-0.848$, $p<0.001$). [Conclusions] Ultrasound has the potential to enable a faster and more convenient diagnosis of rheumatoid sarcopenia.

## W80-4

**Differences in physical function between late-onset rheumatoid arthritis and young-onset rheumatoid arthritis**

Yuki Saito[1], Mochihito Suzuki[1], Takaya Sugiura[1], Hiroto Yamamoto[1], Chinami Ohnishi[2], Kenya Terabe[1], Yoshifumi Ohashi[1], Ryo Sato[1], Hironobu Kosugiyama[1], Junya Hasegawa[1], Yusuke Ono[1], Toshihisa Kojima[3], Shuji Asai[1], Shiro Imagama[1]

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Conflict of interest: None

Objectives: Clarifying the differences in physical function between late-onset rheumatoid arthritis (LORA) and young-onset rheumatoid arthritis (YORA). Methods: Patients (LORA 53, YORA 275) from a prospective cohort study on frailty in RA patients from 2021/3~2022/12 were included. Propensity score was calculated with using age at study entry as a covariate. A comparison was made between the LORA group (48 patients) and YORA group (48 patients). Primary endpoints were [muscle mass (MM), grip strength, walking speed, timed up and go test (TUG), and physical function assessment (HAQ-DI)]. Results: Patient characteristics (LORA vs. YORA) were no significant differences in age (74/74 years) and women (83.3/91.7%), whereas disease duration was 5/20 years ($p<0.001$). Trunk MM mass was significantly higher in the LORA group at 19.9/18.5 kg ($p<0.05$). The weight of the upper limb was 1.6/1.4 kg on the left, 1.6/1.5 kg right, and the weight of the lower limb was 5.8/5.5 kg, 5.8/5.5 kg, with no significant difference. A significant difference was observed for grip strength of 21.2/16.5 kg ($p<0.05$), but not for walking speed 1.2/1.2 m/s, TUG 11.3/9.2 seconds, and HAQ-DI 0.42/0.44. Conclusion: We found that LORA and YORA are characterized by differences in trunk muscle mass and grip strength.

## W80-5

**Health Assessment Questionnaire as a predictor of a fall in the elderly female patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] An elderly person who took more than12 seconds to complete timed up and go (TUG) test is a predictor of a fall. We aimed to clarify the cut-off value of Health Assessment Questionnaire (HAQ) and walking speed for TUG more than 12 seconds. [Methods] In this study, sixty-eight patients with rheumatoid arthritis (RA) were included. We surveyed HAQ, TUG, walking speed, Root Mean Square (RMS). We used a tri-axial accelerometer to measure walking speed and RMS. The patients were divided into 2 groups (the TUG more than 12 seconds group and the TUG less than 12 seconds group). [Results] The mean age of 68 patients was 68.9 ± 12.5. The mean TUG test was 9.0 ± 3.2 seconds. Nine patients (13.2%) took over 12 seconds in TUG test. The receiver operating characteristic analysis showed the cut-off value of walking speed and RMS were 0.82 m/seconds (AUC = 0.988) and 1.973, each (AUC = 0.928). The AUC of HAQ was the next highest (AUC = 0.893). The cut-off value of HAQ was 1.0 (specificity 0.778 and sensitivity 0.864). [Conclusions] The cut-off value of HAQ was 1.0 for TUG more than 12 seconds in the elderly female patients with RA. HAQ is an indicator that can be measured without any instruments.

## W80-6

**Relationship between foot disease activity and foot function in patients with rheumatoid arthritis**

Haruki Kobayashi[1], Takanori Azuma[1], Masakazu Shimizu[1], Yuji Moriyama[1], Takumi Umeno[1], Yasuhisa Ueda[2]

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Conflict of interest: None

[Objective] Many patients with Rheumatoid Arthritis (RA) have foot deformities. This study aims to investigate the relationship between disease activity in the foot and foot function. [Methods] This study included 34 RA patients (age 65.2±14.0 years) who visited our rehabilitation center and consented to measurements from September 14, 2023, to September 30, 2023. Disease activity in the foot was assessed using RADAI-F5. Foot function was assessed using the Japanese Society for Surgery of the Foot

(JSSF) RA Foot Ankle Scale, ankle dorsiflexion range of motion, and toe-tapping test. The correlations between these measurements were examined. [Results] The RADAI-F5 score was 2.0±1.8 (HDA: 3%, MDA: 24%, LDA: 35%, remission: 38%). The JSSF score was 79.8±18.3 points, ankle dorsiflexion range of motion was 12.1±6.6 degrees, and toe-tapping test result was 8.2±3.3 taps. A significant negative correlation was found between RADAI-F5 and JSSF (r=-0.65). JSSF showed significant positive correlations with ankle dorsiflexion range of motion and toe-tapping test results (r=0.67, r=0.59). [Conclusions] Patients with higher RADAI-F5 scores appear to have decreased foot function. RADAI-F5 could be effective in facilitating the prescription of rehabilitation in patients with foot issues.

## W81-1

**A case of interstitial lung disease with dermatomyositis acutely exacerbated by COVID-19 showing improvement with baricitinib**

Masataka Namiki[1], Soshi Takahashi[1,2], Shintaro Yasui[1], Yukina Tanimoto[1], Motoko Katayama[1], Saori Hatachi[1], Shunichi Kumagai[1,2]
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Conflict of interest: None

An 85-year-old man had been diagnosed with interstitial lung disease (ILD) with dermatomyositis (DM) 3 years ago. He had been treated with oral prednisolone and tacrolimus. Because SARS-CoV-2 antigen test kit was found to be positive, he had stayed at home and continued immunosuppressive drugs. After 9 days, his symptoms were worsened and he visited our hospital. He was admitted to our hospital as severe COVID-19, and we started steroid therapy and remdesivir. His symptoms were improved once, but the oxygen demand had worsened again. X-ray showed worsening of pneumonia, and then baricitinib had been added for COVID-19. However, from the clinical course and the results from CT scan, we re-diagnosed as an acute exacerbation of DM-ILD, not COVID-19. Remdesivir was quitted and baricitinib had been continued since his symptoms and oxygen demand had been improved. His ILD was improved, and he was discharged. Conclusion: We experienced a case of acute exacerbation of DM-ILD during treatment of COVID-19, resulting the successful treatment with baricitinib. The result suggested that baricitinib may be effective in the treatment of ILD with autoimmune disease.

## W81-2

**Two cases of anti-TIF-1 gamma antibody-positive dermatomyositis presenting after chemotherapy, with TIF-1 gamma antigen expression in tumor tissue**

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Conflict of interest: None

We report two cases of anti-TIF-1γ-positive dermatomyositis presenting after chemotherapy. [Case 1] A 73-year-old female developed lymphadenopathy, and large cell neuroendocrine carcinoma was diagnosed by lymph node biopsy. Post-chemotherapy, the patient exhibited muscle enzyme elevation, muscle weakness, and rash, leading to a diagnosis of dermatomyositis. Despite treatment, her outcome was poor. [Case 2] A 71-year-old male presented with aphasia. A left temporal lobe tumor was detected by MRI, and a lung tumor and lymphadenopathy were found by CT. A metastatic tumor of small cell lung cancer was diagnosed by a brain tumor biopsy. Post-chemotherapy, he developed muscle enzyme elevation, muscle weakness, and rash, and he was then diagnosed with dermatomyositis. Despite treatment, his outcome was poor. In both cases, the tumor cells were positive by anti-TIF-1γ antibody immunostaining. [Conclusion] Anti-TIF-1γ-positive dermatomyositis has a high incidence of malignancy, but its pathophysiology remains unclear. In our two cases, anti-TIF-1γ-positive dermatomyositis developed after chemotherapy, with proven TIF-1γ expression in the patients' tumor cells. Tumor cell destruction may contribute to anti-TIF-1γ antibody production, and the accumulation of similar cases are necessary.

## W81-3

**Utility of cardiac MRI for evaluating myocarditis in polymyositis/dermatomyositis (PM/DM)**

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Conflict of interest: None

Myocarditis in polymyositis/dermatomyositis (PM/DM) is often undiagnosed by conventional ECG and UCG. In cardiac magnetic resonance imaging (cMRI), parametric mapping has rapidly gained popularity in recent years for an assessment of myocardial involvement. We report a case of DM in a 53-year-old woman with myocarditis, which was done by cMRI and was useful for therapeutic and efficacy decision. She was treated by antibiotics for pneumonia at previous hospital, however her inflammation increased and noted myalgia, so she was referred to our hospital with the possibility of having DM. She had Gottron's sign, elevated CKs, high signal on muscle MRI and findings of myositis on biceps biopsy. ECG and UCG were normal. Troponin I and CK were elevated despite preceeded tacrolimus treatment and cMRI was performed. cMRI showed high signal on T2-weighted imaging and LGE in the septum. Global ECV on T1 mapping was 35%, global T2 value on T2 mapping was 60 ms, suggesting myocardial damage due to DM. After treatment, cMRI showed LVEF improved from 51% to 62%, T2-weighted imaging showed no high signal and LGE was unchanged, but T1 mapping showed global ECV of 30% and T2 mapping showed global T2 value of 54 ms, indicating improvement in cardiac function, ECV and T2 values.

## W81-4

**A case of dermatomyositis with coexistence of anti-TIF1-gamma and anti-ARS antibodies suggested by clinical features and muscle pathology**

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Conflict of interest: None

[Case] A 51-year-old woman was referred to our department because she had fever, dyspnea on exertion, and muscle weakness in her extremities for one month. She had heliotrope rash, shawl sign, periungual erythema, gottron's sign, reverse gottron's sign, muscle weakness in proximal muscles, elevated muscle deleterious enzyme, and positive anti-TIF1-gamma and anti-ARS antibodies. Electromyography showed fibrillation potential. Muscle pathology showed perifascicular necrosis and regeneration of myofibers and ALP expression in the perimysium, while MxA expression was observed. No malignant complications were observed. The diagnosis of dermatomyositis was made according to the 2017 EULAR/ACR classification criteria. She was started on prednisolone 50 mg/day and tacrolimus, and her cutaneous symptoms, myositis, and interstitial lung disease improved. [Discussion] In general, myositis-specific antibodies are considered to be mutually exclusive. In this case, the clinical features and muscle pathology were characteristic of each antibody, as described above. The muscle pathology suggested that both antibodies can coexist pathologically.

## W81-5

**A case of nuclear matrix protein (NXP)-2 antibody-positive dermatomyositis with dropped head syndrom**

Naoki Oya[1], Kotaro Komori[1], Yoshikazu Motomura[1], Asami Kiuchi[1], Nobuhiro Oda[1], Akira Jibatake[2], Ryo Hazue[1], Ryo Rokutanda[1]
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Conflict of interest: Yes

[Case] A 59 year-old female with past history of rectal cancer presented with a 3-week history of general fatigue, muscle pain and weakness. 3 weeks prior to admission, she noticed general fatigue. Swelling and pain in the proximal muscles appeared 2 weeks before admission, and an exacerbation of pain in the thigh was observed. She was referred to our department with suspected myositis due to recent laboratory tests. On admission, she had weakness in the proximal muscles and the neck muscles, and showed a dropped head. MRI showed STIR high signal in the quadriceps femoris, sartorius muscle, sternocleidomastoid muscle, paraspinal muscle, and trapezius muscle. Further examination excluded malignancies. According to the EULAR/ACR classification criteria, the total score was 5.8 points and was classified as "probable". She received methylprednisolone 60 mg/day with rapid improvement of the dropped head. Later, anti-NXP-2 antibody positivity was confirmed, and histopathological findings showed marked infiltrations of lymphocytes and plasma cells with perifascicular atrophy of muscle fibers. [Discussion] In this case, we experienced a case of anti-NXP-2 antibody-positive dermatomyositis with dropped head syndrome. We report a case with a literature review.

## W81-6

**A case of anti-SRP antibody-positive IMNM and IBM following HIV and syphilis infection**

Fumito Inayoshi, Nobuhito Okumura, Keita Okamoto, Takuma Wada, Hiroshi Kajiyama, Kazuhiro Yokota, Yasuto Araki, Yu Funakubo Asanuma, Yuji Akiyama, Toshihide Mimura
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Conflict of interest: None

[Case] Five months ago, a 42-year-old man was diagnosed with HIV and syphilis and treated with penicillin and anti-HIV drugs. His serum creatinine kinase (CK) level was elevated at 4,835 U/L. Over the course of the last four months, He had noticed muscle weakness and myalgia in his extremities. As his symptoms progressed, he developed difficulty with body movements and swallowing, leading to admit to our hospital. Physical examination revealed muscle weakness in both proximal and distal muscles of his extremities, muscle pain in the thigh muscles, elevated CK levels, and a positive anti-SRP antibody test. MRI STIR images showed multiple high-intensity lesions in the anterior part of the bilateral thigh muscles. Muscle biopsy results findings of findings of immune-mediated necrotizing myopathy (IMNM) and inclusion body myositis (IBM). He treated with prednisone at a dose of 1 mg/kg/day, along with high-dose intravenous immunoglobulin. Subsequently, his muscle strength improved from 2 to 4 by manual muscle testing, and his CK levels decreased to 375 U/L. [Conclusions] This is a case of anti-SRP antibody-positive IMNM that may be due to immune activation following HIV and syphilis infection. Additionally, the pathological findings in the muscle biopsy suggest possible features of IBM.

## W82-1

**The efficacy and safety of remission maintenance therapy with rituximab for ANCA-associated vasculitis in clinical practice; single-center analysis**

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Conflict of interest: None

[Objective] To determine the utility of rituximab (RTX) in the remission maintenance therapy of AAV. [Methods] Patients with GPA and MPA who received remission maintenance therapy with RTX or azathioprine (AZA) were included. The two groups were compared for relapse rates, GC dose, and adverse events (AE) for 24 months. RTX was administered when B-cell counts increased above 1 cell/μl. [Results] There were 48 patients in the RTX/AZA group: 19/29. Mean age: 69.8/74.2 years, GPA: 36.8%/20.7%, MPA: 63.2%/79.3%, mean BVAS: 13.3/13.1 points, and mean GC dose: 44.8 mg/day/39.5 mg/day, with no difference. The RTX group was significantly more likely than the AZA group to receive induction remission therapy with RTX (100%/31.0%). Relapse rates within 24 months were 14.3% in the AZA group, with no relapse in the RTX group. The mean GC dose was 2.0 mg/day in the RTX group and 4.4 mg/day in the AZA group at 24 months, and the RTX group received significantly less GC than the AZA group. Within 24 months, 7 patients discontinued AZA due to AEs, but not in the RTX group. 4 patients in the AZA group had Grade 3 or higher infections, but not in the RTX group. [Conclusions] The efficacy and safety of remission maintenance therapy with RTX for AAV in clinical practice were confirmed over 24 months.

## W82-2

**Discussion about Dosage of Rituximab Induction Regimens for Antineutrophil Cytoplasm Antibody-Associated Vasculitis - Retrospective Study**

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Conflict of interest: None

[Objective] The standard regimens of Rituximab (RTX) induction therapy for Antineutrophil Cytoplasm Antibody (ANCA) -Associated Vasculitis (AAV) is 375 mg/m$^2$ administered intravenously every week for four-dose. Depending on patient's physical condition, sometimes we had to reduce the regimen. We will discuss about the efficacy and safety. [Methods] We enrolled AAV patients who we can follow up for 6 months after introduction therapy. We assessed disease status with Birmingham Vasculitis Activity Score (BVAS) and Vasculitis Damage Index (VDI) after 6 months. We also researched the process of steroid reduction and adverse event in the period. [Results] 21 patients were enrolled. The mean age was 77.4 (58-90) yr. 18 of 21 patients (85.7%) were microscopic polyangiitis and 15 of 21 (71.4%) were new diagnosed. The mean number of RTX 375 mg/m$^2$ administered were 2.0 (2-3). Remission at 6 months was observed in 17 of 21 patients (81.0%). The mean of VDI at 6 months was 2.0 (0-5). And there were 12 adverse events including 7 events of infection and 2 deaths (1 progression of AAV and 1 infection). [Conclusions] Our results suggest that we may reduce the dosage of RTX in introduction therapy.

## W82-3

**Prognosis of ANCA-associated vasculitis patients treated with Rituximab maintenance therapy**

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Conflict of interest: None

**Objective.** To investigate the prognosis of ANCA-associated vasculitis (AAV) patients treated with Rituximab (RTX) maintenance therapy. **Methods.** AAV patients who treated with RTX in remission induction and maintenance therapy between 2015 and 2023 were enrolled. **Results.** Nineteen patients (25 times), 5 men and 14 women, median age 73 years old (62-85 years old), 15 MPO-ANCA-positive and 5 PR3-ANCA-positive patients, were included. Relapse during maintenance therapy occurred in 3 patients (3 times). Maintenance therapy was completed in 16 patients (16 times) with a median time from remission induction to the last RTX infusion of 24 months (15-34 months). Outcomes were 7 relapses, 8 in remission, and 1 death, and relapse-free survival from the last RTX was 87% at 2 years and 47% at 3 years. Regarding 7 patients with relapse, a median time from last RTX to relapse was 31 months (15-37 months), all patients showed increased ANCA levels. **Conclusion.** Relapses after completion of RTX maintenance therapy occurred mainly between 2 and 3 years and were more common in MPO-ANCA-positive patients. ANCA levels were increased prior to relapse in all relapsed patients.

## W82-4

**The efficacy of avacopan in remission induction therapy for MPA/GPA**

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Conflict of interest: None

[Objective] To clarify the efficacy of avacopan (AVA) for MPA and GPA under real clinical settinsgs. [Methods] MPA and GPA patients who received remission induction therapy at our institution from January 2017 to June 2023 were included in this study. The achievement rate of BVAS=0, glucocorticoid (GC) dose (/day), and occurrence of adverse events (AEs) up to 6 months after treatment were investigated in two groups (with and without-AVA). [Results] A total of 11/58 patients were included in the with/without-AVA, respectively. Patient background was as follows: mean age, 72.7/73.2 years; MPA, 81.8%/74.1%; mean BVAS, 13.5/13.3 points before treatment; mean GC dose at start of treatment, 38.9/41.7 mg/day. The achievement rate of BVAS=0 at 3 and 6 months was 90.9% and 100% in the with-AVA and 80.0% and 95.8% in the without-AVA. Mean GC doses (/day) at 3 and 6 months were 5.8 and 2.8 mg in the with-AVA and 11.9 and 7.8 mg in the without-AVA. The rate of incidence of GC-related AEs (hypertension, diabetes, severe infection, etc.) within 6 months was 0% in the with-AVA and 50.0% in the without-AVA. [Conclusions] In real-world clinical practice, remission induction therapy with AVA significantly achieved a high remission rate, reduced GC doses, and reduced GC-related AEs.

## W82-5

**Efficacy of mepolizumab during maintenance therapy in patients with eosinophilic granulomatosis with polyangiitis**

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Conflict of interest: None

[Objective] To clarify the efficacy of mepolizumab (MPZ) during maintenance therapy of patients with eosinophilic granulomatosis with polyangiitis (EGPA) compared to standard-of-care (SoC). [Methods] Patients, diagnosed with EGPA and treated at our hospitals between January 2016 and June 2022, were included if they met all of the following criteria: prednisolone ≦ 20 mg/day, Birmingham Vasculitis Activity Score (BVAS) < 10, and more than 6 months after start of treatment for EGPA. Participants comprised patients on MPZ (MPZ group: n = 16) and those on newly taken immunosuppressants (SoC group: n = 16). We investigated disease activity and relapse rates. [Results] The rate of change of BVAS over 12 months was significantly lower in the MPZ group than in the SoC group (MPZ: -59.2 ± 45.6% [mean ± SD]; SoC: -15.4 ± 71.8%, P = 0.009). The rate of change of prednisolone dose over 12 months was not significantly different between the groups (MPZ: -16.1 ± 71.8%; SoC: -37.1 ± 46.9%, P = 0.20). Relapse rates tended to be lower in the MPZ group than in the SoC group (P = 0.08). [Conclusions] Our study demonstrated that administration of MPZ to EGPA during maintenance therapy reduced disease activity and relapse rates.

## W82-6

**Glucocorticoid tapering of Mepolizumab in Eosinophilic Granulomatosis with Polyangiitis**

Takeshi Shoda[1], Hideyuki Shiba[1], Youhei Fujiki[2], Junichi Konma[2], Natsuko Esa[1], Ayana Okazaki[1], Takanori Nakagaki[1], Shogo Matsuda[1], Takao Kiboshi[1], Yumiko Wada[1], Takayasu Suzuka[1], Takuya Kotani[1], Tohru Takeuchi[1]
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Conflict of interest: None

[Objective] To evaluate the glucocorticoid (GC) reduction and treatment optimization of Mepolizumab (MEPO) in Eosinophilic Granulomatosis with Polyangiitis (EGPA). [Methods] Consecutive EGPA cases treated at our hospital and Yodogawa Christian Hospital were included. The use of MEPO, clinical data were evaluated. [Results] A total of 64 cases of EGPA were analyzed with a mean age of 61 years at onset. The median BVAS at onset was 14, and ANCA was positive in 22 cases, with a median ANCA of 138.5 U/mL. 26 cases used MEPO, and 38 cases did not. In the MEPO group, the amount of GC, immunosuppressant, were significantly less (p=0.007, p=0.044). Moreover, cases PSL≦4 mg, MEPO was significantly higher (p=0.047), suggesting a long-term GC reduction effect. MEPO use within 6 months after treatment initiation was observed in about 10%, and showed a trend toward early reduction of eosinophil counts and a reduction in total GC dosage. In the MEPO group, BVAS was 16 and the ANCA positivity rate was 10 cases. Regardless of disease activity or ANCA, there were few relapses, dropouts, or adverse events. [Conclusions] MEPO treatment for EGPA demonstrated a GC reduction effect and tolerability even when introduced at an earlier stage and was effective even in severe conditions.

# English Poster Session

## EP1-01

**Carpal collapse in Patients with Early Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] We hypothesized that early aggressive treatment of patients with early Rheumatoid Arthritis (RA) improved the outcome of carpal collapse over the past decade. We previously reported a 2-year follow-up of carpal height ratio (CHR) in patients with early RA. In this study, we report the results of a longer-term observation. The purpose of this study is to investigate the change in CHR 7 years after the initial visit in patients with early RA who developed and started treatment in 2009 and 2014. [Methods] CHR was measured by radiographs of both hands at the initial visit and 7 years later. [Results] Nineteen patients (17 females) were included in this study. The mean age at the initial visit was 55 years. The mean left CHR changed from 0.549 to 0.539 in the 2009 group and from 0.564 to 0.556 in the 2014 group. The mean right CHR changed from 0.516 to 0.511 in the 2009 group and from 0.536 to 0.523 in the 2014 group. The change in bilateral CHR was not significantly different between the two groups. There was no significant difference in DAS28-CRP between the initial visit and 7 years later for both groups. There were no significant differences in the rates or doses of MTX use in each year. The use of bDMARDs was 3 cases in 2009 and 1 case in 2014. [Conclusions] In this study, there was no significant difference in the amount of change in CHR between RA patients who started treatment in 2009 and 2014, however, both groups had a slight progression of carpal collapse after 7 years.

## EP1-02

**Unraveling the progress of immunotherapy for rheumatoid arthritis through a bibliometric analysis**

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Conflict of interest: None

[Objective] The field of immunotherapy for rheumatoid arthritis (RA) is vibrant and fast-growing, with a broad spectrum of biological and small molecule medicines that are tailored to target distinct immune components. Through the lens of bibliometric analysis, this study aimed to uncover the evolution, research trends, geographical distribution, and emerging themes in RA immunotherapy. [Methods] The research utilized comprehensive bibliometric methodologies. A detailed search was conducted in the Scopus database using the related keywords of "immunotherapy" and "rheumatoid arthritis". The search retrieved all scholarly publications published throughout the timeframe of 2000 to 2023. The co-authorship and co-occurrence analyses were conducted using VOSviewer software version 1.6.19. [Results] A comprehensive search of the Scopus database retrieved a total of 3,102 scholarly articles related to RA immunotherapy within the time frame of 2000 to 2023. According to an analysis of the geographical distribution of research output, the United States, the United Kingdom, China, Germany, and France emerged as the most prominent countries in the field of RA immunotherapy research. Co-occurrence analysis revealed that the primary topics that garnered significant attention encompassed "immune checkpoint inhibitors", "immune-related adverse events", "regulatory T cells", and some frequently studied drugs such as rituximab, infliximab, adalimumab, and tocilizumab. These themes reflected the various approaches conducted by researchers to improve the effectiveness of RA immunotherapy. [Conclusions] In conclusion, this study provides a full picture of the current state of RA immunotherapy studies. Through the analysis of research patterns, this study establishes a fundamental basis for prospective research avenues and contributes to the advancement of knowledge and the development of strategies to improve our understanding of immunotherapy for RA.

## EP1-03

**Implant preservation by using CLAP for postoperative infection after revision elbow arthroplasty in a patient with rheumatoid arthritis; a case report**

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Conflict of interest: None

Purpose: We report a patient with rheumatoid arthritis in which implant preservation was possible with debridement, antibiotics, and implant retention (DAIR) combined with continuous local antibiotic perfusion (CLAP). Case: A patient was 69 years old and female. Her duration of RA was 29 years. She had received primary TEA 15 years before revision. Two years after revision TEA, PJI was observed with swelling, pain, and redness in the left elbow. Because of acute onset and no finding of implant loosening, DAIR with CLAP with Gentamicin was performed as an emergency surgery. Postoperatively, the patient was treated with CLAP and systemic administration of Cefotiam and Minocycline. A small amount of MSSA was detected in intraoperative tissue culture. CLAP was terminated on day 18. Minocycline and Clindamycin were continued for chronic suppression of antibiotics. After removal of CLAP, no relapse was observed. At the last observation, her left elbow kept a similar ROM compared to preoperatively. Conclusion: Local administration and reflux of a high concentration of Gentamicin could destroy the biofilm formed on the implant and prevent infection in our case. CLAP with DIAR may be an effective treatment method for implant preservation in even PJI of TEA.

## EP1-04

**Sero-conversion of anti-cyclic citrullinated peptide antibody during the course of disease in a patient with rheumatoid arthritis; a case report**

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Conflict of interest: None

[Background] We report a patient who revealed positive-seroconversion of anti-cyclic citrullinated peptide antibody (ACPA) along with worsening of her symptoms of rheumatoid arthritis (RA). [Case Report] 54-years-old, female. She felt neck pain four years ago. After that, she was referred to our hospital because of left index finger MP joint pain and high fever. Blood tests at the time of her first visit to our hospital showed ACPA 2.9 U/ml, Rheumatoid factor (RF) 20 IU/ml, antinuclear antibody (ANA) 1: 40, erythrocyte sedimentation ratio (ESR) 33.0 mm/h, C-reactive protein (CRP) 0.32 mg/dl, DAS28CRP4 2.03. We diagnosed her as seronegative RA because ACR/EULAR classification criteria 2010 score was 6 points, followed by initial treatment with salazosulfapyridine. Later, she transferred to another hospital due to relocation. she was withdrawn from the treatment and follow-up due to palliation of the symptom, although ACPA became 18.8 U/ml. After six years, she was referred back to our clinic because her joint symptoms worsened, and the evaluation showed DAS28CRP4 4.67, ACPA 100.8 U/ml, RF 214 IU/ml, ESR 39.0 mm, CRP 0.20 mg/dl, and MMP3 34.8 ng/ml., ACPA titers increased to positive and enhanced inflammatory response. Methotrexate, prednisolone and tocilizumab were applied for her treatment. X-rays at the last observation of both hands and feet showed no joint destruction. [Conclusion] We experienced a patient who revealed seroconversion of ACPA during the course of the disease. In this case, we thought to have been preceded by physical symptoms of RA and later became positive for ACPA. It suggests even if ACPA is negative, it is important to diagnose early RA based on physical examination, blood and biochemical tests as well as imaging, and to initiate treatment to suppress joint destruction caused by RA.

## EP1-05

**A Case report of high tibial osteotomy for a patient with Rheumatoid arthritis patients treated with csDMARDs**

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Conflict of interest: None

[Objective] High tibial osteotomy (HTO) procedure is widely used for osteoarthritis (OA) of the knee, but is generally contraindicated in rheumatoid arthritis (RA) patients. We report a case of RA patients who well controlled by csDMARDs underwent HTO. [Case] A 41-year-old woman visited our hospital with a chief complaint of right knee pain and instability. She underwent anterior cruciate ligament reconstruction at 35 year-old and developed RA at 40 year-old. She was treated csDMARDs. Her right knee showed slightly loss of flexion angle and slight instability. There was no pain and swelling joint other than right knee. Lysholm knee score was 71 points and an average of Knee Injury and Osteoarthritis Outcome Score (KOOS) was 57.7 points. Disease activity at DAS 28 ESR was low. X-ray showed mild medial OA rather than RA and femorotibial angle (FTA) was 180 degrees. MRI showed malposition of reconstructed ACL remnants, medial meniscus (MM) extrusion and medial OA. She underwent centralization of MM and opening wedge HTO. FTA changed from 180 degrees to 171 degrees. After the surgery, she took csDMARDs continuously. After HTO, she underwent arthroscopic examination and removal implants at 14 months postoperatively. Arthroscopically there was no progression of OA and remarkable synovitis. There was no major complication for example deep infection, venous thrombosis. There were no symptoms related to RA. She felt slightly pain and instability at 3 years after HTO. Lysholm knee score is improve to 90 points and average KOOS is improved 85.3 points. There are no symptoms related RA and dose of csDMARDs is reduced. There was no progression of OA and RA in X-ray at the final follow-up. [Conclusions] We think that if RA is well controlled with medication, HTO is one option for patients with OA and RA.

## EP1-06

**Effect of tocilizumab therapy on lipid levels in patients with rheumatoid arthritis: a meta-analysis**

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Conflict of interest: None

**Objective:** To assess tocilizumab and its effect on cardiovascular risk factors, specifically an increase in core lipid levels (total cholesterol, LDL, HDL), and its risk for atherogenic events among rheumatoid arthritis patients. **Methodology:** A meta-analysis was done to determine the side effect of tocilizumab therapy in increasing lipid levels in patients with rheumatoid arthritis. Four studies were appraised and included in the study. The meta-analysis was performed according to the recommendations of the Cochrane Collaboration, and the findings are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. **Results:** This study evaluated the efficacy of tocilizumab therapy in the lipid levels of patients with rheumatoid arthritis. In this systematic review and meta-analysis, four studies met the inclusion criteria and were included in the final analysis and appraisal. This meta-analysis determined that tocilizumab therapy is less efficacious than placebo in total cholesterol and LDL levels in rheumatoid arthritis patients on tocilizumab therapy in comparison to placebo (MD: 13.40 [95% CI: -4.65, 31.44]), (MD: 13.02 [95% CI: -1.62, 27.65]). However, tocilizumab was more efficacious in HDL levels (MD 4.89 [95% CI: -2.20, 11.98]). Additionally, tocilizumab was associated with a three-fold increase in cardiovascular event risk. **Conclusion:** The results of this meta-analysis determined that tocilizumab therapy had no effect in altering lipid level and had no effect in increasing cardiovascular risk in rheumatoid arthritis patients.

## EP1-07

**Positive Correlation between Serum Alkaline Phosphatase (ALP) and the Severity of Rheumatoid Arthritis (RA) in Advanced Medical and Dental Institute (AMDI)**

Mohamed Shafi S Mahboob Ali
Advanced Medical and Dental Institute (AMDI), Malaysia

Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease affecting the joints with varying severity. Risk factors include age, sex, genetics, and environment. RA causes permanent joint damage, rheumatoid vasculitis, and Felty syndrome. The treatment goals are to reduce the pain and stop further damage. The peak incidence is between ages 35 and 50 years. Women are more affected than men. Alkaline phosphatases (ALP) are a group of isoenzymes located on the outer layer of the cell membrane and catalyze the hydrolysis of organic phosphate esters in the extracellular space. Many studies have proven the link between increased ALP levels and RA severity. [Methods] The study aims to prove the correlation between raised ALP and the severity of RA.120 patients diagnosed with RA based on the ACR/EULAR 2010 RA classification were taken in their fasting blood and stored in the lab at 2-8 degrees. Their sera were extracted and subjected to spectrophotometry using the Thermo Scientific Multiskan SkyHigh apparatus. The data were entered into an Excel spreadsheet, and the result calculation was done. Data were analysed using SPSS version 27, and the 'P' value of >0.005 was considered statistically significant. [Results] The ALP values were significant (P=0.005) in the severe grade of RA with a mean value of 224.2 +/- 80.4 IU/L. The higher the ALP value, the higher the ARA score and the severity of the disease. The mean age of our subjects was 62 years old. Kruskall Wallis test was applied as we also measured the level of CRP. Other related variables with RA were described using the ANOVA test. [Conclusions] There is a positive correlation between raised levels of IL-6 and the severity of RA. Drugs that block the activity of IL-6 should be explored to find the potential cure for this debilitating disease.

## EP1-08

**Rheumatoid Arthritis -Undergraduate teaching experience from a tertiary care centre rheumatology clinic in Peshawar, Pakistan**

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Conflict of interest: None

**Objective** To evaluate medical student feedback following a stuctured rheumatology clinical rotation. **Methods** The students of 4th year MBBS at Northwest School of Medicine attend the outpatient rheumatology clinic for their clinical rotation. During the rotation students get an opportunity to take musculoskeletal history, learn examination using the GALS (Gait, arms, legs and spine) technique as well as learn common medications used in rheumatology. In addition students attend physiotherapy unit to get awareness about its utility in musculoskeletal conditions. At the end of the rotation students complete an open text feedback form. **Results** During the session 2023,50 students provided feedback as follows with regards to their learning experience: 1. Learnt history taking: 20 2. Learnt common drugs: 20 3. GALS (Gait, Arms, Leg, Spine) examination: 7 4. Common conditions: 6 5. Physiotherapy: 5 6. Classification of arthritis and its management: 5 7. Difference between rheumatology and orthopedics: 3 8. Learnt patient interaction: 3 9. Comfortable environment: 1 10. Learnt clinical skills: 1 11. Awareness of investigations: 1 **Conclusions** With limited number of rheumatologists and the growing burden of musculoskeletal diseases, undergraduate clinical rheumatology teaching can help in early diagnosis of patients in particular rheumatoid arthritis. Further teaching opportunities in the clinic can help improve student learning experience. In the future innovation in clinical teaching needs to be considered to enhance the learning experience of medical students.

## EP2-01

**A case of bilateral hip arthritis with osteoarthritis following treatment with immune checkpoint inhibitors**

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Conflict of interest: None

We report a case of bilateral hip osteoarthritis following treatment with nivolumab due to malignant vaginal melanoma in a 56-year-old woman. She was diagnosed as bilateral developmental hip dysplasia in childhood and underwent right hip osteotomy at age 19. At age 53, she developed malignant vaginal melanoma and was treated with nivolumab for two years beginning from age 54. At age 55, she was referred to us because of worsening bilateral hip pain. At the time of her initial examination, she had multiple joint pains. Blood biochemistry indicated an elevated inflammatory response, however, anti-CCP antibodies were negative. PET-CT after nivolumab treatment showed uptake in both hip joints. Due to worsening pain in both osteoarthritic hip joints, she underwent left THA in July at age 56, followed by right THA in October. Synovial tissue pathology showed lymphocyte aggregation and synovial hyperplasia, with positive immunostaining for CD68, TNF-α, IL-6, PD-1, and PD-L1. The patient had a good postoperative course, with the improvement of her polyarthralgia. The development of musculoskeletal symptoms after the administration of immune checkpoint inhibitors after THA is increasingly well known. In this case, the patient presented with polyarthritis following the immune checkpoint inhibitor therapy, suggesting an immune-mediated adverse effect.

## EP2-02

**Smoking, the silent killer of the bones too?**

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Conflict of interest: None

[Objective] we present the case of an 76 years female patient, diagnosed with postmenopausal osteoporosis (T score lumber spine -3.1), for which, in 2019, treatment is initiated with Vitamin D 2000 IU and 1,200 mg of calcium daily. She is also known with high blood pressure, schemic heart disease, aortic atherosclerosis, chronic bronchitis due to smoking (10-15 cigarettes per day for about 50 years). [Methods] after 1 year, in January 2020, she repeats DXA exam that shows the progression of the T score in the lumbar spine (-3.4) and osteopenia at the hips (mean T score -1). In this context, in association with Vitamin D/Calcium we add risedronic acid 35 mg/weekly. Also, the patient is encouraged to perform daily physical activity within tolerance and quit smoking. [Results] in February 2021, the patient presented for re-evaluation, complaining of pain in the thoracic spine. At the physical examination we note kyphosis, and x-rays of the spine shows thoracic vertebral fractures. The DXA exam indicates a T score progression (-3.6 vs -3.4) compared to the last 1 year assessment. The FRAX score is also achieved: 10 years probability of fractures 8.8% for major osteoporotic fracture and 1.9% for hip fracture. Calcium and vitamin D are dosed with normal values. We add to the basic treatment for osteoporosis Denosumab 60 mg subcutaneously at 6 months. Several laboratory investigations are also being performed to rule out the secondary cause of osteoporosis as thyroid function tests, cortisol levels, parathormone, glycated hemoglobin-normal values, no inflammatory tests present. The evaluation from February 2022, we find again the progression of the T score (-4). The patient tells us that due to the psychological stress of the last year, the number of cigarettes smoked daily has been increased to 20. [Conclusions] given the progression of T-score values, in terms of identifying a secondary cause of osteoporosis, is smoking the real candidate for progression of osteoporosis?

## EP2-03

**Onset of SLE with spontaneous pneumothorax and subcutaneous emphysema after recent Covid-19**

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Conflict of interest: None

[Background] There are only a few known cases of the onset of SLE with spontaneous pneumothorax and subcutaneous emphysema. We describe the onset of SLE with pulmonary involvement during active Covid-19. [Case Report] An 18-year-old man consumed up to 1 liter of energy drinks per day for one year. He was hospitalized with severe anemia, splenomegaly, T 38C, shortness of breath during exercise, cough with mucous sputum, decreased appetite, general severe weakness, dizziness and headache. Severe subtotal polysegmental pneumonia was diagnosed as a result of Covid-19, which was treated with Remdesivir 100 mg No. 6, Glucocorticosteroids 250.0 mg No. 3 without much effect. Analyzes showed: proteinuria up to 26g/day, erythrocyturia 300Er/µl, hypoalbuminemia 24.14g/l, increased creatinine 189µmol/l, urea 26.9 mmol/l, lactate dehydrogenase 1105U/l, CRP 280 mg/l, decrease in absolute lymphocytes 0.35x109/l. The condition was complicated by the appearance of spontaneous pneumothorax, subcutaneous emphysema, severe dyspnea at rest, a decrease in saturation to 50%, and polyserositis. Immunotests confirmed SLE: positive antibodies to ANF, dsDNA, Sm, decreased complement components C3 and C4. His treatment had a positive effect: hemodialysis with ultrafiltration, GCS, IVIG, Cyclophosphamide, transfusion of erythrocyte suspension. The patient was discharged with improvement for further treatment at home. [Conclusion] The reasons for the activation of a systemic autoimmune disease after Covid-19 are still not known, but recent studies have shown that in severe cases of Covid-19, B cells are activated, which secrete a large number of antibodies involved in the autoimmune process. In our case, Covid-19 could provoke latent SLE, which debuted with spontaneous pneumothorax, subcutaneous emphysema and lupus nephritis. Despite the severe course of Covid-19, timely pathogenetic therapy of SLE contributed to the relief of symptoms and improvement of the patient’s condition.

## EP2-04

**Severe COVID-19 in a lupus patient presenting with lupus enterocolitis and decompensated liver failure: a case report**

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Conflict of interest: None

**Introduction**: Systemic lupus erythematosus is a multi-systemic autoimmune disease with extremely variable and heterogeneous clinical presentation. Liver cirrhosis and liver failure are extremely rare in patients with SLE accounting to about 1-2%. There is paucity of information about the treatment of SARS-CoV-2 in a patient with autoimmune disease and liver cirrhosis. In this paper we present the successful management of an SLE patient initially presenting with gastrointestinal symptoms and pancytopenia who later developed pneumonia and COVID-19. **Case**: A 26-year-old Filipino female presenting with a 5-month history of watery diarrhea, joint paints, and generalized body weakness. She had seizures during admission. Laboratory data indicated pancytopenia, RTPCR revealed positive results. Whole abdominal CT scan revealed cirrhosis, splenomegaly, dilated portal vein with porto-venous collateral formation and moderate ascites. Upper and lower gastrointestinal endoscopy revealed esophageal varices, portal gastropathy, antral gastritis, duodenitis, non-specific colitis, small rectal varices and internal hemorrhoids. She was started on methylprednisolone pulse therapy 1g for 3 days, IV Ig, hydroxychloroquine, spironolactone, cyclophosphamide infusion. She was eventually weaned off oxygen support with resolution of diarrhea and partial improvement on blood parameters. The patient’s treatment of RRT and cyclophosphamide infusions continued as outpatient. **Conclusion**: Cirrhosis which is a rare and severe manifestation of SLE has a poor prognosis. Management starts with an in-depth understanding of disease-specific complications and associated comorbidities. Those patients with hematological system involvement and impaired liver function should be closely monitored and timely management should be initiated.

## EP2-05

**A case of juvenile systemic lupus erythematosus with thrombotic thrombocytopenic purpura: Successful management with caplacizumab and rituximab**

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Conflict of interest: None

[Objective] Acquired thrombotic thrombocytopenic purpura (aTTP) is a life-threatening condition caused by inhibitory autoantibodies targeting ADAMTS13. Plasma exchange (PE) and immunosuppressive agents are available for its treatment. Caplacizumab reduces the need for PE and transfusions but does not inhibit inhibitor production. In contrast, rituximab is effective against autoimmune diseases but lacks guidelines for use in pediatric aTTP with underlying conditions. [Case] We present the case of a 14-year-old girl with systemic lupus erythematosus (SLE)-TTP who was treated with caplacizumab and rituximab, in addition to concurrent PE and immunosuppressive therapy during the acute phase. She had a history of headaches and nausea and was diagnosed with SLE based on laboratory results. After a renal biopsy, she experienced seizures and altered consciousness, accompanied by low platelet counts. ADAMTS13 activity was undetectable, and inhibitor levels were elevated. Emergency treatment included catheter therapy, PE, and immediate initiation of methylprednisolone pulse therapy. Caplacizumab was also started three days after the onset of TTP. The patient showed gradual improvement with the administration of hydroxychloroquine, mycophenolate mofetil, and caplacizumab. Although her platelet counts initially increased, they later decreased, prompting the initiation of rituximab treatment. After two months of rituximab treatment, inhibitors were undetectable, and ADAMTS13 activity exceeded 10%, leading to the discontinuation of caplacizumab. Subsequently, the patient demonstrated sustained improvement without inhibitor recurrence and returned to her normal life. [Conclusions] SLE-TTP carries a 10% mortality rate, underscoring the importance of early and comprehensive treatment. Further research is needed to determine the optimal timing and indications for the use of caplacizumab and rituximab in pediatric SLE-TTP. This case illustrates their benefits in managing this condition.

## EP2-06

**Lupus in a patient with ankylosing spondylitis and vitiligo: a case report**

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Conflict of interest: None

**Introduction** Co-existence of lupus, AS, and vitiligo is rare. Each have distinct features and pathogenesis. This syndrome may be due to a rare genetic combination or an adverse drug effect. Data is very limited on this condition and found in only in case reports. Prognosis is uncertain. We report a case of ankylosing spondylitis who developed atypical features of lupus. **Case** A 30yo male consulted due to fever. He is diagnosed with AS and vitiligo for a decade. He was previously on etanercept and methotrexate, followed by short-term secukinumab, then infliximab. 8 months ago, he had febrile episodes for a month. Infection work-up was negative, CT scan showed splenomegaly; multiple axillary, abdominal, and inguinal lymphadenopathies (LAD). Biopsy showed reactive follicular hyperplasia. A month ago, he was apparently well, but tests showed leukopenia, thrombocytopenia, and transaminitis. Resolution of the latter two findings were noted on follow-up. Few hours prior to admission, he presented with seizures. PE showed hypopigmented lesions. Lymphadenopathies, oral ulcers, or synovitis were absent. Tests still showed leukopenia. Repeat CT scan revealed hepatosplenomegaly with stationary LAD. No acute infarcts or focal mass seen on MRI. BMA, infection work-up were negative. Due to the multiorgan involvement, immunopanel was requested revealing positive ANA-IF, elevated anti-dsDNA, low C3. Prednisone 1mkd, HCQ, and levetiracetam were started. Symptoms resolved. On follow-up, there was no recurrence of fever and leukopenia. **Conclusion** Occurrence of lupus with AS and vitiligo may be multifactorial: genetics, use of anti-TNFi. Establishing a diagnosis of SLE is challenging, especially with uncommon initialfeatures such as LAD, splenomegaly. Work up is necessary to rule out infection, malignancy, and other autoimmune diseases. Larger studies are needed to fully describe the epidemiology, natural disease course, risk factors, and prognosis surrounding this rare overlap syndrome.

## EP2-07

**Chronic Tophaceous Gout in a Young Adult Female with Genetic Variants of Uncertain Significance: A Case Report**

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Conflict of interest: Yes

**Objective** We report a case of a 31-year-old young adult Filipino female diagnosed with chronic tophaceous gout at the age of 20 but has hypersensitivity reactions to both Allopurinol and Febuxostat. **Methods/Results** Serial monitoring of serum uric acid since eleven years ago ranges from 9 to 11 mg/dL, with normal creatinine, liver function and thyroid function tests. At present physical examination showed multiple tophi on multiple areas such as feet, knees and hands and with limitation of motion. Determination for the cause of early-onset chronic hyperuricemia showed fractional excretion of uric acid was 3.78% with random uric acid and creatinine ratio of 0.42, compatible with underexcretion of uric acid. Ultrasound of kidney, ureter and bladder were unremarkable. Consideration then was a possible Familial juvenile gouty nephropathy probably from a rare autosomal dominant genetic condition. Patient then underwent Invitae expanded renal disease panel which evaluated 401 genes for variants that are associated with genetic disorders. The four genes of interest - UMOD, REN, HFN1B and SEC61A1 - were normal. However, four variants of uncertain significance were identified: ITGB4, STX16, SYNPO and WNK1. At present, the presence of these four variants with uncertain significance still need to be explored. **Conclusion** This case is rare and unusual in several ways. The onset of gout occurred early in a young adult female. Genetic work up for primary hyperuricemia secondary to underexcretion is also unknown and rarely done in the Philippines. This case revealed the presence of four genetic variants of uncertain significance which later need to be explored. Lastly, treatment is challenging due to hypersensitivity to both Allopurinol and Febuxostat which are the only urate-lowering agents in the Philippines. Desensitization to Allopurinol or Febuxostat and genetic counselling are highly recommended.

## EP2-08

**Persistent and chronic diarrhea as an initial manifestation of lupus in Filipino females: a case series**

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Conflict of interest: None

**Introduction** Prevalence of lupus GI manifestation ranges from 4-18% in Asia. Diarrhea is a rare initial lupus presentation. It can be due to enterocolitis, protein-losing enteropathy, or pancreatitis. There is limited literature on this condition, but overall prognosis is good. We report 3 cases of SLE initially presenting with acute and chronic diarrhea. **Case** Case 1 is a 19yo female with chronic diarrhea and progressive edema. Tests showed anemia, thrombocytopenia, hypoalbuminemia. Ultrasound revealed ascites. Endoscopy showed severe pancolitis. Biopsy exhibited chronic non-specific ileitis, lymphoid aggregates & chronic non-specific proctitis. Case 2 is a 26yo female with chronic diarrhea, arthritis. She had seizures during admission. Tests showed pancytopenia, nephrotic range proteinuria, elevated creatinine. CT scan revealed cirrhosis, splenomegaly, portal hypertension. Endoscopy showed esophageal varices, portal gastropathy, non-specific colitis, small rectal varices. Case 3 is a 30yo female with persistent diarrhea, decreased urine output, anasarca. Tests displayed anemia, elevated creatinine, nephrotic range proteinuria, and hypoalbuminemia. 2DE showed a low EF. All had positive ANA, elevated anti-dsDNA, low serum C3. Diagnosis of SLE was made. Case 1 presented with protein losing enteropathy, bicytopenia while Case 2 & 3 had enterocolitis

with life-threatening organ involvements like pancytopenia, nephritis, neuropsychiatric lupus, cirrhosis, myocarditis. All were given MPPT 1g for 3 days and hydroxychloroquine was started. Case 2 & 3 underwent hemodialysis then IV cyclophosphamide. Symptoms gradually resolved. Case 1 was lost to follow-up. Case 2 & 3 continue RRT and IV cyclophosphamide as outpatient. **Conclusion** Diagnosis of SLE is challenging in those who present with diarrhea, and in the absence of typical lupus symptoms. SLE should be included in the differential diagnosis in young female with persistent diarrhea. Timely diagnosis is critical for appropriate management.

## EP2-09

**Covid Infection In A Young Boy On Immunosuppression For The First Presentation Of Cerebral Lupus: A Management Challenge**

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Conflict of interest: None

A 19-year-old previously healthy male presented with low grade fever for 2 months with myalgia, oral and palatal ulcers. He had a history of recurrent abdominal pain for 3 months leading to an apparent weight loss of 6 kg and hair loss for 6 months. There was bilateral lower limb swelling with periorbital swelling for 3 weeks and recent onset focal fits with secondary generalization and change in sensorium. On examination he had palatal ulcers with hemorrhagic mucositis and evidence of non-scarring alopecia. There was lower extremity edema with periorbital swelling and inguinal lymphadenopathy. He was hemodynamically stable, but had fluctuating GCS without focal neurological signs. His initial investigations revealed, pancytopenia with normal inflammatory markers, creatinine, marginally high serum amylase and liver enzymes. and subnephrotic range proteinurea without active sediments. Both kidneys were normal in size and echogenecity. His MRI brain and the NCCT brain revealed cerebral atrophy. Patient had a normal 2D Echo. Bone marrow showed early bone marrow hypoplasia. Upon clinical disease progression and the biochemical evaluation, the potential of SLE with cerebral involvement was taken into consideration. He had markedly reduced C3 and C4 levels with highly positive ANA with nuclear pattern. ANCA and APLS screening were negative. In the mean time he was tested positive for covid infection. However, considering the higher possibility of SLE with cerebral involvement, early aggressive treatment with IV methyl Prednisolone and IV Cyclophosphamide were commenced and the patient achieved a remarkable clinical and biochemical response. The effect of COVID-19 infection varies greatly based on gender, age, and ethnicity. However, certain patient populations are especially at high risk. As a result, it is pertinent and crucial to evaluate the effects of COVID-19 and use patient-specific features to inform treatment decisions in order to reduce mortality and morbidity.

## EP2-10

**The Correlation Between Interleukin-6 (IL-6) And The Development Of Systemic Lupus Erythematosus (SLE) In Advanced Medical and Dental Institute (AMDI)**

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Conflict of interest: None

[Objective] Interleukin-6 (IL-6) is a Pro-Inflammatory cytokine with many biological activities. IL-6 is mainly involved in immunity and inflammatory processes. It induces the terminal differentiation of B lymphocytes into antibody-forming cells and the differentiation of T cells into effector cells. Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by antibodies to nuclear and cytoplasmic antigens, multisystem inflammation, protean clinical manifestations, and relapsing course. We designed a study to establish the correlation between IL-6 and the severity of the SLE [Methods] About 52 SLE-diagnosed patients were recruited based on the 1997 Updated American College of Rheumatology Revised Criteria for Classification of SLE in our centre. Their venous blood was taken and centrifuged at 4500RPM for about 5 minutes, and the serum was collected. ELISA test was done on these sera, and the data obtained was recorded in the form of a scatter plot and statistics, in which any 'P' value of >0.05 was significant. The severity of the subject's SLE was quantified using the BILAG Index. The index allocates alphabetic scores to each of the ten organ-based systems, and then a total score is calculated. [Results] We found a direct correlation between the level of IL-6 (statistically significant P=0.005) and the severity of the SLE. The IL-6 mean value was taken as 132.6pg/ml, while a linear scatter plot was obtained. Pearson correlation coefficient showed a linear correlation between the two variables. Thus, the higher the IL-6 levels, the higher the BILAG score. [Conclusions] Serum IL-6 levels can be used to screen, diagnose, and act as a prognostic factor in the development and progression of SLE. These findings may open the opportunity for a new horizon in the early detection and treatment of SLE patients, which will greatly implicate the disease's complications and the cost of treating it.

## EP2-11

**The great masquerador presenting as unilateral sacroilitis: a case report**

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Conflict of interest: None

**Background** Tuberculosis (TB) is one of the commonest infectious diseases which has a range of presentations. Out of its range of presentations, musculoskeletal TB is the third most common site of extrapulmonary TB after pleural and lymphatic disease. The absence of concomitant lung disease may lead to delayed diagnosis of TB related musculoskeletal manifestations unless there is a high degree of clinical suspicion. **Case** A 43 year old male, presented with left sided low back pain of one year duration, along with significant morning stiffness. There were no evidence of other articular or extra-articular manifestations and his clinical examination was unremarkable. Investigations revealed normocytic anaemia with elevated APRs, positive Tuberculin test (13 mm) and negative HLA B27. Chest X-ray and abdominal US scan was normal. MRI of the sacroiliac (SI) joints revealed a focal area of contrast enhancement with joint effusion in left SI joint suggestive of infectious sacroiliitis. The patient was commenced on conventional 4 drug anti TB treatment. After 1 month of treatment patient presented with unilateral painful knee joint swelling with restricted joint movements. The joint fluid analysis favours the evidence of crystal arthropathy with raised serum uric acid levels. This was attributed for the Pyrazinamide, hence it was replaced with Levofloxacillin for the conventional treatment. Symptomatic treatment with Allopurinol was commenced for Gout, although switching to Febuxostat required due to adverse effects of Allopurinol. Our patient showed clinical improvement and complete radiographic resolution of sacroilitis after the completion of anti TB therapy. **Conclusions** Higher degree of clinical suspicion is required on patients presenting with sacroilitis as the delay in diagnosis may lead to increased risk of deformity. Prompt identification and treatment of TB scaroilitis has promising outcomes.

## EP2-12

**A case of late onset and rapid progression of Granulomatosis with Polyangiitis**

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Conflict of interest: None

[Background] We present a case of late onset of granulomatosis with polyangiitis (GPA), where the patient underwent massive antibiotic therapy before the development of the classic triad of symptoms: inflammation of the ENT organs, changes on CT of the chest and nephritis, as well as an urticarial erythematous-papular rash on skin. [Case Report] 60 y.o. female was treated with 13 different type of antibiotics for 2 months without any effect due to the nonspecific complaints for shortness of breath, dry cough, hearing loss in the right ear, fever up to 39C, general muscle pain, loss of appetite and general weakness. Chest CT found multifocal lesions of both lungs, polysegmentalpneumonia and brain MRI: signs of microangiopathy, right-sided mastoiditis. Despite intensive antibiotic therapy, the pa-

tient retained T 39C of a non infectious nature, as she had moderate anemia, elevated procalcitonin, ESR, CRP and thrombocytosis. On the 33-35th day of hospitalization patient had pain in the calf muscles, very painful erythematous papular rashes on the skin, aphthous stomatitis, otitis media and 3rd degree hearing loss of the right ear, ulcerative rhinitis with perforation of the septum, eustachitis, erythrocyturia, proteinuria, increased blood creatinine, and positive pANCA, c ANCA, MPO, PR3, ANF. She was treated with positive effect: pulse therapy Methylprednisolone with the transition to GCS per os, Cyclophosphamide (CP) and Rituximab. [Conclusion] It is noteworthy that the debut occurred in old age. Due to poor data at the onset of the disease, the initial consultation of a rheumatologist was late. Also, the symptoms rapidly began to increase within 3 days with the involvement of the central nervous system, kidneys and skin. High doses of GCS, CP and Rituximab stopped the disease activity and helped to stabilize the patient's condition.

## EP2-13

**Overlap Syndrome presenting as Recurrent Guillan-Barre Syndrome in an Adult Female: A Case Report**

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Conflict of interest: Yes

Introduction: We aim to highlight a case of Overlap Syndrome - Mixed Connective Tissue Disease (Systemic Sclerosis, mRSS 18, Systemic Lupus Erythematosus, Pre-Clinical Rheumatoid Arthritis, with features of Myositis), a severe systemic inflammatory syndrome, presenting as dysphagia in an adult female with history of Guillian-Barre Syndrome. Case Report: We present the case of a 34 year old female, recently treated for Guillian-Barre Syndrome with intravenous immunoglobulin infusion, with history of recurrent hypokalemia, initially presenting with progressive dysphagia, shortness of breath and generalized muscle weakness. She was noted to have thick skin on the chest, both forearms, abdomen, superior femoral area and both legs with sclerodactyly on both hands and feet and hyperpigmentation of the volar aspect of her hands and feet. Patient had a diffuse cytoplasmic pattern ANA 1:160 with low C3 and C4. Highly elevated Anti-dsDNA was observed at 447.5. On Electromyography and Nerve Conduction Studies of all extremities, electrophysiologic changes consistent with a diffuse distal and proximal symmetric generalized sensory-motor polyradiculoneuropathy were observed. Patient was given three days of Methylprednisone Pulse Therapy with marked improvement of symptoms after each day of infusion. Conclusion: Our study shows that Overlap Syndrome - Mixed Connective Tissue Disease may present as neurologic disorders. Prompt recognition of rheumatologic illness is needed to start treatment and avoid complications of the disease.

## EP2-14

**An inconceivable coalesce: A rare case of Hepatocellular carcinoma with polymyositis**

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Conflict of interest: None

**Introduction** Polymyositis is one of rare diseases under inflammatory myopathies which are chronic in nature and causes muscle inflammation, pain and weakness that worsens over several weeks to months. Interestingly, the association of polymyositis and propensity to any type of malignancy is lesser than that of other myopathies such as dermatomyositis. The objective of this report is to present a case of a hepatocellular carcinoma in a patient with polymyositis. **Case** A 62-year-old female who is a known case of chronic hepatitis B infection with liver cirrhosis presents at the ER with intermittent quadrilateral proximal extremity weakness. Upon evaluation, CKMB, AFP and lipid profile revealed elevated results. HBT ultrasound and triphasic CT scan showed irregular heterogeneously enhancing mass. Furthermore, electrophysiologic studies showing a myopathic process which predominantly affects the proximal muscle of the four extremities were also established. A diagnosis of polymyositis was made. There were no apparent skin lesions that is essential in diagnosing dermatomyositis and it is rarely associated with hepatocellular carcinoma. Patient was eventually started with tenofovir and prednisone which showed significant improvement in her condition. She was improved discharged with noted decreased extremity weakness. Muscle biopsy was offered however patient was lost to follow up. **Conclusion** This case report elucidates the correlation between hepatocellular carcinoma and polymyositis. Profound understanding of diverse myopathies and their potential etiologies is a critical resource that significantly influences the approach to case management. The article highlights the significance of varied diagnostic methods.

## EP2-15

**The Effect of Interleukin-6 Blocking in Patients with Polymyalgia Rheumatica: A Retrospective Study**

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is an inflammatory disease which has pain and stiffness around the shoulder girdle and proximal hip and thigh, and usually occur elderly people. In the treatment of PMR, low-to-moderate dose of the glucocorticoid is very effective. However, long term use of the glucocorticoid induces many adverse events like a diabetes mellitus and osteoporosis. To prevent these adverse events, the use of a monoclonal antibody to interleukin-6 receptor (IL-6R) may be another option. The purpose of this study is to assess the effect of IL-6R on PMR in our clinical practice. [Methods] Consecutive patients with PMR in our hospital, who were included in our retrospective cohort, were reviewed between 2018 and 2022. A total of 65 patients with an average age of 72 years were enrolled. Following the diagnosis of PMR, all patients were prescribed the prednisolone at low-to-moderate dosage. Following the 4 to 6 weeks, if the symptoms and laboratory data found the difficulty to decrease the dosage of prednisolone, IL-6Rs (tocilizumab or sarilumab) were applied to those patients. The prednisolone dose at the initial time and latest follow-up was compared. [Results] The prednisolone dose at the last follow-up was lower (12.5 vs. 1.1 mg/day, $p<0.002$) and the prednisolone discontinuation rate was 55/65 (77%). [Conclusions] This study suggested that IL-6Rs have a steroid-sparing effect in PMR. IL-6Rs can be an option in the management of PMR. Further study would be needed the safety and long-term availability of this method.

## EP2-16

**Case series of patients with low back pain who have hypercalcaemia induced by malignant tumour of the lung**

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Conflict of interest: None

[Objective] To clarify the importance of the measurement of the value of serum calcium when elderly patients come to the hospital. [Methods] Two patients were shown here with low back pain who have hypercalcaemia induced by malignant tumour of the lung. [Results] (Case 1) 84 years-old male with low back pain because of the fracture of the 11th thoracic vertebra with honey-comb lung and pleural effusion. Serum calcium level was 14.4 mg/dl and became higher up to 16.3 mg/dl. He was treated by administration of calcitonin plus saline hydration but he died on the 6th day after administration. After his death, high level of parathyroid hormone-related protein (PTHrP) was informed (17.1pmol/l). (Case 2) 81 years-old male with low back pain with old thoracic fracture, which was determined by MR Imaging. Serum calcium level was 17.5 mg/dl and treated with calcitonin plus saline hydration. The small cell lung cancer was diagnosed because chest CT scan revealed large tumour and serum levels of neuron-specific enolase and ProGastrin-releasing peptide were elevated. But he died on the 9th day after administration. After his death, high level of PTHrP was revealed high (2.5pmol/l). [Conclusions] Hypercalcaemia induced by malignant tumour is the serious state which drive patients renal insufficiency, cardiac arrhythmias and death. Some elderly patients complain low back pain but have no complaints about signs and symptoms of hypercalcaemia. We must examine the value of serum calcium when elderly patients come to the hospital. Some patients have hyper-

calcaemia because of vitamin D toxicity or some because of the malignancy. In addition to calcitonin, intravevous bisphosphonate or subcutaneous denosumab could be considered to lower the serum calcium concentration.

## EP2-17

**Kienböck disease with a subchondral bone cyst of distal radius: a case report**

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Conflict of interest: None

[Objective] In the previous reports, there is little information regarding Kienböck disease with a subchondral bone cyst of distal radius. This study aimed to report a case of Kienböck disease with a subchondral bone cyst of distal radius. [Methods] A 45-year-old male presented to us complaining of right wrist pain while playing tennis for the past two years. He has no previous history of trauma. The active range of his right wrist motion was 0° in volar flexion and 40° in dorsal flexion. Tenderness on the site of the radiolunate joint was confirmed. A plain radiograph of his right wrist showed that the lunate was collapsed and separated, and a subchondral bone cyst at the distal radius was confirmed. He was diagnosed with Kienböck disease with Litchman classification stage IV. CT showed that the subchondral bone cyst (size: 10 mm x 10 mm) was at the dorsal side of the lunate fossa. MRI showed that the subchondral bone cyst had low signal intensity in T1-weighted images and high signal intensity in short-tau inversion recovery (STIR) images. After 9 months of conservative therapy, the patient subsequently had surgical treatment. Arthroscopic findings showed the proliferation of synovium in the radiocarpal joint and an unstable fragment of lunate. After synovectomy, an open dorsal incision at the distal radius was made, and monocortical bone harvested from the iliac crest was grafted into the subchondral bone cyst. A splint was applied for 3 weeks. The bone graft in the subchondral bone cyst was united, and the patient was allowed to return to play tennis at 3 months postoperatively. Nine months after the surgery, the patient played tennis without wrist pain, and the range of wrist motion was improved with 35° in volar flexion and 50° in dorsal flexion. A radiograph showed no further progression of the lunate collapse. [Conclusions] The patient was healed with wrist arthroscopic synovectomy and bone grafts for a subchondral bone cyst.

## EP2-18

**Early onset polymyalgia rheumatica at a age of 41 diagnosed with 18-fluorodeoxyglucose positron emission tomography and computed tomography**

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Conflict of interest: None

[Case] A 41-year old male was admitted to our hospital for fever of 38°C, morning stiffness, and myalgia in shoulders and thighs for a week. On admission serum CRP was elevated to 12 mg/dl with mild leukocytosis (9340/μl), while ANA, RF, and anti-CCP antibodies were all negative. $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography and computed tomography (PET/CT) revealed accumulation of $^{18}$F-FDG in both shoulder and hip joints, and lumbar interspinous bursae, consistent with typical findings of polymyalgia rheumatica (PMR). Based on the symptoms and these findings, the diagnosis of PMR was made according to some older criteria including the Bird/Wood criteria (Ann Rheum Dis 1979;38:434-9.). As there was also a prominent $^{18}$F-FDG uptake in pancreatic head besides aforementioned region, the area was intensively examined, but no pancreatic tumor had been found. With 20 mg of prednisolone, all symptoms promptly disappeared and CRP became negative, supporting the diagnosis of PMR. Over the next 2 years, prednisone was tapered and discontinued, and the patient remained healthy without pancreatic abnormality. [Discussion] We presented a singular case of PMR with onset at a young age, early 40s. The diagnosis of PMR was established by some superannuated criteria and $^{18}$F-FDG PET/CT findings. As the newest widely used diagnostic criteria, 2012 EULAR/ACR (Ann Rheum Dis. 2012;71:484-92.) include a required criterion: “age 50 years or older”, PMR is considered extremely rare in people under the age of 50. The clinical significance of this case is that it showed that PMR can occur even before the age of 50 years and that $^{18}$F-FDG PET/CT is useful not only for examining the presence or absence of concomitant giant cell arteritis or neoplastic complications, but also for diagnosing such atypical PMR cases.

## EP2-19

**Neutrophilic infiltration in subacute tenosynovitis of finger by psoriatic arthritis requires differential diagnosis from septic change**

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Conflict of interest: None

Background: Psoriatic arthritis (PsA) is often difficult to diagnose in the early stages. We report a case of dactylitis associated with psoriatic arthritis, required differential diagnosis from purulent tenosynovitis, and with pathologic analysis. Case report: A 16-year-old female patient presented with pain and swelling of left middle finger. The patient was referred to our hospital because MRI showed synovitis of the flexor tendon sheath with bone marrow edema of the middle phalanx. The clinical course of the patient suggested tenosynovitis associated with subacute inflammation. In addition, infectious pyogenic tenosynovitis with elevated CRP (1.1 mg/dl) could not be ruled out due to persistent Kanavel’s signs. Therefore, we operated a tendon synovectomy for diagnostic treatment as an emergency surgery. Although tissue culture was negative, the macroscopic findings were consistent with pyogenic tendinitis. Histopathology of the synovial tissue showed many neutrophils and CD14-positive monocytes. However, the swelling recurred 6 weeks after surgery, and the patient was referred to a rheumatology department. The patient was diagnosed with dactylitis caused by PsA, combined with past history of its diagnosis at 14 years old. The skin rash resolved quickly after administration of methotrexate, and her dactylitis and knee arthritis improved by adalimumab. Discussion: Neutrophilic infiltration with clinical signs of inflammation is an important pathomechanism to characterize an infectious purulent thread, requiring consideration of immediate surgical intervention. Subacute tenosynovitis of PsA should be taken into account as its differential diagnosis, as well as a careful interview of past history.

## EP2-20

**Rheumatoid arthritis with extraarticular manifestations, osteoporosis and malignancies in the era of biological therapies, can we make it safe?**

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Conflict of interest: None

[Objective] We present the case of a male patient, 64 years old, who is hospitalized in January 2023 for left hip pain and petechial lesions all over his body [Methods] The patient is known to our clinic from 2008, when he was diagnosed with rheumatoid arthritis. During this time he was treated with csDMARDs (now on Methotrexate 20 mg weekly and Leflunomide 20 mg daily) but he had frequently high activity levels of the disease needing also corticosteroids. From the patients’s history: total right hip prosthesis for aseptic osteonecrosis of femoral head without a definite cause (1998), bladder cancer (2012), surgical intervention for lumbar spine herniated disc (2012), chronic myeloid leukemia under treatment with Imatinibum (2014), complete left subtrochanteric fracture that required intramedullary nail fixation after a minor traumtism (2015). In May 2021 the patient was diagnosed with osteoporosis (T Score-3) and started treatment with bisphosphonate (Ibandronic acid 150 mg monthly), calcium 1g and vitaminD3 2000 UI daily. In June 2022 DXA shows a T score -3.2 and FRAX score 26.5%. We decided to increase vitamin D 4000 IU and switch

to intravenous bisphosphonates (Ibandronic acid 3 mg every 3 months) Following investigation in January 2023, we found severe thrombocytopenia and xray showed intramedullary nail with atypical left subtrochanteric fracture. The orthopedic surgery is temporized and after consultations with hematologists, we decided to start treatment with Rituximab, with good evolution regarding the number of platelets. In July 2023 DXA shows T score -3.5 [Results] Although the patient is treated with biphosphonate, calcium and D3 vitamin for osteoporosis, he presented fracture on fragile bone, causes of osteoporosis beeing multiple. [Conclusions] Given the important associated pathology and immunosuppressive therapy (Imatinbum, Rituximab, csDMARDs, corticosteroids) can we may take into consideration antiosteoporotic biological treatment (Denosumab)? Could we consider another option?

## EP2-21

**Laugier-Hunziker Syndrome in a middle-aged Filipino woman with Rheumatoid Arthritis: A Case Report**

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Conflict of interest: None

**Introduction:** Laugier-Hunziker Syndrome (LHS) is a rare, benign, idiopathic disorder characterized by brownish-black spots on oral mucosa associated with longitudinal melanonychia of nails supported by a dermatoscopic assessment. However, oral and esophageal mucosa or skin biopsy is more accurate and confirms the changes as basal cell hypermelanosis and acanthosis. Thus, intensive screening for pigmentary syndromes entails diagnosis of LHS after exclusion of potential causes. **Case:** This is a case of a 54yo Filipino female with diagnosis of rheumatoid arthritis established for 5 years, according to 1987 ACR Criteria. Pertinent physical examination revealed brown to black hyperpigmented macules in the oral mucosa, longitudinal melanonychia of the nails of the hands; all skin changes appeared even before the start of RA treatment. To add, the patient was also diagnosed with autoimmune thyroiditis and primary myelofibrosis. Metabolic work up was unremarkable. Whole Abdominal Ultrasound revealed multiple cholelithiasis, hepatic steatosis and mild splenomegaly. EGD revealed negative for polyps, presence of gastric ulcers and esophagitis. Antibody testing for anti-CCP, anti-dsDNA, C3, and ANA were within the normal range. Bone marrow aspiration and biopsy showed normocellular marrow with adequate erythroid, myeloid and megakaryocytic series, noting focal fibrosis. Thus, the most common syndromes noting presence of an active mucocutaneous hyperpigmentation were ruled out. Thus, LHS was diagnosed based on the clinical findings and evaluations made by the Dermatology Clinic. The patient's blood count and metabolic profile were serially monitored and medications such as Levothyroxine, Methotrexate, Folic acid and steroids were adjusted accordingly. **Conclusion:** Laugier-Hunziker Syndrome is a rare disease commonly affecting middle-aged women and the coexistence of LHS and RA may shed new light on the role of autoimmunity in the etiopathogenesis of this uncommon disease.

## EP2-22

**Early identification and prompt treatment of severe lupus flare in a patient with lupus nephritis shown promising evidence in reversing kidney damage caused by systemic lupus erythematosus**

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Conflict of interest: None

**INTRODUCTION** Systemic lupus erythematosus (SLE) is a chronic autoimmune multi systemic disease with heterogeneous manifestations and Lupus nephritis (LN) is one of the common manifestations. The treatment of LN is complete remission, achieved through immunosuppressive drugs and steroids. **CASE HISTORY** 32-year-old Sri Lankan female, a diagnosed patient with class III LN and secondary APLS presented with fever, cough, shortness of breath for one week. She was in disease remission for 2 years with HCQ, MMF and low dose steroids. On admission, she was hemodynamically unstable with massive right sided pleural effusion and pericardial effusion warranting intensive care admission. Her inflammatory markers were high, with low C3 and C4 levels and FBC showed bi-cytopenia. CXR and 2D ECHO showed massive pleural and pericardial effusions. Her UFR showed RBC with nephrotic range proteinuria with rising creatinine. US scan KUB showed AKI without chronic parenchymal changes. Her blood, pericardial, pleural fluid and urine cultures were negative. She was diagnosed to have a severe lupus flare with serosal and renal involvement. Therefore, induction therapy was commenced with IV methyl prednisolone 1g daily for 3 days and IV Rituximab 1 gram. She underwent pericardiocentesis, right sided IC tube insertion and hemodialysis for AKI. Later the induction was followed by oral prednisolone 1 mg/kg/day, MMF, HCQ and Tacrolimus. As this presentation was life threatening, the induction therapy was commenced prior to the histological confirmation with a renal biopsy. Renal biopsy done 4 weeks later showed the evidence of class II LN. **DISCUSSION** In a patient with LN the clinical and the biochemical parameters are not sufficient to predict the extent and severity of kidney damage. It is advisable to confirm the extent of renal involvement histologically. **CONCLUSION** This case highlights early identification and the prompt treatment of severe lupus flare having a significant impact on renal disease progression.

## EP2-23

**Chilblain Lupus Erythematous-A Rare Encounter**

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Conflict of interest: None

[Objective] Chilblain lupus erythematosus (CHLE) is a rare, chronic variant of cutaneous lupus erythematosus that occurs during cold or damp periods on the hands, fingers, or feet. Like idiopathic chilblains such as perniosis, CHLE presents with tender, reddish-blue papules, nodules, or plaques on the toes, fingers, nose, or ears precipitated by cold exposure. The prevalence of the disease is about 3-20%; moreover, it occurs more frequently in women. Purpuric erythematous-violet plaques characterize it in the distal regions, such as the ears, nose, fingers and toes. [Methods] CHLE is defined by the Mayo Clinic criteria, which include two major and four minor. Two major and at least one minor criterion are required to diagnose a patient. Patients with chilblain lupus erythematosus may also display hypergammaglobulinaemia, positive rheumatoid factor, antinuclear antibody, antiphospholipid or anti-Ro antibodies. They are usually negative for anti-double-stranded DNA antibodies. [Results] The first-line treatment for mild and localised symptoms is topical corticosteroids. Second-line systemic treatments consist mainly of immunomodulators and immunosuppressants. Studies have shown benefits from the use of topical tacrolimus and pimecrolimus. We want to report a case of a young lady who presented to our centre with CHLE. [Conclusions] Chilblain lupus erythematosus is a rare and chronic disease mainly affecting women. Although it is not as severe as Systemic Lupus Erythematosus (SLE), it may be the sentinel sign of a range of underlying auto-immune diseases. Physicians should be vigilant in dealing with CHLE as their symptoms may be subtle and mimic other similar pathologies.

## EP2-24

**A Case of Viral Pneumonia Associated with Disseminated Herpes Zoster Posing Differential Diagnostic Challenges with SLE**

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Conflict of interest: None

Introduction: SLE is an autoimmune disorder that can affect various organs. Immunosuppressive therapy, while effective for managing SLE, predisposes patients to opportunistic infections, including those caused by the Varicella-Zoster Virus (VZV). We report a case in which it was difficult to diagnose pneumonia in a patient with SLE. Case Presentation: An 89-year-old female, diagnosed with SLE achieved remission with steroids and MMF treatment. Subsequent outpatient therapy reduced her prednisolone dosage to 9 mg/day. 1 month before hospitalization, she developed disseminated, bean-sized erythema on her limbs and trunk. Three days later, some lesions progressed to vesicles. Six days post-onset of erythema, she was emergently admitted with progressive dyspnea. A chest CT scan revealed bilateral interstitial shadows. On admission, with 2L nasal oxy-

gen, her SpO2 was 93%. Multiple oral ulcers and vesicular lesions on her trunk and limbs were noted. Differential diagnoses included bacterial and fungal pneumonia, SLE relapse (bullous lupus and lupus pneumonia). Treatment with levofloxacin, micafungin, and steroid pulse therapy was initiated. However, a skin biopsy revealed epithelial cell ballooning, raising suspicion for VZV infection. Rapid antigen testing VZV was positive, and a serological pattern indicated past VZV infection. Disseminated herpes zoster, including the pulmonary lesions attributed to VZV infection, was diagnosed. Treatment with acyclovir and immunoglobulin was initiated, leading to improvement of cutaneous and pulmonary manifestations. Conclusion: We report a case of disseminated herpes zoster with a rare manifestation of viral pneumonia in a patient with SLE undergoing immunosuppressive therapy. While viral pneumonia secondary to disseminated herpes zoster is rare, it can be fatal. It's crucial to consider this diagnosis in immunosuppressed patients presenting with rash and pneumonia and to promptly conduct skin biopsy and rapid antigen testing.

## EP2-25

**Hypocomplementemic Urticarial Vasculitis As An Initial Presentation Of Systemic Lupus Erythematosus**

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Conflict of interest: None

49-year-old, female a known patient with hypothyroidism and BA, presented with sudden onset SOB after applying a cosmetic product over her face and neck. She had been on over the counter steroids in short courses for more than a year for chronic urticaria. On admission she was treated for anaphylaxis. Though she responded to adrenaline initially, subsequently developed cardiorespiratory arrest which required intubation and ventilation. Her hemodynamics were maintained with the support of ionotropes. Her lungs had fine crepitations with scattered rhonchi and no pleural effusions. Investigations revealed bicytopenia with normal inflammatory markers. Her blood picture, coagulation, liver and the renal profile was normal. C3 and C4 levels were very low. CXR: alveolar shadowing bilaterally. HRCT: Aggravation of pneumonitis superimposed with alveolar edema or alveolar hemorrhage. Bronchoscopy: evidence of pulmonary hemorrhage. US Scan abdomen and KUB: moderate splenomegaly, features of AKI, 2D ECHO: EF=41%, impaired LV function and anterior wall hypokinesia, no pericardial effusion. ANA: positive (>1:100, Nuclear homogeneous pattern). Vasculitic and the infection screening were negative. Therefore, the working diagnosis was entertained as SLE in a background of hypocomplementemic urticarial vasculitis. She was started on IV steroids. Due to secondary nosocomial infection, commencement of immunosuppressions were crucial and commenced on PLEX combined with IV Ig. Despite this intensive treatment, the patient deteriorated and succumbed to death due to worsening respiratory distress and cardiac instability secondary to sepsis. Key Message: Histological evaluation is necessary when a patient presents with inadequate treatment response for conventional treatment for urticaria. In the presence of leuko-cytoclastic vasculitis on histology, complement levels should be measured and monitored, even though the association between HUV and SLE is not clearly defined.

## EP2-26

**Bilateral retinal vasculitis in first presentation of Systemic Lupus Erythematosus**

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Conflict of interest: None

[Objective]-Background- Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disorder that can result variety of eye manifestations. While Keratoconjunctivitis sicca is the most common one, retinal vasculitis is one of the rare manifestations with a poor prognosis. Its presentation varies such as eye pain, visual disturbances, dry eye symptoms, eye discharges, redness and sometimes asymptomatic. A 27-year-old Sri Lankan lady with a history of migraines presented with a month's history of fever with constitutional symptoms, anemic symptoms and occipital headache for two weeks. On examination, she was pale but did not have alopecia, oral ulcers, rashes or synovitis. Her fundoscopy examination revealed bilateral disc oedema. [Methods]- In her evaluation, she was found to have elevated ESR>100, normal CRP, leucopaenia with absolute lymphopaenia, moderate anaemia with warm type autoimmune haemolytic anaemia (AIHA), ANA-1:160 (nuclear pattern), DsDNA-positive with thriple positive APLS antibodies. For the evaluation of disc oedema, MRI/MRA/MRV brain was arranged and became normal. CSF manometry-normal. Finally, ophthalmic assessment revealed evidence of retinal vasculitis which includes vascular sheathing in both eyes. Her diagnosis was made as SLE, warm AIHA and bilateral retinal vasculitis. [Results]- She was started intravenous methylprednisolone three pulsus followed by oral prednisolone, 4 cycles of Rituximab and Azathioprine were commenced later on. In addition to that Hydroxychloroquine and Aspirin were also initiated. She responded well to the therapy and went into disease remission. [Conclusions]- Retinal vasculitis is a rare but known eye manifestation in SLE and the majority present with active SLE. Early suspicion, detection and treatment can minimize morbidity.

## EP2-27

**Co-occurrence of polyarteritis nodosa and cold agglutinin disease manifesting as cold-induced painful purple digits**

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Conflict of interest: None

[Case] A 90-year-old man was referred in winter with anemia, weight loss, 2-week history of fever, and Raynaud's phenomenon (RP). Initial skin presentation was a reversible white-blue-red discoloration of the fingers with rewarming. However painful purple digits (PPD) developed on the next visit leading to hospitalization for ischemic digital gangrene. Lab findings revealed CRP 9.07 mg/dl and anemia. Serological tests for infections and antibody panels were negative. X-ray, ultrasound and contrast CT were unremarkable. Arteriography of left forearm showed aneurysms in the finger vessels, and abdominal arteriography revealed irregular stenoses of mesenteric and renal arteries; finding consistent with polyarteritis nodosa (PAN). Additionally, cold agglutinins, direct Coomb's test with anti-C3bC3d, and direct antiglobulin tests were positive, leading to the co-diagnosis of cold agglutinin disease (CAD). Hematology consultation was performed, however consent for bone marrow exam could not be obtained. Alprostadil, mPSL 1g x 3 day pulse therapy followed by PSL 60 mg/day was initiated. Presence of poor prognostic factors warranted the addition of cyclophosphamide 500 mg/month. His serum hemoglobin level increased and CRP normalized. Subsequently, progression of digital ischemia was halted. [Clinical Significance] Small to medium vessel vasculitis may manifest as PPD, with RP being an infrequent presentation. In contrast, CAD can exhibit both presentations. Our case presented with digital ischemia worsened by cold temperatures, along with vasculitis symptoms, prompting a comprehensive evaluation, leading to the diagnosis of PAN and CAD. Reports on the association between vasculitis and CAD are scarce, with no reports of PAN and CAD co-occurrence. When patients with vasculitis experience cold-induced digital ischemia, it is crucial to investigate potential associated conditions like CAD. Timely evaluation is essential to prevent potential complications.

## EP2-28

**Physical and Biological Treatment Plan Evaluation of IMRT for Brain Cancer**

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Conflict of interest: Yes

Introduction: Brain cancer is an affliction characterized by the abnormal proliferation of cells within the brain or the central nervous system, originating from either the brain or surrounding tissues. This study aims to evaluate the IMRT treatment plan in case of brain cancer by using different physical parameters and biological models. Materials & Method: The

beam arrangement of all IMRT plans consisted of seven or nine beams for each case, and the prescription dose was set at 60 Gy for 30 fractions. All treatment plans were generated using the Eclipse treatment planning system (Version 13.6). The physical evaluations were conducted using various parameters, including Conformity Index (CI), Homogeneity Index (HI), Quality Coverage (QC), Conformation Number (CN), Lesion Coverage Factor (CVF), Lesion Underdosage Factor (LUF), Healthy Tissue Overdosage Factor (HTOF), Healthy Tissue Conformity Index (HTCI), and Geometric Conformity Index (g), as proposed by the American Association of Physicists in Medicine (AAPM). Result & Discussion: The Conformity Index (CI) for case 5 and 7 are below 1 but not below 0.8, indicating that the isodose confirms the PTV volume above 80%. The homogeneity indexes (HI) for all cases are within the limits defined by the RTOG protocol. However, in case 3 and 9, the QC falls below 80% due to adjacent contouring of PTVs to the skin beyond the dmax. Nevertheless, the TCP and NTCP results remain within the acceptable limits, demonstrating no major violations and indicating that the IMRT plans are biologically acceptable. Conclusion: The comprehensive evaluation of all ten plans in this study revealed that the IMRT plans were successful. Optimal dose distribution within the PTV ranged from 95% to 108%, while the administered dose to the OARs remained below their respective tolerance levels.

## EP3-03

**Rate and causes of hesitancy in COVID-19 vaccination in Korean patients with autoimmune rheumatic diseases: a survey study**

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Conflict of interest: Yes

**Objective** The Coronavirus Disease-19 (COVID-19) vaccines were developed and used to control the COVID-19 infection and pandemic. According to the Korean college of rheumatology guidelines, patients with autoimmune rheumatic diseases (AIRDs) are recommended to take COVID-19 vaccination. The purpose of this study was to identify the COVID-19 vaccination rate and causes of the vaccine hesitancy in Korean AIRDs patients. **Methods** In this paper-based survey study, we enrolled 118 patients with AIRDs who visited a single tertiary university hospital from March 2022 to April 2022. The questionnaire included the subject's demographic details, diagnosis, disease duration, medication, side effects after the vaccination and questions regarding the vaccine hesitancy. The vaccinated group refers to a group that took at least one vaccination and the hesitancy group refers to a group that did not take any vaccination. **Results** Of the 118 patients with AIRDs, 101 (85.6%) were the vaccinated group and the 64 (63.4%) has completed 3rd vaccination whereas 17 (14.4%) were the hesitancy group. The most common AIRDs was ankylosing spondylitis (38.6%) in the vaccinated group and systemic lupus erythematosus (52.9%) in the hesitancy group, respectively. The frequency of glucocorticoids, conventional disease modifying anti-rheumaitc drugs (DMARDs) and immunosuppressants use were significantly higher, but the frequency of biologic DMARDs were significantly lower in the hesitancy group compared with the vaccinated group. The most common cause of vaccine hesitancy was a fear related to the side effects of vaccine (33%) followed by concerns for flare of AIRDs (20.8%). **Conclusion** COVID-19 vaccination rate was suboptimal in Korean patients with AIRDs and concerns for side effect of vaccination and flare of underlying diseases were leading causes for vaccination hesitancy, suggesting that rheumatologists should provide more accurate information to these patients regarding the need for COVID-19 vaccination.

## EP3-04

**Comparison of anti-inflammatory and anti-angiogenesis effects of JAK inhibitors in IL-6 and TNF alpha-stimulated fibroblast-like synoviocytes derived from patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] In this study, we investigated the anti-inflammatory and anti-angiogenesis effects of each JAK inhibitor in IL-6 and TNFα-stimulated fibroblast-like synoviocytes derived from patients with rheumatoid arthritis (RA-FLSs) to clarify the effect of JAK inhibitors targeting the JAK-STAT pathway involved in the pathogenesis of RA. [Methods] RA-FLS were stimulated with estimated blood concentrations of JAK inhibitors (Tofacitinib (TOF) 0.3μM, Baricitinib (BAR) 0.3μM, Peficitinib (PEF) 1μM, Upadacitinib (UPA) 0.3μM, Filgotinib (FIL) 2μM), followed by IL-6 (100 ng/ml) and sIL-6R (100 ng/ml) or TNFα (10 ng/ml) stimulation for 24 hr. Relative mRNA expression levels of the inflammatory factors ICAM1 and MMP1 and the angiogenetic factors VCAM1, VEGF, and MCP1 were evaluated by qRT-PCR. Phosphorylated STAT1 (pSTAT1) and pSTAT3 were assessed by western blot. To assess angiogenesis, synovial tissue was evaluated. RA-FLSs were divided into two groups based on RA treatment received: non-BIO group (not using biologics), or JAK group (JAK inhibitor used). Tissue samples were subjected to hematoxylin and eosin staining, and immunofluorescence staining. [Results] Under IL-6 stimulation, the expression levels of all targets for both inflammatory and angiogenic factors (ICAM1, VCAM1, VEGF, MCP1 and MMP1) were lower in all JAK inhibitors. On the other hand, all targets showed no significant differences between groups in TNFα stimulation. Western blot results showed that pSTAT1 and pSTAT3 levels were significantly lower in all JAK inhibitors than control. The immunofluorescence demonstrated that angiogenesis markers including αSMA and VEGF were expressed higher in non-BIO RA-FLS than JAK group. [Conclusions] In RA joint, JAK inhibitors suppress synovial inflammation and angiogenesis induced by IL-6.

## EP3-05

**Enhanced Expression of Semaphorin 4A in Lupus Dendritic Cells and Kidneys: Implication for Therapeutic Potential**

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Conflict of interest: None

[Objective] In this study, we aimed to explore the expression of semaphorin 4A (SEMA4A) in the context of systemic lupus erythematosus (SLE) and investigate its potential correlation with lupus activity in both a lupus mouse model and SLE patients. [Methods] Bone marrow-derived dendritic cells (BMDCs) and renal tissues from control mice and Toll-like receptor (TLR)-7 agonist (R848)-induced lupus mice were investigated for the expression of SEMA4A. Immunohistochemistry was performed to examine the expression of SEMA4A in the kidney of the patients with SLE and they were analyzed according to the activity index of lupus nephritis. [Results] The SEMA4A was highly expressed in the BMDCs of the lupus group compared to the control group. The immunocytochemistry also showed enhanced fluorescence intensity of SEMA4A in BMDCs of the lupus mouse group compared to the control group. The kidneys, one of the main target organs of SLE, were analyzed for the protein level of SEMA4A in the murine lupus group and control group. The mean fluorescence intensity of SEMA4A in the kidneys of lupus mice was significantly enhanced compared to the control group. In the analysis of immunohistochemistry of SEMA4A in kidneys of the patients with SLE, the positivity of SEMA4A staining was markedly higher in lupus nephritis with higher activity score compared to those of lupus nephritis with lower activity score. [Conclusions] The expression of SEMA4A is significantly increased in the dendritic cells and kidneys of the lupus murine group and the patients with SLE compared to the control group. The expression of SEMA4A correlates with the severity of lupus nephritis. These results indicate the possible contribution of SEMA4A in the pathogenesis of SLE and the potential of targeting SEMA4A for the treatment of SLE.

## EP3-06

**A clinical audit on use of non-steroidal anti-inflammatory drugs (NSAIDs) among degenerative arthritis in out patient clinics at a Rheumatology tertiary care hospital in Sri Lanka, in relation to the NHSGGC NSAIDs guidelines**

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Conflict of interest: None

Objective] - NSAIDs are effective treatments for the relief of pain, swelling and stiffness of arthritis. It is being used increasingly in patients with degenerative arthritis. There are several guidelines on NSAIDs. However, only a few audits have been carried out to check whether the NSAIDs are used according to the guidelines. Here we aimed to assess adherence to guidelines when prescribing NSAIDs in patients with degenerative arthritis. [Methods] - A structured audit form was developed and distributed to consulting medical officers in rheumatology clinics and the form was interviewer-administered focusing on factors that should considered when prescribing NSAIDs according to NHS Greater Glasgow and Clyde (NHSGGC) Oral Non-Steroidal Anti-inflammatory guidelines. Initial sixty outpatients who presented within two weeks were enrolled in the study. Data was analyzed using a paired t-test. Reauditing was arranged after the introduction of the same guidelines, in 2 months for the same cohort and data was analyzed to complete the audit cycle. [Results]- Before the introduction of guidelines, the observed percentages of checking the status of blood pressure, serum creatinine, full blood count, use of Proton pump inhibitors, consideration of comorbidities, consideration of other medications, duration of NSAIDs use (as required/ < 1 month) were 0%, 0%, 0%, 98.33%, 20%, 11.67% and 23.33% respectively. After the introduction of guidelines, the observed percentages were 93.33%, 58.33%, 53.33%, 98.33%, 96.67%, 96.67% and 78.33% respectively. Then all the factors were analyzed using a paired t-test and p-values were calculated. All p values were < 0.001, except the use of PPI (p=0.659). [Conclusions] - There were deficiencies when prescribing NSAIDs in degenerative arthritis. After the introduction of NSAID guidelines, there was a statistically significant improvement in prescription. The limitation of the study includes small population size.

## EP3-07

**All-new screening apparatus for cold syndrome-positive people**

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Conflict of interest: None

[Objective] The present invention has been made to provide reference information for determining instructions or an amount of medication to each cold syndrome-positive person by accurately evaluating whether or not each cold syndrome-positive person is a true positive person based on a surface temperature of right and left EIFU parts (WHO standard acupuncture point locations: TE17) measured for and subjective symptoms of discomfort in right and left pharynx regions (a subjective evaluation item) heard from the cold syndrome-positive people and notifying the evaluation results. [Methods] All clinical data was collected at the Hiroshima Prefectural Office COVID-19 Countermeasures Office from February 2022 to December 2022. The right EIFU temperature, the left EIFU temperature, the difference value between the right EIFU temperature and the left EIFU temperature, and whether or not the difference between discomfort in the right and left pharynx regions is present for 50 PCR-positive people determined to be infected with Omicron strain, which is a type of COVID-19, by PCR test. All subjective and objective data were statistically analyzed using multiple regression analysis ($p<0.05$). [Results] A correlation was observed between the left and right EIFU temperatures and the direct forehead temperature. The difference in EIFU temperature between the left and right sides was correlated with the subjectively evaluated difference in discomfort in the pharynx between the left and right sides. [Conclusions] The apparatus may be useful for early detection and drug treatment of patients with cold syndromes, including coronavirus pneumonia (PCT/JP2023/0119875).

# Poster Session

## P1-001

**Analysis of factors and affected joints in relation to working status in patients with rheumatoid arthritis under 65 years of age using the FRANK registry**

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Conflict of interest: None

[Objective] Using rheumatoid arthritis (RA) patient registry data, we will clarify the factors that influence the working status of RA patients and the affected joints. [Methods] 1658 RA patients aged 65 years or younger who were registered in the FRANK registry by September 2022 were analyzed. The 141 people who were unable to work due to RA were classified as the non-working group, and the 1112 people who were working at the time of registration were classified as the working group. [Results] Compared with the working group, the non-working group was significantly older, had a longer disease duration, had higher disease activity (CDAI), and lower ADL index (mHAQ). The non-working group had a high rate of joint symptoms, and univariate analysis showed that symptoms in the elbows, hands, fingers, knees, and ankles were significantly related to working status. In multivariate analysis, finger, elbow, and knee joints were significantly associated with working status. [Conclusions] Symptoms of the fingers, elbows, and knee joints may influence the working status of RA patients. These results suggest that appropriate control of disease activity at an early stage may be important for social participation in RA patients.

## P1-002

**The impact of each joint on pain visual analog scale (VAS) in rheumatoid arthritis-Analysis using NinJa 2021 and joint index vectors-**

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Conflict of interest: None

[Objective] We reported in JCR 2023 that the impact of lower small joint involvement on pain VAS is smaller than that of upper small joint in rheumatoid arthritis (RA), based on joint index vectors and the *NinJa* 2019 study. The aim of this study was to analyze the impact of each joint based on *NinJa* 2021. [Methods] We analyzed 15,360 RA patients using multiple regression analysis with pain VAS as the objective variable and tender joint index and number of tender joints of each joint region as explanatory variables. [Results] The tender joint index of upper large joints had the largest impact on pain VAS, followed by lower large joints, upper small joints, and lower small joints. In the elderly group, stage II-IV group, and class II-IV group, the tender joint index of lower small joints did not have a significant impact on pain VAS. The wrist joint, a large upper joint, had the highest impact on pain VAS. Tarsometatarsal, MTP and IP joints had little impact on pain VAS. [Conclusions] The impact of lower small joints on pain VAS was relatively small, especially in the elderly group and the

patient group with advanced stage on x-ray and dysfunction. It is important that physicians carefully examine the forefoot, as RA patients may not report lower small joint pain.

## P1-003

**Clinical characteristics of patients with rheumatoid arthritis (RA) exhibiting disproportionate articular pain (DP) in Japan: Analysis based on Ninja2019 and joint index vector**

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Conflict of interest: None

[Objective] Choy et al defined Disproportionate Articular Pain (DP) as TJC - SJC more than 7 in a 28-joint count. DP was reported to occur in 23% in moderate to high disease activity patients in MONARCH. This study aimed to analyze the clinical characteristics of DP using *NinJa*2019. [Methods] Clinical data, including joint index vectors, were analyzed from 13,653 RA patients registered in *NinJa*2019. Data were compared between DP and non-DP groups. [Results] Among 653 patients with moderate to high disease activity, DP was observed in 180 (27.6%), which was similar to that reported by Choy. Disease duration, DAS28, mHAQ, x (upper extremity index), and y (lower extremity index) were significantly higher in DP than in non-DP groups. while z (large joint predominance index) was significantly lower. With all patients included, DP was rare at 0.03%, but the clinical characteristics were similar. Furthermore, DP was associated with a significantly higher frequency of positive discordance (patient > physician). [Conclusions] RA with DP was associated with high disease activity, predominance of small-joint involvement, and positive patient and physician discordance of overall disease activity assessment. Further studies are needed to explore the role of DP as poor prognosis factor in RA.

## P1-004

**The onset age of rheumatoid arthritis is higher, the disease duration is shorter and more deaths occur due to interstitial lung diseases and respiratory tract infections in men. -NinJa2021 cohort investigation-**

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Conflict of interest: None

[Objective] To examine the differences of age of onset, number of deaths and causes of death, etc. by gender in *NinJa2021* database. [Methods] We examined 17181 cases (3645 men, 13536 women) from the *NinJa2021* database. [Results] Patient backgrounds are as follows (male/female): average age: 67.8 (69.4/67.3) y. o, onset: 53.4 (58.5/52.1) y. o, disease duration: 14.3 (10.9/15.2) years, CDAI: 5.24 (4.68/5.39), RF positive: 73.0%, anti-CCP antibody positive: 71.5%, history of smoking: 33.3 (74.8/21.9) % In 199 cases of deaths, male: 81 cases (2.22%). female: 118 cases (0.87%). age: 78.6 (78.0/79.1) y. o, onset: 60.6 (64.9/57.6) y. o, disease duration: 18.1 (21.5/15.2) years, CDAI: 6.6 (5.28/7.46), DMARDs use 79.1 (77.8/79.7) %, steroids 70.4 (69.4/71.1) %, history of smoking: 44.1 (78.3/19.3) %, major causes of death were malignant disease: 42 (14/28) cases, interstitial lung disease: 16 (11/5) cases, respiratory tract infection: 34 (17/17) cases, heart failure: 16 (1/15) cases. [Conclusion] 1) Although the age of onset and average age is higher in men, the disease duration is shorter, and there is no difference between men and women in the age structure over 75 y.o. 2) The mortality rate is higher in men, and the deaths by interstitial lung disease and respiratory tract infection are higher than women.

## P1-005

**Validation of NinJa data using post marketing Surveillance of JAK inhibitors**

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Conflict of interest: None

[Objective] The National Database of Rheumatic Diseases in Japan (NinJa) covers around 2% of rheumatoid arthritis (RA) patients nationwide. This study compared NinJa data with post marketing surveillance (PMS) data of JAK inhibitors to verify whether NinJa captures the actual clinical practice for RA in Japan. [Methods] Registered patients in PMS studies of baricitinib (BAR), upadacitinib (UPA), and filgotinib (FIL) were compared to NinJa patients using those drugs at the time of the respective PMS studies regarding attributes and drug use. Statistical analyses used t-test, chi-square test, and Fisher's exact test. [Results] Number of patients compared were: BAR (PMS 4731, NinJa 286), UPA (2106, 39), FIL (655, 43). Comparisons between PMS and NinJa patients for each drug showed no statistically significant differences. [Conclusion] Verification through real-world use of JAK inhibitors suggested NinJa data may capture actual RA clinical practice in Japan without bias.

## P1-006

**Characteristics of patients who underwent total ankle arthroplasty for rheumatoid arthritis: a study using NinJa**

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Conflict of interest: None

[Objective] The purpose of this study was to clarify the characteristics of patients undergoing TAA for rheumatoid arthritis (RA) using NinJa, a nationwide database of rheumatic diseases. [Methods] Information on patients who underwent TAA, total knee arthroplasty (TKA), total hip arthroplasty (THA), and total elbow arthroplasty (TEA) was extracted from NinJa registration data from 2007 to 2021. Comparisons were made between sites and over time. [Results] A total of 3,776 relevant surgeries were performed, of which 83 were TAAs. The number of TAAs per 100 RA patients per year was calculated from 0.057 in 2007-2011 to 0.034 in 2017-2021, a decrease of 40%, but the decrease was smaller than TKA and TEA. The TAA group had an average of 1.7 previously inserted prostheses, significantly more than the other groups. The discrepancy between patient and physician ratings was significantly greater in the overall RA evaluation than in the other groups. There was also a large increase in mean age. [Conclusions] TAA for RA patients showed a decreasing trend, although not as much as TKA and TEA, with a 40% decrease over 10 years; TAA group had several characteristics, including a higher number of previous joint replacements and a greater discrepancy between patients' and physicians' general RA evaluation.

## P1-007

**Progressive Pulmonary Fibrosis (PPF) in Anti-aminoacyl-tRNA Synthetase Antibody-Positive / Autoantibody-Negative Polymyositis/ Dermatomyositis Complicated by Interstitial Lung Disease**

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Conflict of interest: None

[Objective] This study investigates PPF progression characteristics in anti-aminoacyl-tRNA synthetase antibody (ARS)-positive/autoantibody-negative polymyositis and dermatomyositis (PM/DM) associated with interstitial lung disease (ILD). [Methods] A cohort of 59 continuous cases with anti-ARS antibody-positive/autoantibody-negative PM/DM-ILD, seen from 2015 to 2022, underwent analysis. Clinical data, evolving respiratory symptoms, respiratory function tests, and high-resolution chest computed tomography (HRCT) scans were assessed. Factors linked to PPF progression were examined. Chest HRCT images were evaluated by two specialized radiologists. [Results] Among 59 cases, 8 met PPF criteria, with 7 meeting progressive fibrosing interstitial lung disease (PF-ILD) criteria. Median durations to PPF and PF-ILD were 2.2 (0.6-3.0) and 1.9 (0.3-3.1) years, respectively. PPF cases had significantly higher pre-treatment serum KL-6 levels ($P$ = 0.048), reduced %FVC and %DLCO ($P$ = 0.01, 0.03), more cumulative cyclophosphamide ($P$ = 0.024), and more ILD-related hospitalizations ($P$ = 0.01). [Conclusion] Elevated pre-treatment serum KL-6 and declining lung function may predict PPF progression.

## P1-008

**Comparison of the treatment courses and the prognoses of anti-synthetase antibody-positive and anti-MDA5 antibody-positive idiopathic inflammatory myopathy-associated interstitial lung disease (IIM-ILD): a single center retrospective study**

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Conflict of interest: None

[Objective] To compare prognoses of anti-synthetase (ARS) antibody and MDA5 positive inflammatory myopathy-associated interstitial lung disease (IIM-ILD). [Method] We collected data of MDA5 and ARS IIM-ILD, as well as ARS ILD patients, who were treated at our institution between Jan 2004 to Aug 2023, and compared the rates of remission, recurrence, and lung-related death (LRD). Remission was defined as no disease activity for > 3 months, with GC dose of < 10 mg/day of prednisolone. LRD was defined as death from respiratory failure of any cause. [Result] Of 37 MDA5 patients (62% female, median age 53 [26-77], median observation 5.5 years [0.1-16.1]), 33, 30, and 8 patients achieved more than one remission, GC-free (GF), and Drug-free (DF) remission. In 4 patients, no remission was achieved, leading to death. There were 8 relapses (0.8/person-years), with no relapse after GF remission achievement, and 5 LRD's after 0.14 years [0.09-0.21]. Of 34 ARS patients (82% female, age 54 [34-81], observation 4.8 years [1.1-17.7]), 33, 15, and 0 achieved remission, GF, and DF remission. There were 58 relapses (0.27/person-years), and 4 LRD's after 3.3 years [1.1-8.7]. [Conclusion] LRD's occur early in MDA5 and later in ARS patients. New treatment options for treatment-resistant cases are required.

## P1-009

**anti-EJ antibody positive polymyositis/dermatomyositis with interstitial pneumonia: A Three-case series**

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Conflict of interest: None

[Background] Anti-synthetase syndrome (ASS) is systemic autoimmune diseases characterized by the anti-ARS antibodies. anti-EJ (anti-Glycyl-tRNA synthetase) antibody is observed at 2-5% and is detectable with ARS-ELISA test. We identified 3 Japanese cases of anti-EJ positive PM/DM with Lineblot assay. [Case 1] 58 yo male, developed interstitial pneumonia (IP) and steroid was started. At 67 yo, myositis, mechanic's hand, elevation of CPK, aldolase, anti-ARS (EJ) antibody was noted and diagnosed as dermatomyositis. Bacterial pneumonia triggered IP progression to death. [Case 2] 55 years old male showed elevation of KL-6 and UIP was diagnosed. At 64 yo, Gottron, mechanic's hand, EJ antibody diagnosed with Amyopathic dermatomyositis (DM). Nintedanib was started for the progression of IP. [Case 3] 78 years old male, who developed IP, swallowing difficulty, pericardial effusion. The elevation of KL-6, CPK made a diagnosis of polymyositis. Rectum carcinoma was found. steroid and IVIG was used. [Conclusions] anti-EJ antibody is associated with DM and IP. Elevation of KL-6, IP was noted in all three cases. Polymyositis was found in 2/3. EJ antibody was also reported to be associated with pulmonary hypertension, malignancies, such were also seen in our cases.

## P1-010

**A case of multidisciplinary treatment including double membrane filtration plasma exchange (DFPP) for relapse of myasymptomatic dermatomyositis (CADM) positive for anti-PL-7 antibodies**

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Conflict of interest: None

A woman in her 70s. She developed interstitial pneumonia in month Y of X-1, and although Godron's sign was observed, there were no muscle symptoms, and she was diagnosed with CADM, which was positive for anti-PL-7 antibodies. She underwent steroid pulses, simple plasma exchange (PE), tacrolimus, rituximab, cyclophosphamide pulses, and high-dose gamma globulin therapy, and achieved remission. Although the steroid dose was reduced, she developed dyspnea on exertion in month Y+7 the same year. She was diagnosed with CADM relapse. She received the same initial treatment. She also received PE, but it was discontinued due to anaphylactic shock. She was switched to DFPP and could complete it a total of 7 times without experiencing anaphylactic shock again. After that, we again administered methylprednisolone steroid pulse for 3 days, and rituximab once a week for a total of 4 times. Since DFPP performs plasma exchange using albumin without using plasma, it is difficult to completely remove pathogenic substances, but it can reduce the risk of allergies and infections. Anti-PL-7 antibody is one of the anti-ARS antibodies, and although muscle weakness, arthritis, and skin symptoms are relatively common, we consider this to be a valuable case of CADM relapse.

## P1-011

**A case of anti PL-7 antibody positive-anti ARS antibody syndrome treated with immunosuppressant and plasmapheresis**

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Conflict of interest: None

From June 20XX, she complained of fever, dyspnea on exertion, and noticed with Gottron's sign. Diagnosed with common acquired pneumonia, she was admitted to the previous hospital. Her pneumonia did not improve with antibiotic treatment, and plain chest CT imaging revealed interstitial shadows. During the investigation of the cause of interstitial pneumonia, she was found to be positive for anti-ARS antibody/anti-PL-7 antibody. In early July, she was transferred to our department for further treatment. Based on the above course and muscle weakness in her proximal extremities, she was diagnosed with interstitial pneumonia, associated with anti-ARS antibody syndrome. She was started treating with steroid pulse, cyclophosphamide pulse, and tacrolimus, only to find that their response was poor. Therefore, she was also treated with plasmapheresis three times a week for three weeks. As a result, her respiratory status, hematological markers, and chest images all showed improvement, and she was weaned from the ventilator in early August while tapering glucocorti-

coid. She was transferred to a convalescent hospital in early September. In this case report, we would like to discuss efficacy and validity of plasmapheresis as a treatment of anti-ARS syndrome.

## P1-012

**A case of anti-ARS antibody-associated interstitial pneumonia with severe respiratory failure successfully treated with ECMO**

Chifumi Akiyama, Takanori Nakagaki, Mahiro Yamamoto, Kota Imaizumi, Aya Sakamoto, Takao Kiboshi, Takayasu Suzuka, Takeshi Shoda, Takuya Kotani, Tohru Takeuchi
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Conflict of interest: None

[Case] A 64-year-old male patient with dyspnea on exertion began to experience respiratory distress at the end of December, X-1, and visited his previous physician on January 4, X. A CT scan of the chest showed extensive frosted glass shading and methylprednisolone (mPSL) 1g/day was started, but his respiratory condition worsened further. On January 6, respiratory status at the time of transfer was P/F: 90, and V-V ECMO was started on the first day. Based on positive anti-ARS antibody and elevated serum CK level, we diagnosed anti-ARS antibody-associated interstitial lung disease (ASS-ILD). On the first day, 1g of intravenous cyclophosphamide (IVCY) and 3 mg/day of tacrolimus (TAC) were started, followed by plasma exchange on the 5th day. Respiratory condition improved, and steroids were tapered off. Oxygen administration was discontinued on the 86th day, and the patient was discharged on the 129th day. [Discussion] This is a case of a patient with rapidly progressing severe respiratory failure with ASS-ILD who was successfully treated with ECMO. ECMO may be useful as a respiratory replacement therapy until the onset of immunosuppressive therapy in patients with severe respiratory failure who are difficult to rescue with ventilators. This report includes a review of the literature.

## P1-013

**A case of anti-ARS antibody syndrome complicated by pulmonary hypertension and treated with intervention while waiting for a lung transplant for interstitial lung disease**

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Department of Respiratory Medicine and Clinical Immunology, Nippon Life Hospital, Osaka, Japan

Conflict of interest: None

[Case] 54-year-old male [Chief complaint] Shortness of breath [History of present illness] Diagnosed with interstitial lung disease (ILD) due to anti-ARS antibody syndrome (ASS) in year X-8. In year X-1, he was registered for a lung transplant at University A. In May of X, shortness of breath during exertion worsened. He was admitted for further investigation. [Course after admission] Chest CT showed no signs of worsening of ILD compared to when he was registered for lung transplantation. However, at RHC, mPAP: 33 mmHg, PVR: 6.2 WU, which was not recognized at the time of lung transplant registration, was noted. Various tests excluded group II and IV factors, and imaging and pulmonary function tests showed no worsening of ILD, so immunosuppressive treatment was performed as a complication of group I PH due to ASS. We also attempted to use a PDE5 inhibitor as a cardiopulmonary comorbidity. After 8 weeks, RHC showed improvement with her mPAP: 24 mmHg, PVR: 3.9 WU, without deterioration of pulmonary hemodynamics. [Discussion] In collagen disease-related PH complicated by ILD, the extent to which group I elements are included in group III PH is extremely important in determining treatment policy. Based on past literature, we will discuss the PH pathology in this case.

## P1-014

**A case of dermatomyositis with lung transplantation that weaned the patient from home oxygen therapy induction**

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Conflict of interest: None

A 40-year-old woman began coughing at around 37 years of age and had shortness of breath on exertion at around 40 years of age. She was suspected to have collagen disease and was referred to our hospital. She had bilateral lower lung fine crackles since her initial admission, and was diagnosed with dermatomyositis due to fever, myalgia, arthralgia, and elevated aldolase. She had interstitial lung disease and was treated with high-dose prednisolone and immunosuppressive therapy, but her lung function declined over time. The patient was strongly motivated to continue working in her fields at home, and the decision was made to continue immunosuppressive therapy while considering lung transplantation. After a lung transplant consultation, a partial left lung transplant was performed at the age of 56, and the patient was able to wean off home oxygen therapy. Discussion The treatment of interstitial lung disease associated with collagen disease is mainly drug therapy, and glucocorticoids and immunosuppressive agents are used for treatment. This patient was successfully weaned from home oxygen therapy by lung transplantation. This is a valuable case and will be reported with some literature review.

## P1-015

**NOD2 mutation associated Blau syndrome case with BCG-tuberculid and painless cystic tumors**

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Conflict of interest: None

Case: At the age of 8 months, purple-red papules appeared on the extremities and on the face after BCG vaccination. Skin biopsy was performed, and the pathological finding was non-caseating epithelioid cell granuloma. At the age of 4 years, corneal ulcers of unknown cause and posterior iris adhesions appeared. At the age of 5 years after visits to many local clinics (dermatology, orthopedics, and ophthalmology). He had painless cystic masses on both limbs and arthritis of the fingers. A skin biopsy was performed again, and pathological findings were suspicious for BS. Genetic testing revealed a mutation R334W in the NOD2 gene, confirming the diagnosis. He was treated with anti-TNF-α inhibitors and showed rapid trend improvement. Discussion: BS has been reported with an autosomal dominant inheritance pattern, but similar mutations was identified in sporadic cases. BS can be sometimes confused with juvenile idiopathic arthritis or rheumatoid arthritis. Due to multiorgan involvement, it takes long time for final diagnosis. To avoid the progression of clinical coarse, awareness of this disease required.

## P1-016

**A case of infantile sarcoidosis with granuloma in the kidney**

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Conflict of interest: None

[Case] A 3-year-old boy. He visited hospital because of recurrent fever for the past 3 months. Ga scintigraphy showed accumulation in the lungs and bilateral kidneys. Suspecting sarcoidosis, he underwent ophthalmologic examination and renal biopsy. Retinal vasculitis and epithelioid cell granuloma in the kidneys were observed, without any skin rash or arthritic symptoms, and no *NOD2* mutation was found. U-TP/U-Cr, and U-β2MG/U-Cr (UBCR) were 0.27 g/gCr, and 1.79 μg/mgCr, respectively. He was diagnosed as sarcoidosis with tubular interstitial nephritis, and PSL 1 mg/kg/day was started. UBCR did not normalize and AZA was added, but UBCR increased to 4.6 as the PSL dose was reduced. After 4 months, Ga scintigraphy showed that the accumulation in the lungs had disappeared, but in the kidneys remained mildly. AZA was changed to MMF and PSL was gradually reduced. After 17 months, renal accumulation became less noticeable by Ga scintigraphy, but UBCR has not yet normalized. PSL has been reduced to 0.22 mg/kg/day, but there is no prospect for discontinuation. [Clinical Significance] Renal sarcoidosis is a rare disease in adults,

too. Treatment methods have not been established. The use of PSL in children can cause growth retardation, so treatment should be discussed.

## P1-017

**Analysis on the disease relevance of two potential disease-causing variants identified on a patient suspected of cryopyrin-related periodic fever syndrome**

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Department of Pediarics and Child Health, Kurume University School of Medicine

Conflict of interest: Yes

[Objective] Cryopyrin-associated periodic fever syndrome (CAPS) is of an autosomal dominant inheritance caused by a gain-of-function mutation in the NLRP3 gene. We experienced a case of CAPS diagnosed in adulthood with chronic meningitis, hearing loss, epilepsy, and persistent inflammation. This case was characterized by the absence of the skin rash often seen in CAPS. We seek to elucidate the genetic background that explains these clinical findings. [Methods] NLRP3 gene analysis using NGS was performed at Orphan net Japan Kazusa. TA cloning was performed to examine whether the variants were cis or trans. Two in vitro assays were performed to investigate the disease relevance of the obtained variants. All the experiments were approved by the ethics committee of Kurume University. Written informed consent was obtained from the patients or their legal guardians. [Results&Conclusions] NLRP3 genetic tests identified two rare missense variants, NLRP3 R262Q heterozygous (reported, VOUS) and E691K heterozygous (novel). Genetic analysis of this case, as well as of the maternal and paternal family members, revealed the two missense variants were present in separate alleles and compound heterozygous. Disease relevance is currently being investigated by the in vitro assay systems.

## P1-018

**Two cases of subcutaneous panniculitis-like T-cell lymphoma with mutant TIM-3**

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Conflict of interest: None

Subcutaneous lipoid-like T-cell lymphoma (SPTCL) is a lymphoproliferative disease characterized by subcutaneous adipose tissue infiltration by activated αβ-type CD8-positive cytotoxic T cells. Although the prognosis is relatively good, there is no established treatment for SPTCL, and it may be complicated by hemophagocytic lymphohistiocytosis (HLH), which is refractory to treatment. There have been reports of cases of complications with autoimmune diseases such as systemic lupus erythematosus (SLE), which are often difficult to diagnose due to the similarities in clinical and histological findings with lupus erythematosus profundus. Recently, HAVCR2 (TIM-3) gene mutations have been reported to be involved in the pathogenesis of the disease. We will report two cases of SPTCL and the results of genetic testing on HAVCR2 gene, TIM-3 protein expression, and cytokine analysis.

## P1-019

**A review of our pediatric rheumatology outpatient clinic**

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Conflict of interest: None

[Objective] Early detection and treatment of pediatric rheumatic diseases is important, and treatment must be continued from childhood into adulthood. We have established a pediatric rheumatology outpatient clinic. [Methods] 35 patients under 18 years of age who attended our pediatric rheumatology outpatient clinic from April 2022 to September 2023 were reviewed. [Results] 19 patients were diagnosed with and suspected of having a rheumatic disease. Of these, 7 patients were newly diagnosed in our clinic. Patients were referred by medical institutions (12 patients), websites (6 patients), and friends (1 patient). The details of rheumatic diseases are juvenile idiopathic arthritis (4 patients), systemic lupus erythematosus (3 patients), PFAPA syndrome (3 patients), dermatomyositis (2 patients), and Sjogren's syndrome, mixed connective tissue disease, and microgeodermatitis (1 patient each) [Conclusions] Few parents chose the collagen disease unit because of fever and other symptoms, suggesting the need for closer collaboration with local pediatric units. The number of patients newly diagnosed at clinic was relatively high and the diseases varued. Many of the patients were in the age group with remarkable development. Ongoing support is therefore needed to match the timing and growth of each patient.

## P1-020

**Investigation about the use of DMARDs results for patients with rheumatoid arthritis in our hospital**

Shin Furukawa
Internal Medicine, Kushiro Red Cross Hospital

Conflict of interest: None

[Objective] Eastern Hokkaido district secondary care area is about 300,000 population. It is two rheumatic specialist full-time employment and part-time service system 2 times in the month at our hospital. It was intended to grasp our local rheumatic medical treatment state by an investigation by the use of DMARDs results of our hospital. [Methods] By medical information system of our hospital electronic chart, I investigated a change of rheumatic medical treatment information from February, 2002 to December, 2022. [Results] The target rheumatic number of patients was 660 in 2002 survey first year, increased to 1715 in 2022. Dosage results in 2022 of csDMARDs: MTX850, SASP63, IGU351, TAC180, MZR98, BU2. Dosage results in 2022 of bDMARDs: IFX36, ADA67, ETN11, GOL66, CZP5, ABT54, TCZ115, SAR7. Dosage results in 2022 of tsDMARDs: TOFA17, BARI36, PEFI4, UPAD2, FILG10. [Conclusions] The rheumatic number of patients of our hospital suddenly increased from 2018. The rheumatic specialist who worked in a neighboring hospital was retired from, and this was because that rheumatic patients moved in our hospital. So, support of rheumatic care nurses and the rheumatic foundation registration pharmacists is in an indispensable situation.

## P1-021

**Real-world Practice of nintedanib (NTB) for connective tissue disease-associated interstitial lung disease (CTD-ILD)**

Yosuke Sakamoto[1], Tomoki Tanaka[1], Ayano Ando[1], Nao Tsugita[1], Keisuke Ikeda[1], Yosuke Iwadate[1], Nana Kinoshita[1], Shunsuke Kyoda[1], Hirotomo Asakura[1], Eri Shishido[1], Kosuke Shimode[1], Risa Shindo[1], Kazuma Ino[1], Yoshiro Kanayama[1], Junichi Kondo[1], Takumi Muramatsu[1], Yasuhiro Hasegawa[1], Yu Matsueda[1], Tatsuhiko Wada[1], Yoshiyuki Arinuma[1], Jun Okada[1], Kenji Oku[1], Sumiaki Tanaka[1,2], Kunihiro Yamaoka[1]
[1]Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, [2]Division of Rheumatology, Kitasato University Medical Center

Conflict of interest: None

[Objective] The purpose of this study was to clarify the treatment with NTB and the factors leading to discontinuation in a real-world setting in our department. [Methods] We analyzed the retention rate and factors leading to discontinuation of NTB in CTD-ILD patients treated with NTB at our department from April 2020 to July 2023. [Results] The median age of the 45 patients analyzed was 55 years, and the main underlying diseases were SSc, PM/DM and RA. The major adverse events were gastrointestinal symptoms. Twenty-five patients discontinued within 1 year of initiation, mainly due to gastrointestinal symptoms. Comparing the continuation group with those who discontinued due to gastrointestinal symptoms, the mean age of the continuation group was significantly younger than that

of the discontinuation group. 55% (11/20) of the continuation group and 33% (6/18) of the discontinuation group started NTB at the initial dose of 300 mg/day and 200 mg/day or less, respectively, showing a tendency for more patients to continue NTB at the initial dose of 300 mg/day. [Conclusions] Although there were numbers of discontinuations due to gastrointestinal symptoms, our results suggests that the initial dose adjustment of NTB may not contribute to drug persistency.

## P1-022

**Investigation of clinical course of patients with rheumatic diseases receiving azathioprine**

Aiko Hirano, Takashi Kida, Shunsuke Fujieda, Junya Kitai, Masayuki Yoshioka, Motoko Hanatani, Hironori Inoue, Takuya Yanagida, Satoshi Omura, Yuichiro Nakanishi, Akiko Kasahara, Naoka Kamio, Kazuki Fujioka, Wataru Fujii, Takahiro Seno, Makoto Wada, Masataka Kohno, Yutaka Kawahito
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Conflict of interest: None

[Objective] While azathioprine (AZA) is widely used for refractory rheumatic diseases, recent approvals of novel therapeutics have broadened the therapeutic options. We investigated the status of AZA use within our department post-initiation of NUDT15 genotyping test. [Methods] We evaluated the clinical course of patients who started AZA between February 2019 and September 2023 based on their electronic medical records. [Results] The number of patients who newly started AZA was 86 (female: 65%; median age: 69 years; 56 patients with vasculitis, 11 with myositis, 4 with systemic lupus erythematosus, and 15 with other diseases) and 35 patients started AZA as the first-line therapy. The NUDT15 gene genotyping was conducted for 51 patients (90% ARG/ARG and 10% ARG/CYS). The one-year retention rate for AZA was 42%. AZA was discontinued in 40 patients within 24 weeks; the primary reason was hepatic injury (55% (22/40 patients)) (median time to onset: 52 days) and the second reason was inadequate response (18% (7/40 patients)). The median reduction in glucocorticoid (GC) dose was 3 mg/day (24 weeks). [Conclusions] Despite AZA's GC-reducing effect, many patients stopped it early. Hepatic injury remains a concerning adverse effect of AZA, irrespective of the NUDT15 gene polymorphism.

## P1-023

**A case of SLE involving a patient with azathioprine-induced anaphylactic shock**

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Conflict of interest: None

[Case] A 37-year-old female [Chief complaints] Fever, chills, low back pain [Medeical history] At the age of 10, she developed systemic lupus erythematosus (SLE). She was being treated with belimumab, betamethasone, hydroxychloroquine, and tacrolimus. Peripheral circulation disorder and fingertip ulcers began to appear from 3 years ago. For initiation of bosentan, tacrolimus was changed to azathioprine (AZP) from 4th/X. On 20th/X, she visited our hospital due to fever, left lower back pain, and leg edema. She showed facial flushing and her systolic blood pressure was 60-mmHg range. Septic shock due to pyelonephritis was suspected, and she was treated with noradrenaline and meropenem. As her symptoms improved, she then resumed AZP, and was discharged on 28th/X. However, on the same day, she developed fever, chills, and back pain again. Her vitals were in shock, her face, neck, and chest were flushed, and her peripherals were cold. It was suspected that she had AZP-induced anaphylactic shock. She was treated with adrenaline, antihistamines, and corticosteroids, and she recovered. [Discussion] Anaphylactic shock due to azathioprine is rare but can cause serious symptoms. We will compare this case with previous reports, and report it for reference when using AZP in the future.

## P1-024

**Improvement of peripheral neuropathy associated with eosinophilic granulomatosis with polyangiitis by intravenous immunoglobulin (IVIg): a report of two cases**

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Division of Rheumatology, Department of Internal Medicine, National Hospital Organization Nagoya Medical Center

Conflict of interest: None

[Case 1] A-4X-year old female has past history of asthma. She complained of lower limbs neumbness and pain in 20XX-2. Her ankles presented dorsiflexion and plantarflexion disorder. The results of the nerve conduction study showed tibial, peroneal and sural nerve damage. Her eosinophil increased to 7100/μL. She was diagnosed with EGPA. She was treated with and predonizolone (PSL) 1 mg/kg/day and IVIg twice, but peripheral neuropathy didn't resolve. We administered mepolizumab and third IVIg, peripheral neuropathy improverd. [Case 2] A-4X-year old female. She was suspected to have eosinophilic fasciitis in and treated with PSL0.5 mg/day. In 20XX-2, her eosinophil count increased and numbness appeared in both palms and fingers, and grip strength in both hands decreased. Nerve conduction study revealed median and ulnar neuropathy, and based on history of asthma, she was diagnosed with EGPA, and IVIg was performed. The grip strength in both hands improved and the numbness was limitted to the fingers. [Conclusion] Peripheral neuropathy associated with EGPA is resistant to treatment and IVIg is effective. In our cases, peripheral neuropathy improved by administration of IVIg early after the onset of symptoms. We think it was important to diagnose and treat peripheral neuropathy associated with EGPA early.

## P1-025

**Successful treatment with IVIg for a case of EGPA complicated with myocarditis relapsed even on both high dose steroid and cyclophosphamide**

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Department of Rheumatology, Suita Municipal Hospital

Conflict of interest: None

[Case] A 71-year-old man with a history of asthma presented to our hospital for weight loss, numbness in upper and lower limbs, myalgia in left lower limb. Mononeuritis multiplex, elevated CRP (6.11 mg/dL), and eosinophilia (7165/μL) led to the diagnosis of EGPA. As elevated troponin T and contrast-enhanced MRI indicated coexistent myocarditis, combination therapy with high dose steroid and IVCY was initiated promptly, resulting in stopping worsening of neurological symptoms, normalization of CRP and disappearance of eosinophilia. EF on echocardiography improved from 50% to 59%. After reducing PSL to 50 mg, CRP reelevated to 0.67 mg/dL and eosinophil rose to 144/μL, suggesting a mild flare of EGPA. Soon after increment of PSL to 60 mg and employment of IVIg, negative CRP and eosinophil disappearance were achieved. It is notable that the dose of PSL could be rapidly reduced this time to 50 mg, and then 40 mg weekly. [Clinical Significance] IVIg therapy for EGPA has been reported to be effective against peripheral neuropathy. However, there has been few reports on the its effects on myocardial damage or on the steroid sparing effects for refractory patients who relapsed during high-dose steroid use. Our case suggests IVIg could be used successfully for such patients.

## P1-026

**Outcomes of total hip arthroplasty in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The present study was undertaken to investigate outcomes of total hip arthroplasty in patients with RA. [Methods] This study includ-

ed 1255 hips (932 osteoarthritis, 130 idiopathic osteonecrosis of the femoral head, 117 RA, and 76 femoral neck fracture) who underwent primary THA in Nagoya Medical Center from September 2009 to July 2022. We examined the implant survivorship of THA in patients with RA compared with non-RA. [Results] Revision THA was underwent in 34 hips (2.7%). The incidence of primary THA in patients with RA decreased over time (2009-2012: 16.4%, 2013-2016: 8.7%, 2017-2019: 5.6%, 2020-2022: 4.1%). The risk for revision THA due to aseptic loosening was significantly higher in RA (HR: 8.0, 95%CI: 2.68-23.88) and femoral neck fracture (HR: 5.1, 95%CI: 1.23-21.24) compared with OA. [Conclusions] Although the incidence of primary THA in patients with RA decreased, RA patients still have the risk for aseptic loosening after total hip arthroplasty.

## P1-027

**The middle-term results of total hip arthroplasty for rheumatoid arthritis**

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Conflict of interest: None

The middle-term results of total hip arthroplasty for rheumatoid arthritis Objective. The purpose of this study was to evaluate the clinical outcomes of total hip arthroplasty (THA). Patients and Methods We conducted a retrospective survey of primary THA performed between 2006 and 2018 based on medical records. The survey items included age at surgery, gender, implant type, complications, reoperation, and reason for reoperation. Results. There were 58 THA cases performed during the study period, age at surgery: 66.7±8.3 years, 10 males and 48 females, mean follow-up: 5.7±4.0 years. All implants were cemented stems, 44 cemented cups and 14 cementless implants on the acetabular side, and the JOA score improved significantly from 44.1 preoperatively to 69.4 at the last follow-up ($P<0.05$). Complications included dislocation in 2 cases (3.4%) and peri-prosthetic femur fracture in 1 case (1.7%), and revision was performed only in the dislocated case. 10-year survival was 90% with all revisions as endpoints and 100% with revision for aseptic loosening. Discussion. Excellent mid-term results of THA for rheumatoid arthritis have been reported for both cemented and cementless THA, and the results of cemented THA and hybrid THA in this study were stable.

## P1-028

**Study on short-term postoperative results of total hip arthroplasty in elderly aged 75 and over**

Toki Takemoto, Takeshi Oguchi, Kaori Sato, Shiro Urata
Department of Orthopedic Surgery, Anjo Kosei Hospital, Aichi, Japan

Conflict of interest: None

[Objective] We investigated whether muscle mass and gait speed are associated with postoperative outcomes in patients with THA in elderly patients. [Methods] Among the THA cases performed at our hospital, 63 patients with OA were investigated (the elderly (Group E), under 75 years old (Group C)). Based on the AWGS2019 sarcopenia diagnostic criteria, SMI <5.7 kg/m2 was considered low, and gait speed <1 m/s was considered low. [Results] Patients with low muscle mass had low BMI and GNRI values in both groups E and C, but there was no difference in outcomes. Regarding low gait speed before surgery, hospitalization periods and number of days able to walk with a cane was significantly longer in Group C. In Group E, most cases have low gait speed. Patients who were able to walk with a cane early after surgery had significantly better hospitalization periods and JOA scores after 6 months, and their gait speed tended to be faster. [Conclusions] Although it is possible that patients with low muscle mass are in worse condition, there was no significant difference in outcomes. In group E, it was considered that walking speeds lower than 1 m/s could be useful indicator for good postoperative outcomes in elderly patients.

## P1-029

**Examination of prosthetic joint infection risk factor in metal-on-metal total hip arthroplasty**

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Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Mie, Japan

Conflict of interest: None

[Objective] It has been reported that metal-related events (ARMD) occur frequently in metal-on-metal total hip arthroplasty (MOM-THA), but it may be difficult to differentiate them from postoperative infection. We compared periprosthetic joint infection (PJI) cases of MOM-THA cases with ARMD cases. [Methods] The subjects were 247 joints of 230 MOM-THA cases performed at our department from 2006 to 2011. The average age at the time of surgery was 64.1 years (34-85), and the average observation period was 10.5 years. [Results] Seven patients infected 9 joints (3.6%), and the underlying diseases were osteoarthritis (OA) in 6 joints and rheumatoid arthritis (RA) in 3 joints. Revision THA was performed at an average of 6.9 years and a median of 3.6 years (1.9-14.7 years) after the initial THA surgery. After revision an average of 8.7 years, there was no relapse of infection. When compared with 28 patients (28 joints; 11.3%) who underwent revision for ARMD, the CRP value and white blood cell count before revision were significantly higher in infected cases. There were significantly more RA cases among infected case. [Conclusions] In MOM-THA cases, patients with RA and elevated CRP and white blood cell counts should be examined and treated with consideration to the onset of infection.

## P1-030

**Risk factors for dislocation after total hip replacement using the supine anterolateral approach**

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Department of Orthopaedic Surgery, Tohoku University Graduate School of Medicine

Conflict of interest: None

[Objective] The rate of postoperative dislocation has decreased with the use of the supine anterolateral approach to total hip arthroplasty (ALS-THA), but the risk factors for dislocation have not been established. In this study, we retrospectively investigated postoperative dislocation after ALS-THA performed at our hospital. [Methods] The subjects were 226 groins (180 patients) who underwent ALS-THA between June 2013 and November 2021, 47 males (37 patients) and 179 females (143 patients). The mean age at surgery was 64.1 years and the mean observation period was 1 year and 11 months. The underlying diseases were osteoarthritis (OA) in 160 hips, osteonecrosis of the femoral head (AN) in 63 hips and fracture of the neck of the femur (FNF) in 3 hips. The causes of dislocation and the size and placement of implants were investigated. [Results] The dislocation rate of first THA in our department was 2.6% (6/226). Disorder-specific dislocation rates were 0.6% (1/160) for OA, 7.9% (5/63) for AN and 0% (0/3) for FNF. There were no significant differences in placement of implants between the groups. [Conclusions] Particular attention should be paid to hyperflexion and hyperextension within the first postoperative month and to postoperative falls in ALS-THA with AN as the primary disease.

## P1-031

**Six months postoperative clinical outcomes of total hip arthroplasty using UNIVERSIA stem in three rheumatoid patients with destructive hip joints**

Kazuyoshi Mitani, Yasuhiro Terashima, Koji Tateishi, Takahiro Suzuki
Department of Orthopaedic Surgery, Kohnan Kakogawa Hospital

Conflict of interest: None

[Object] We recently encountered 3 RA patients who got surgery of THA usinig UNIVERSIA stem, and we report six months postoperative clinical outcomes of them. [Case 1] A 64-year-old woman with RA complained right hip pain. Before THA, JOA hip score for hip function was 43, and JHEQ was 20. Six months after THA, JOA hip score was 84, and

JHEQ was 64. In radiograph, spot welds appeared around the stem and another bone reactions didn't appear. There were no postoperative complications. [Case 2] A 78-year-old man with RA complained right hip pain. Before THA, JOA hip score was 61, and JHEQ was 31. Six months after THA, JOA hip score was 84, and JHEQ was 80. In radiograph, no bone reaction appeared. There were no postoperative complications. [Case 3] A 79-year-old woman with RA complained left hip pain. Before THA, JOA hip score was 54, and JHEQ was 18. Six months after THA, JOA hip score was 87, and JHEQ was 68. In radiograph, spot welds appeared around the stem and another bone reactions didn't appear. There were no postoperative complications. [Clinical Significance] In this study, there was no bone reaction without spot welds and no postoperative complication including thigh pain, so we found that THA using UNIVERSIA with RA patients could get good postoperative clinical outcomes.

## P1-032

**A case of cTAA for ankle OA with Seronegative RA**

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Department of Orthopaedic Surgery, St. Marianna University School of Medicine

Conflict of interest: None

[Background] Combined total ankle arthroplasty (cTAA) is indicated for ankle osteoarthritis (OA) patients with OA in adjacent joints and those at high risk of talus fracture. We report a case of cTAA for an OA ankle joint that developed seronegative RA during the preoperative period. [Case description] A 74-year-old woman had been treated conservatively by her local doctor with a diagnosis of OA of the ankle joints. X-rays revealed end-stage OA and CT and MRI showed OA changes in the subtalar joint and numerous cystic lesions. During an outpatient clinic for preoperative evaluation, the patient developed worsening pain and edema, and Seronegative RA was diagnosed as polyarthritis with upper extremity edema over time. Anti-rheumatic drugs were introduced, and cTAA was performed after RA's improvement. After the surgery, there was no recurrence of RA. [Discussion] It has been reported that cTAA can provide good hindfoot flexibility even in patients with arthropathic changes in the subtalar joint by replacing the entire talus. In this case, OA changes were observed in the subtalar joint, and there were concerns about the progression of joint destruction due to RA, but we believe that good treatment results were obtained by combining talus replacement with OA.

## P1-033

**Two cases of salvage surgery with retrograde intramedullary nail with auto or allogeneic femoral head bone grafting for loosening after total ankle arthroplasty (TAA) in patients with rheumatoid arthritis (RA)**

Sho Kuwazoe[1], Yuya Takakubo[2,3], Suran Yang[2], Yoshihiro Wanezaki[2], Masashi Aso[2], Ryusuke Honma[4], Yasushi Naganuma[5], Akiko Sasaki[6], Hiroshi Orui[7], Michiaki Takagi[2,3]
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Conflict of interest: None

[Objective] The aim of this study was to report salvage surgeries using a retrograde intramedullary nail in combination with autogenous or allogeneic femoral head bone grafting for TAA loosening in two patients with RA [Case 1] The patient is an 83-year-old male. His duration of RA was 34 years. Three years ago, TAA was performed for his left ankle joint. However, a salvage procedure was performed using a retrograde intramedullary nail in combination with an autologous femoral head graft due to TAA loosening and sinking of talar implant. Bone union had been achieved at 11 weeks. The JSFF-RA improved from 26 points preoperatively to 68 points at 14 months postoperatively. [Case 2] The patient is a 76-year-old female. Her duration of RA was 15 years. Six years ago, a TAA was performed for her right ankle joint. However, a retrograde intramedullary nail was used in combination with a homologous femoral head to perform salvage surgery due to TAA loosening and a fracture of her ankle. Bone union had been achieved at 9 weeks. the JSSF-RA improved from 38 points preoperatively to 70 points at 2 months postoperatively. [Conclusions] Retrograde intramedullary nailing with a femoral head grafting for loosening after TAA relieves pain and improves walking ability in patients with RA.

## P1-034

**Risk factors for recurrence after modified scarf and Akin osteotomy for hallux valgus deformity in rheumatoid arthritis**

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Conflict of interest: None

Objective To investigate recurrence risk after modified scarf and Akin osteotomy for hallux valgus deformity in rheumatoid arthritis (RA). Methods A retrospective study was conducted on 49 feet of 41 patients who underwent modified scarf and Akin osteotomy for hallux valgus deformity in RA. Recurrence defined as (Hallux Valgus Angle (HVA) more than 20 ° at the 2 years after surgery. Results HVA significantly improved from 46° preoperatively to 8.4°. Nine feet (7 patients) experienced recurrence. Significant differences existed in preoperative M1/M2 angle ($p<0.01$), M1/M5 angle ($p<0.01$), T1-MT angle ($p=0.025$), and Hardy grade ($p=0.03$) between the recurrence and non-recurrence groups. Multivariate logistic regression analysis showed significant differences in the preoperative M1/M5 angle (odds ratio=0.94, $p=0.044$) and T1-MT angle (odds ratio=1.11, $p=0.048$). When comparing preoperative Hardy grade 7 with those of 6 or less (Fisher's exact test), postoperative recurrence was significantly higher in the preoperative Hardy grade 7 group ($p=0.041$). Conclusions Preoperative open foot, flat foot, and sesamoid position represent risk factors for recurrence after modified scarf and Akin osteotomy for hallux valgus deformity in RA.

## P1-035

**Perioperative withdrawal period of janus kinase inhibitors in patients with rheumatoid arthritis who underwent joint surgery**

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Conflict of interest: None

[Objective] BOur Department has been performing orthopedic surgery on RA patients receiving JAK inhibitors since 2015, and has gradually shortened the withdrawal period while confirming safety. In this study, we report a review of perioperative management in 11 RA patients on JAK inhibitors. [Methods] The 11 patients underwent surgery between January 2020 and May 2023 while receiving JAK inhibitors. 4 patients underwent wrist arthroplasty 2 patients underwent wrist arthroplasty, 1 patient underwent finger arthroplasty, 1 patient underwent shoulder synovectomy, and 3 patients underwent TKA. 6 patients were treated with tofacitinib, 3 with baricitinib, and 2 with filgotinib. [Results] The mean perioperative withdrawal period was 6.7 days for the 11 patients, no SSI occurred, and DWH was observed in one patient. Symptom flare-ups were observed in 3 patients, and the onset of symptoms was observed an average of 9.3 days after drug withdrawal. [Conclusions] The Japan College of Rheumatology Guidelines for Rheumatoid Arthritis 2020 does not include information on perioperative withdrawal of JAK inhibitors. Although the perioperative management was generally good in this case, we will discuss the appropriate period of perioperative drug withdrawal, including a review of the literature.

## P1-036

**Five cases of rheumatoid arthritis patients taking JAK inhibitors who underwent limb surgery**

Toshiharu Okuda

Okuda Orthopedic Clinic

Conflict of interest: None

[Purpose] we investigated the postoperative course of a patient with rheumatoid arthritis (RA) who underwent surgery while taking JAK inhibitors. [Method] The subjects were 5 cases (5 women, mean age 65.2 years) who underwent orthopedic surgery while receiving JAK inhibitors (baricitinib 3 tofacitinib 1 upadacitinib 1). Disease activity (DAS28-CRP) at the time of surgery was in remission in all cases. The surgeries included 2 cases of finger (2-5) MP arthroplasty, 1 case of wrist arthroplasty, 1 case of finger PIP arthroplasty, and 1 case of toe arthroplasty. The drug was administered for 7 days and resumed after the wound had healed. [Results] There were no cases in which relapse of RA activity was observed due to drug discontinuation before or after surgery. Furthermore, no complications such as postoperative infection or delayed wound healing were observed. Two patients who underwent finger MP joint arthroplasty and one patient who underwent toe arthroplasty achieved cosmetic and functional improvements. [Conclusion] Surgical treatment such as limb arthroplasty and synovial resection is recommended in RA patients who have limb deformity and residual swelling and pain in small joints even if the disease activity is clinically stabilized with the use of JAK inhibitors.

## P1-037

**Current status of hip joint destruction modes in Rheumatoid Arthritis**

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Department of Orthopaedic Surgery, Saitama Medical University Hospital, Saitama, Japan

Conflict of interest: Yes

[Objective] The purpose of this study is to investigate the current status of RA-THA in our hospital in recent years. [Methods] From November 2020 to October 2023, 429 THA joints were performed at our hospital. Of these, 25 cases with 28 joints (6.5%) were included during RA treatment. The average age was 70 years, males: 3 cases with 3 joints, females: 22 cases with 25 joints. [Results] The mean disease duration from RA onset to THA was 10.6 years. Medications were MTX: 15 patients (60%, 4-12 mg/week), steroids: 10 patients (40%, 1-7.5 mg/day), bDMARD: 3 patients (12%). CRP on admission averaged 0.47 mg/dl, and 14 joints (50%) were within the normal range. Preoperative pelvic radiographs were typical rheumatoid arthritis in 13 joints, osteoarthritis with acetabular dysplasia in 6 joints, RDC-like joint destruction in 5 joints, femoral neck fracture in 3 joints, and traumatic osteonecrosis of the femoral head in one joint. [Conclusions] In recent years, the use of MTX has increased in RA-THA, and the proportion of patients with typical rheumatoid arthritis of the hip joint is decreased. On the other hand, RA-THA in cases of secondary osteoarthritis of the hip joint with acetabular dysplasia or RDC, which may be due to bone fragility, is currently on the increase.

## P1-038

**Validation of the Coronal Plane Alignment of the Knee classification (CPAK) in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the distribution of Coronal Plane Alignment of the Knee (CPAK) classification in patients with rheumatoid arthritis (RA) and to examine differences by gender. [Methods] 300 knees in 159 patients with RA were included in this study. LDFA and MPTA were measured on full-length standing frontal X-ray images of lower extremities, and arithmetic HKA (aHKA=MPTA-LDFA) and Joint Line Obliquity (JLO=MPTA+LDFA) were calculated and classified. Patient background and gender differences in each parameter were compared. [Results] 300 knees were classified as Type I: 32.7%, II: 51.7%, III: 11.0%, IV: 1.7%, V: 2.3%, VI: 0.7%, VII, VIII, IX: 0%. There were significant differences in height (166.7 cm vs. 153.8 cm, $p<0.01$) and weight (65.4 kg vs. 54.9 kg, $p<0.01$) between males and females, but not in age or BMI. There were also significant differences in MPTA (85.1 vs. 86.0), LDFA (86.6 vs. 87.1), and JLO (171.6 vs. 173.0), but not in aHKA (-1.5 vs. -1.1). [Conclusions] The distribution of CPAK classification in this study differs from previous studies of osteoarthritis in Japan. It is important to evaluate radiographs at a time of minimal deformity in order to know the innate alignment.

## P1-039

**Risk factors for delayed diagnosis of rheumatoid arthritis in the knee joint**

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Conflict of interest: None

[Purpose] We examined risk factors for delayed diagnosis of rheumatoid arthritis (RA) in the knee joint. [Patients and Methods] The main symptoms were knee arthritis and knee joint pain, and 29 cases and 48 knees were diagnosed as RA. The time required for diagnosis was 6.5 months. The patients were divided into two groups: 25 knees whose time from initial diagnosis to RA diagnosis was less than 6 months (early diagnosis group) and 23 knees whose time from initial diagnosis to RA diagnosis was 6 months or more (delayed diagnosis group), and risk factors for delayed diagnosis were examined. [Results] Age was younger in the early diagnosis group, 65.4 years in the early diagnosis group and 69.7 years in the delayed diagnosis group. The proportion of cases with other joint symptoms was higher in the early diagnosis group, at 56% and 26%, respectively. CRP at the first visit was 4.3 and 4.4, with no difference. RF value 74, 44 IU/mL, anti-CCP antibody 207, 50 U/mL, percentage meeting classification criteria 80%, 56.5%, CDAI 23, 19, all of which were higher in the early diagnosis group. [Conclusion] Diagnosis of initial knee joint RA is often difficult, especially when localized to the knee joint or when the patient is seronegative, tending to take time to make a definitive diagnosis.

## P1-040

**Experience with high tibial osteotomy for patients with rheumatoid arthritis**

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Department of Orthopaedics Surgery School of Medicine Toho University

Conflict of interest: None

We report a case in which opening wedge high tibial osteotomy (OW-HTO) was performed for knee joint disorder associated with RA, and good clinical results were obtained. The patient is a 48-year-old woman. Three years ago, OW-HTO was performed on her right knee at another hospital with a diagnosis of knee osteoarthritis. After the surgery, her pain did not improve, so she visited our department. When she was first seen at our department, she had swelling and pain in multiple joints, so a detailed examination led to the diagnosis of RA. She was treated with methotrexate and adalimumab, and her disease activity improved. One year after starting treatment at our department, she had a pain in her left knee joint, which interfered with her daily life. Plain X-ray images of her left knee showed Larsen grade 2, so OW-HTO was performed, and the postoperative pain was alleviated, and the KOOS pain score improved from 33.3 points preoperatively to 88.9 points postoperatively. Arthroscopic findings during the second look showed cartilage regeneration. Joint-preserving arthroplasty may be an option for surgical treatment for patients with knee joint disorders associated with RA in relatively young patients, as long as low disease activity can be maintained.

## P1-041

**Cause and Risk Factor for Revision Surgery After Thoracolumbar Posterior Spine Fusion for Patients with Rheumatoid Arthritis**

Hirofumi Bekki[1], Takuya Oda[1,2], Tetsuya Tamaru[1], Atsushi Kimura[1], Masamitsu Hara[1], Koji Sakuraba[1], Yasuharu Nakashima[2], Junichi Fukushi[1]
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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patient has the risk of revision surgery after spine fusion due to the bone erosion or osteoporosis. There are few reports regarding the outcome of thoracolumbar posterior spine fusion for patients with RA. [Methods] A total of 193 patients underwent thoracolumbar posterior spine. We examined the detail and risk factor for the Revision Surgery (Re) group. The alignment of spine was measured by using X-ray preoperatively and one year after the operation. The clinical and radiographic data were compared with who didn't require second operations (Ctrl group). [Results] The Re-group consisted of 56 cases (29%), who underwent additional operation in three years on average. Adjacent segment diseases were the most frequent cause of revision surgery (50%). For the Re-group, the number of fixed vertebral bodies were larger than Ctrl group (3.5 vs 2.7), and the scoliosis angle was improved postoperatively (4.2 vs 1.8). Disease activity of RA and dose of prednisolone were similar between both groups. [Conclusions] Risk factors for revision surgeries were wide range of fixation and the overcorrection of scoliosis. The timing of surgery may be determined appropriately to reduce the range of fixed vertebral bodies and prevent the overcorrection of scoliosis.

## P1-042

**Arthroscopic Bone Grafting for Lunate Fracture with Intraosseous Ganglion Cyst: A Case Report**

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Conflict of interest: None

[Backgrounds] Symptomatic wrist intraosseous ganglions are treated by arthroscopic curettage and bone grafting. We report a case of intraosseous lunate ganglion accompanied by lunate fracture treated under arthroscopy. [Case] A 60-year woman. She had a month of right wrist pain. X-ray and CT scan confirmed a cystic lesion inside the lunate with a thin and partially deficit cortex. Surgical treatment was performed under arthroscopy. The cartilage of the lunate was normal but easily depressed with a probe. This indicated the fracture. The synovial wall of the lesion was curated. The cavity was packed with cancerous bone from the iliac crest through a needle cap. CT scan at 6 months postoperatively showed bone union. 1 year postoperatively, the patient regained normal grip strength and range of motion. qDASH improved from function: 22.7 and work: 25 to both 0. HAND20 improved from 31 to 0. [Clinical Significance] An intraosseous ganglion differs from a secondary bone cyst in osteoarthritis and rheumatoid arthritis in that there is no chondral lesion. The ganglion with fracture can be treated under arthroscopy. Previous reports recommended the use of a soft-tissue protector or a trocar. We used a needle cap without preparing a special device. This technique is easy and low-cost.

## P1-043

**A case of Sjogren's disease carrying isolated anti-SSB/La antibodies that was diagnosed by salivary sonography and labial salivary gland biopsy**

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Conflict of interest: None

[Background] Isolated anti-SSB/La antibodies are rare in Sjogren's disease. In this case, although isolated anti-SSB/La antibodies were positive and the titer was low, Sjogren's disease was diagnosed. [Case] The patient was a 45-year-old woman who showed subclinical hyperthyroidism from the symptom of fatigue. Thyroid sonography performed by an endocrinologist coincidentally revealed hypoechoic area in the salivary glands. Thereafter, her laboratory data showed isolated anti-SSB/La antibodies with a low titer. She was therefore referred to a rheumatologist. Saxon's test results were 1.9 g per 2 minutes, and Schirmer's test showed 3 mm per 5 minutes. Labial salivary gland biopsy showed 7 foci in 11 specimens. Sjogren's syndrome was confirmed by these results. [Key message] If the antibody profile is atypical and its titer is low, work up for Sjogren's disease should be done, when we think pretest probability is high.

## P1-044

**A case of Sjögren's syndrome complicated by mesenteric lipoatresia**

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Conflict of interest: None

[Case] Female, 73 years old [Chief complaint] Abdominal pain [Recent medical history] The patient was referred to our hospital 3 months ago due to persistent abdominal pain for 9 months. The patient had undergone endoscopic resection of gastric adenoma and anal cancer, respectively, but the abdominal pain continued and the patient had a fever for 2 weeks. She underwent additional workup and ceCT that revealed increased contrast enhancement of mesenteric membrane and multiple enlarged mesenteric lymph nodes. Mesenteric lymph node biopsies showed mesenteric infiltrates of lymphocytes, plasma cells, and foam cells, indicating that the site of inflammation was the mesenteric rather than the lymph node. Bacteriology was negative. Additional testing showed antinuclear antibodies 320x (speckled) and anti-SS-A antibodies >240 IU/mL. A lip biopsy was performed and Sjögren's syndrome was diagnosed. IgG4 was not elevated (IgG 2181 mg/dL, IgG4 < 5 mg/dL). Prednisolone 30 mg/day was started and the abdominal pain and fever improved. In this case, the absence of findings consistent with infection or malignancy led us to suspect an autoimmune mechanism. Mesenteric lipoiditis associated with Sjögren's syndrome is rare, and this case is considered a valuable case.

## P1-045

**A case of leukoencephalitis in a patient with Sjögren's syndrome requiring differentiation from brain tumor and positive MOG antibody in spinal fluid**

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Conflict of interest: None

A 33-year-old woman was diagnosed with Sjögren's syndrome (SS). She was admitted to the hospital two weeks prior to admission because MRI showed contrast effects in the bilateral temporal lobes, parietal lobes, and periventricular areas of the lateral ventricles. The MRI showed enlarged areas of T2WI/FLAIR high signal in the bilateral cerebral white matter, suggesting autoimmune encephalitis or lymphoma. An open brain biopsy was performed, pathological findings showed leukoencephalitis, marked plasma cell infiltration, and myelin oligodendrocyte glycoprotein (MOG)-predominant myelin sheath loss. Spinal fluid analysis also revealed MOG antibody positivity, suggesting that the patient had a combination of features of both autoimmune encephalitis due to SS and MOG antibody-associated disease. After starting steroid pulse and PSL 1 mg/kg, MMSE and FAB were improved, but the loss of computation remained, but the edematous lesions on head MRI were reduced and the loss of computation was improved with rituximab. We have experienced a case of leukoencephalitis in a patient with positive spinal fluid MOG antibody and SS background. Although there have been reports of MOGAD combined with SS, we report here a case in which both elements were found in a brain biopsy.

## P1-046

**A case of TAFRO syndrome complicated by Sjögren's syndrome**

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[1]Shizuoka Hospital, Juntendo University School of Medicine, [2]Juntendo University School of Medicine Juntendo Hospital

Conflict of interest: None

[Case] 34-year-old female [Chief complaints] Fever, abdominal distension, lower limb edema [Present history] In September X, she was raced to our hospital with fever and abdominal distension. As a result of close examination, Blood samples showed increased inflammatory response and thrombocytopenia, and plain CT showed pleural and ascitic effusion, hepatosplenomegaly, and multiple lymph node enlargements, and eventually she was admitted to our hospital. [Course after hospitalization] After starting antibiotics, there was little improvement in fever and increased inflammatory response and progressive renal damage and increased ascites were observed. As a result of various examinations, the diagnosis was a combination of TAFRO syndrome and Sjögren's syndrome. Treatment with high-dose glucocorticoids and tocilizumab were administered and Cell-free Concentrated Ascites Reinfusion therapy (CART) was performed for severe ascites. After the treatment, various findings and symptoms were improved. [Discussion] TAFRO syndrome is an extremely rare disease with many treatment-resistant cases and still have no established treatment yet. Based on literature review, we report on the coarse of treatment.

## P1-047

**A case of Sjogren's syndrome associated with protein-losing gastroenteropathy treated with high dose corticosteroids and intravenous cyclophosphamide**

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Conflict of interest: None

[Case] A 57-year-old woman was referred to our hospital for further investigation of a two-week history of abdominal distention, anorexia and dyspnea on exertion. Computed tomography scan demonstrated bilateral pleural effusion, which was tapped and classified as transudative base on Light's criteria. Serum biochemistry and urinalysis showed hypoalbuminemia (2.2 g/dL), normal liver function and mild proteinuria (1 g·g/Cr). Immunological tests showed hypocomplementemia and anti-SSA and anti-SSB antibody positivity. 99mTc-HSA-D scintigraphy detected protein leakage from gastrointestinal tract. Salivary gland dysfunction was detected by salivary gland scintigraphy. From these findings, she was diagnosed with Sjogren's syndrome associated with protein-losing gastroenteropathy (PLGE). The administration of high dose corticosteroids and intravenous cyclophosphamide (IVCY) gradually improved her anasarca, and hypoalbuminemia. [Discussion] In most of the previous case reports, Sjogren's syndrome associated with PLGE has been treated with moderate to high dose corticosteroid monotherapy. In our case, high-dose corticosteroids and IVCY were required because of the rapid progression of her disease.

## P1-048

**Treatment results of JAK inhibitors in PMR patients**

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Conflict of interest: Yes

[Purpose] To investigate the treatment results of patients using JAKi for PMR. [Methods] Disease activity in PMR patients was evaluated using PAIN-VAS and the doses of CRP, ESR, MMP3 and glucocorticoid (GC). Missing data were filled in using LOCF (last observation carried forward). [Results] There were 10 PMR patients (6 males) who used JAKi, mean age at onset: 77.0 years, mean CRP: 9.36 mg/dl, mean MMP-3: 305 ng/ml, average RDCI (rheumatic disease comorbidity index); 2.5. The JAKi were upadacitinib in 9 patients and baricitinib in 1 patient. The average observation period after JAKi administration was 206 (56-343) days. PAIN-VAS, CRP, and ESR significantly decreased within 7 days of starting JAKi therapy and continued to decrease thereafter. MMP3 was also significantly reduced after 8 weeks. In all cases, GC was discontinued after an average of 65 days after starting JAKi without increasing the dose. In particular, these values did not worsen and improved in the 6 patients who discontinued GC very early (within 21 days). [Discussion] Although further follow-up is required for safety, the results of this study suggest the possibility of JAKi as an alternative to GC for patients with PMR.

## P1-049

**Examination of Cs responsivity with patients of Polymyalgia rheumatica**

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is often responsive to corticosteroid (Cs), but in some cases, symptoms flare up, and are difficult to treat. Also, predictors of Cs reactivity are not clear, and some cases are difficult to differentiate. We evaluated the responses to Cs therapy. [Methods] We examined 13 patients who met Bird's classification criteria or 2012 provisional classification criteria for PMR (EULAR/ACR). Response to treatment was defined as those patients who could reduce Cs to <5 mg/day were defined as response group, and those who required re-titration or concomitant use of DMARDs, or had difficulty reducing Cs to <5 mg/day during the first year of treatment were defined as resistance group. [Results] The age of onset was 84/77.5 (response/resistance, median), the time from onset to diagnosis was 1.0/2.2 months, the Cs dose at the start was 0.31/0.53 mg/kg, and reduction rate after 6 months was 67%/66%, none of which showed significant differences. However, Cs reduction rate after 12 months was significantly higher in the response group at 94%/75%. Three cases in the resistance group had additional DMARDs. [Conclusions] The results of this study suggests that PMR with difficult to treat undergo Cs dose escalation or additional DMARDs after 6-12 months of treatment.

## P1-050

**Two cases of dementia dialysis patients diagnosed with polymyalgia rheumatica by imaging diagnosis**

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Rakuwa-kai Otowa Hospital

Conflict of interest: None

Polymyalgia rheumatica occurs in the elderly, and its diagnosis is very difficult in patients with dementia who do not have clear complaints. In this report, we describe two cases of unexplained elevated CRP detected in periodic blood sampling in hemodialysis patients who took a long time to be diagnosed and treated. Case 1: A man in his 80s. He was found to have elevated CRP in periodic blood collection during dialysis, and periarthritis of the right shoulder joint and bilateral hip iliopsoas bursitis were observed on CT scan. He was seen by an orthopedic surgeon and antimicrobial agents were started, but his symptoms did not improve and it took 3 months to diagnosis. Case 2: 70s, female. She had fever and elevated CRP, and was treated with antimicrobial agents as an outpatient. CT on admission suspected right shoulder periarthritis and right breast cancer. It took 3 months from the onset of symptoms to the start of treatment. In both cases, steroids were very effective and the patients were very pleased with the results. We realized that polymyalgia rheumatica is not well understood outside of the rheumatology department and that imaging findings are useful in patients with unclear complaints.

## P1-051

**Response to ibuprofen (ibu) in polymyalgia rheumatica (PMR)**

Hidehisa Nagakawa[1], Shusui Hatta[1], Shigeko Inokuma[1], Satoshi Miike[1], Koto Hattori[1], Kazuaki Hara[2,3]
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Conflict of interest: None

[Objective] With the advent of an aging society, the plevarence of PMR is on the rise. Currently, steroids are the first choice. However, the affected patients are elderly and should better avoid them if possible. We have successfully treated many cases of PMR with ibuprofen (ibu) without steroids. [Methods] We searched the cases administered ibu, colchicine, prednisolone (PSL), and/or methotrexate (MTX) in cases with PMR diag-

nosed according to EULAR/ACR criteria at our hospital over a 5-year period from August 2017. [Results] 101 patients (70 females, 31 males, 79.3±6.9 years) were diagnosed with PMR and received one of the above drugs: ibu 69, colchicine 49, PSL 76, MTX 37. Twenty patients had ibu and colchicine simultaneously, 29 patients colchicine after ibu, 46 patients PSL after ibu. Ibu alone or in combination with colchicine without PSL/MTX was administered in 17 cases. All of them achieved a remission. [Conclusions] Ibu could be effective for PMR. even in monotherapy.

## P1-052

**Increase of Polymyalgia Rheumatica (PMR) cases in Kameoka Hospital**

Tatsuo Fukushima
Kameoka Hospital

Conflict of interest: None

[Objective] In the past few years, especially since 2023, there has been an impression that the number of patients with polymyalgia rheumatica is rapidly increasing. Therefore, we will plot the number of PMR cases over time and examine whether the number of PMR cases is actually increasing. [Methods] We observed the number of cases diagnosed with PMR in our hospital over time from 2014, when we opened a rheumatology outpatient clinic, to 2023. [Results] The average number of initial cases in the 7 years after the opening of the specialized outpatient clinic was 3.14 cases/year. Therefore, in 2022 and 2023, the number of cases was more than double that of the previous year, and it seemed that the number of cases was clearly increasing. [Conclusions] The reasons for the increase in the number of cases in recent years include the fact that our hospital's specialized outpatient clinic has become well-known within the city, a simple increase in the incidence of PMR, the spread of the disease concept of PMR, and external factors that increase the incidence of PMR. Examples include existence. Is the recent increase in PMR cases a phenomenon unique to our hospital? I would like to take this opportunity to inform you about the situation in each area.

## P1-053

**A case of refractory relapsing polychondritis treated with filgotinib**

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Conflict of interest: None

A 65-year-old woman was diagnosed with recurrent polychondritis in June X-4 and was initially treated with prednisolone 55 mg (1 mg/kg) and intravenous cyclophosphamide. In April X-3, when the prednisolone dose was tapered to 13.5 mg, CT imaging revealed worsening bronchial wall thickening, prompting initiation of methotrexate therapy. In June X-2, while on methotrexate 8 mg/week and prednisolone 10 mg, she experienced a relapse of subglottic laryngitis. Following steroid pulse therapy, the prednisolone dose was escalated to 25 mg, and the treatment was shifted from methotrexate to tocilizumab. In April X, while on 10 mg prednisolone and tocilizumab, the subglottic laryngitis recurred. After another round of steroid pulse therapy, the prednisolone dose was increased to 20 mg, tocilizumab was discontinued, and filgotinib was initiated. In the management of refractory relapsing polychondritis, various therapeutic agents, such as methotrexate, azathioprine, cyclophosphamide, tocilizumab, TNFα inhibitors, abatacept, rituximab, and JAK inhibitors, have been reported in combination with steroids. To the best of our knowledge, this is the first reported case of recurrent polychondritis successfully treated with filgotinib. We present this case along with a literature review.

## P1-054

**A study of 3 cases of relapsing polychondritis treated with PET-CT**

Takuya Nishi[1], Satoshi Suzuki[1], Tomoya Ohtani[1], Nozomi Kawamata[1], Yukino Taniguchi[2], Ken Yamaji[2], Naoto Tamura[2], Keigo Ikeda[1], Shinji Morimoto[1]
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Conflict of interest: None

Case 1: A 55-year-old woman presented with sore throat and barking cough since April 2023, tracheal wall thickening on CT. PET-CT was performed for tenderness of nasal cartilage, FDG was accumulated in tracheal wall and nasal cartilage. We considered relapsing polychondritis (RP) and treated with steroid pulse and prednisolone (PSL) of 1 mg/kg/day with improvement of clinical symptoms. Case 2: A 47-year-old man presented with fever, polyarthritis and swelling of both auricular cartilages since 2018. He was referred to our department in May 2023, PET-CT was performed after biopsy of auricular cartilage failed to show significant finding, showed FDG accumulation in both auricular cartilage, nasal cartilage, and polyarticular joints, we treated with PSL of 0.5 mg/kg. Case 3: A 75-year-old man presented with fever, sore throat and hoarseness, and treated with antibiotic since July 2023. PET-CT was performed for refractory to antibiotic, FDG accumulation in tracheal wall and nasal cartilage showed. We treated with steroid pulse and PSL of 1 mg/kg. RP is rare disease, but we experienced 3 cases in 6 months. While RP is critical due to airway involvement, difficult to diagnose for multiple affected organs, nonspecific histological evaluation, and risk of biopsy, suggesting utility of early PET-CT.

## P1-055

**A case of sarcoidosis requiring differentiation from Tolosa-Hunt syndrome**

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Conflict of interest: None

[Case] A 68-year-old woman. Diplopia and left eye pain appeared on February 17, X. On March 1, she was referred to the ophthalmology and she had bilateral IOP and left oculomotor nerve palsy. Brain MRI showed a slight bulge in the left cavernous sinus, and Tolosa-Hunt syndrome was suggested. On March 13, she was referred to the Immunology due to positive antinuclear antibody. On April 18, she was diagnosed with uveitis by retinal perivasculitis and perivascular nodules. On May 15, PET-CT showed abnormal FDG accumulation in the hilar, mediastinal, and periaortic lymph nodes. Based on the PET-CT findings, high serum ACE level, and uveitis, she was clinically diagnosed with sarcoidosis with ocular and neurological lesions. A half-pulse steroid was administered, and 24 mg of mPSL was started as post-therapy. Her symptoms improved, and mPSL was tapered off without recurrence. [Clinical Significance] Neurological lesions occur in 5-10% of patients with sarcoidosis, but the diagnosis may be difficult without non-neurological symptoms. In this report, we describe a rare case in which the patient was diagnosed with sarcoidosis due to the appearance of uveitis during the course of the disease, but was difficult to differentiate from Tolosa-Hunt syndrome.

## P1-056

**A case of cardiac Sarcoidosis diagnosed by FDG-PET/CT in dialysis initiation period**

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Conflict of interest: None

Case presentation: A 68-year-old male with past medical history of type2 diabetes mellitus for more than 20 years presented to the hospital with dyspnea. Myocardial biopsy and gallium scintigraphy were performed on suspicion of cardiac sarcoidosis 8 years ago, and renal biopsy was done to evaluate renal sarcoidosis 2 years ago, but none of them revealed positive results. He was admitted to our hospital and treated with diuretics and inotropic agents, but his symptoms didn't improve. His dys-

pnea and malaise persisted even after hemodialysis was started for uremia and congestive heart failure. FDG-PET/CT was taken to evaluate sarcoidosis activity. Eventually cardiac sarcoidosis was diagnosed with active inflammation from the results of localized high uptake value of FDG in left ventricular myocardium. His symptoms improved immediately after starting 20 mg/day (0.5 mg/kg/day) of prednisolone. Ejection fraction also improved from 24.5% to 45%. Conclusion: Patients with cardiac sarcoidosis sometimes have nonspecific symptoms such as dyspnea and malaise. In this case, uremia was differential diagnosis because he had progressed renal failure. FDG-PET/CT was a very useful tool for diagnosis and evaluating activity of sarcoidosis.

## P1-057

**Two Cases of Cardiac Sarcoidosis successfully treated with TNF-alpha inhibitors**

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Conflict of interest: None

[Case 1] A 73-year-old woman was admitted because of arrhythmia. She was diagnosed as ocular and pulmonary sarcoidosis 7 years before admission. ECG revealed multiple ventricular premature contraction (mVPC) with CRBBB. UCG showed decreased wall motion of the anterior wall and septum. Myocardial contrast-enhanced MRI revealed delayed staining in the ventricular septum and inferior wall, in addition to abnormal staining in the anterior wall. She was diagnosed as cardiac sarcoidosis She was treated with PSL 40 mg and infliximab (IFX), which reduced mVPC by 70%. [Case 2] A 52-year-old woman presented with palpitation. She was diagnosed as sarcoidosis with iritis and interstitial nephritisin 15 year before admission. ECG revealed mVPC. FDG-PET showed focal abnormal accumulation in the ventricular septum and posterior wall. Cardiac scintigraphy showed ischemia in the inferior venticulr wall. The patient was diagnosed as cardiac sarcoidosis. She was initially treated with high dose glucocorticoid (pulse therapy and PSL 50 mg), which failed to control mVPC. Then, MTX and IFX were added, which reduced mVPC by 75%. [Clinical Significance] TNF-αinhibitors could be useful in patients with cardiac sarcoidosis with preserved cardiac function.

## P1-058

**One case each of pemphigus and pemphigoid introduced as suspected Behcet's disease**

Tsuyoshi Kobashigawa[1,2], Yuki Nanke[1,3]
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Conflict of interest: None

[Clinical Significance] We experienced one case each of pemphigus or pemphigoid with oral lesions as a differential diagnosis of oral lesions in Behcet's disease based on the differences in its characteristics. [Case] Case 1 is a 59-year-old male. One month ago, an oral lesion appeared, and the patient was referred to our hospital after seeing a local dentist. A mucosal biopsy was performed, and he was suspected to have pemphigus vulgaris. At the time of his first visit without his skin symptoms including Nikolsky phenomenon. Anti-desmoglein (DG) 3 antibody was positive; then, PSL 0.5 mg/kg/day was started. Whenever himself-interrupted, the trunk lesions recurred. His PDAI score was 10 points, which was moderate. Case 2 is a 68-year-old female who developed pemphigoid 22 years ago. At that time, she was mainly suffering from polyarticular pain, oral lesions, and skin lesions, and the diagnosis was not confirmed, so she was referred to another university's hospital on suspicion of BD. Since she was HLA-B51 positive, suspected of having BD. Five years ago, she first visited our hospital. IgG, IgA, and C3 were positive on DIF, and IgG was 256 times on IIF without his anti-DG 1 or 3 antibodies nor anti-BP180 antibodies; then, she was diagnosed with pemphigoid.

## P1-059

**A case of granulomatous mastitis with erythema nodosum strongly suspected**

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Conflict of interest: None

[Background] Granulomatous mastitis (GM) is a chronic inflammatory disease of unknown cause, and is known to be often accompanied by erythema nodosum (EN). I would like to report a case in which I strongly suspected. [Case] A 36-year-old female had noticed swelling of her left mammary gland and visited a nearby breast clinic. She was diagnosed with mastitis, which improved after treatment with antibiotics, but a few days later she developed an abscess in the same area and drainage was started. After that, she developed swelling and pain in both knees, lower legs, elbows and thighs, so she visited a orthopedic clinic. She was referred to our department with suspicion of collagen disease. As a result of examination on admission, she was found to have an inflammatory response, but her autoantibodies were negative. The skin findings spontaneously improved, and her skin biopsy did not reveal EN. She was discharged from the hospital on the 17th day. Her mammary gland drainage improved without drugs. This case was strongly suspected as GM combined with EN. [Discussion] There are only a limited number of reported cases of GM, and treatments include drainage, steroids, and MTX. Recurrence has been reported, so follow shoud be contiuned. This report includes a literature review.

## P1-060

**A case of erythema nodosum with edema and arthralgia as initial symptoms**

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Yamagata University Faculty of Medicine Department of Orthopaedic

Conflict of interest: None

A 74-year-old man visited our department in March 2023 with edema in both lower limbs and arthralgia in the left knee since February 2023. He had pain in both knees and ankle joints, marked edema in both lower limbs and left forearm, erythema and subcutaneous induration in both elbows and lower legs. There were subcutaneous masses in both precuneus. Blood biochemical tests revealed CRP 7.06 mg/dL, WBC 8570/μL, ASLO 24 IU/mL, sIL2r 846.0U/mL, RF <3 IU/mL, ACPA <0.5U/mL, ANA <40x, CT showed no infection or tumor lesions. Skin biopsy showed septal panniculitis and erythema nodosum (EN) was suspected. Four weeks after the initial diagnosis, the patient was in good health, with normalized CRP <0.10 mg/dL and sIL2r 382.0U/mL. There has been no recurrence of erythema nodosum to date. EN may occur in the setting of infectious diseases or autoimmune diseases, but it may also be idiopathic. It is often associated with high fever and arthralgia, and often resolves within a few weeks, but recurrence is also common. It is necessary to search for underlying diseases and to cooperate with dermatology, and since some cases resolve spontaneously, this disease should be kept in mind in the identification of arthralgia. Clinical Significance: EN should be listed as a differential diagnosis of arthralgia.

## P1-061

**Osteomyelitis of jaw after tooth extraction in two patients with rheumatoid arthritis**

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Conflict of interest: None

[Background] There are predisposing factors (PF) for osteomyelitis of jaw (OMJ) and RA is one of them. Meanwhile characteristics of RA asso-

ciated with OMJ were unknown. We report two cases of RA complicated by OMJ. [Case 1] A 69-year-old woman had been diagnosed with RA, hypertension (HT), and hyperlipidemia (HL). She was managed with leflunomide and mPSL. She was disabled to open mouth after extraction of right lower tooth. Blood examination showed elevated CRP level (19 mg/dl), while CT and 99mTc scintigraphy showed findings compatible to OMJ. She was treated with drainage and antibiotics (ABX). [Case 2] A 75-year-old man has suffered from RA, HT, atrial fibrillation (AF), and a history of AMPC allergy. He was managed with MTX and PSL. He was disabled to open mouth due to perimandibular inflammation. Once his symptoms improved after ABX and extraction of left lower tooth, suppuration and exposure of left mandible occurred 19 days later. Laboratory tests showed elevated CRP level (32 mg/dl) and CT findings were compatible to OMJ. He was treated with ABX, incision and drainage. [Clinical Significance] History of tooth extraction and another PF (HT, HL, AF, immunosuppressive state (PSL and immunosuppressant), and AMPC allergy) may be characteristics of RA associated with OMJ.

## P1-062

**Two cases of implant preservation with CLAP combined with DAIR for Prosthetic Joint Infection after total hip arthroplasty (THA) in patients with rheumatic diseases**

Akitsugu Suzuki[1], Yuya Takakubo[1,2], Suran Yang[1], Yasushi Naganuma[3], Ryusuke Honma[4], Yoshihiro Wanezaki[1], Masashi Aso[1], Michiaki Takagi[1]
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Conflict of interest: None

[Objective] To report two cases of PJI in patients with rheumatic diseases in which debridement and antimicrobial chemotherapy for implant preservation (DAIR) combined with continuous local antimicrobial infusion (CLAP). [Case] Case 1: The patient was a 79 year-old man with a 10 year history of RA underwent right THA. On 11 days after THA, because PJI was revealed, DAIR was performed on the same day with setting of CLAP and starting systematic antibiotics. Intraoperative fluid culture found Enterobactor cloacae complex. On day 12 after DAIR, CLAP was quitted, and the oral antibiotics started instead of the intravenous antibiotics. There has been no relapse at 19 weeks after DAIR. Case 2: The patient was a 56 year-old man. He had a history of palmoplantar pustulosis. THA was performed for his right hip because MRI showed necrosis of the femoral head. On 4 weeks after THA, because PJI was revealed, DAIR was performed on the same day with setting of CLAP and starting systematic antibiotics. Intraoperative fluid culture found staphylococcus aureus. On 14 days after DAIR, CLAP was quitted. There has been no relapse at 4 weeks after DAIR. [Conclusions] The combination of DAIR and CLAP may achieve a local biofilm destruction concentration and preserve the joint prosthesis.

## P1-063

**Intramuscular abscess in the popliteal fossa in an elderly patient with rheumatoid arthritis: a case report**

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Conflict of interest: None

Case presentation: A 75-year-old male had pain in both fingers and wrist joints since April X. In January X+1, he was diagnosed with RA and started MTX treatment. In May of the same year, iguratimod (IGU) was added, and he was in remission with CDAI of 2.6 in August. One month later, right popliteal pain occurred. At the time of visit, his temperature was 38.7°C. Swelling and tenderness were observed in the area. Laboratory findings were as follows: WBC 20000, CRP 17.1, RF 57.9, and MMP-3 78.1. MRI showed abscess formation in the semimembranosus muscle, and he was hospitalized for antibiotic therapy. MRSA was detected in the abscess puncture fluid culture before the start of treatment, and cefazolin was switched to vancomycin. Subsequently, minomycin was added orally, and symptoms improved. The patient is now doing well with no recurrence. Clinical significance: IGU is effective for RA both in combination with MTX and as a single agent, and is often used in relatively elderly patients. Although no significant increase in adverse events has been reported with the combination therapy, infection is always a side effect to be aware of in patients treated for RA. The patient underwent cystoscopy frequently after bladder cancer surgery, which may have been a trigger for MRSA infection.

## P1-064

**A case of rheumatoid arthritis presenting with Lemierre's syndrome during treatment with JAK inhibitor**

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Conflict of interest: None

[Background] Lemierre's syndrome is a syndrome in which anaerobic bacteremia in the oral cavity and pharynx leads to thrombophlebitis of the internal jugular vein and septic embolism of distant organs. We report this rare case of an elderly woman presenting with Lemierre's syndrome while receiving a JAK inhibitor, with some discussion of the literature. [Case] The patient is a 71-year-old woman. She was being treated with prednisolone and filgotinib for rheumatoid arthritis. She presented to the emergency department with right neck pain. She underwent CT/MRI of the head, which revealed no abnormalities. Two days later, she came to our outpatient clinic with severe pain and elevated inflammatory response. CSF examination was negative for meningitis. A simple CT scan showed multiple nodules with cavities in both lungs, and septic pulmonary embolism was suspected, so treatment was started with broad-spectrum antibiotics and antifungal agents. Blood culture tests identified Fusobacterium necrophorum. Contrast-enhanced MRI showed edematous changes in the right maxilla that were suspicious of osteomyelitis, and a contrast-impaired area in the right internal jugular vein. The patient was diagnosed with Lemierre's syndrome and is still undergoing treatment. COI: none

## P1-065

**A case of immune reconstruction inflamatory syndrome was suspected due to discontinuation of JAK inhibitors**

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Conflict of interest: None

The patient was diagnosed with rheumatoid arthritis 15 years ago. She was treated with methotrexate, salazosulfapyridine, tacrolimus, tofacitinib, prednisolone but the disease was difficult to control. She had been treated with FIL 1 year ago. She noticed loss of appetite and general fatigue in July. She was rushed to our hospital because she had difficulty breathing. Chest CT revealed multiple miliary and ground glass shadows on both sides. Her respiratory condition and chest CT image findings worsened after discontinuing FIL. As tuberculosis bacteria was detected through a sputum culture test, the patient was diagnosed with pulmonary tuberculosis. Therefore, immune reconstruction inflamatory syndrome was suspected due to discontinuation of JAK inhibitors. This was a rare case, so we report it.

## P1-066

**A case of tuberculous lymphadenitis requiring differentiation diagnosis with paraneoplastic syndrome with PMR-like symptoms**

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Conflict of interest: None

[Case Study] A woman in her 70s. [Chief complaint] polyarticular arthritis. [Current medical history] Surgery and adjuvant chemotherapy were performed for transverse colon cancer. 2 years later, joint pains of both

shoulders and hip joints appeared which suggested PMR. Considering paraneoplastic syndrome, CT scan was performed and revealed swelling of the abdominal cavity and cervical lymph nodes, and painful nodules appeared in the limbs. Skin biopsy and cervical lymph node biopsy were performed and revealed no malignancy but fat necrosis with multinucleated giant cells was found in the skin samples, and necrotizing granulomatous lymphadenitis was found from the lymph nodes ones. TB-PCR of lymph nodes was negative, but Mycobacterium tuberculosis was found in mycobacteria culture, and tuberculous lymphadenitis was diagnosed. She was treated with anti-tuberculosis treatment. Subsequently, the lymph nodes were reduced on the images, and the inflammatory response and joint symptoms disappeared. [Discussion] PMR-like joint symptoms appeared and lymphadenopathy was found by CT scan for malignancy exclusion and tuberculous lymphadenitis was diagnosed by biopsy. In patients with suspected PMR, it is important to make an exclusion diagnosis by close examination.

## P1-067

**A case of latent tuberculosis infection with chronic erythema nodosum and cervical lymphadenitis which was needed to be differentiated from Takayasu arteritis**

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Conflict of interest: None

A 58-year-old female had intermittently presented with erythema nodosum in her extremities for 10 years. She also had the swelling of right supraclavicular lymph node and the obstruction of right axillary artery with unknown origin for 5 years. These symptoms were exacerbated in June 202X with intermittent fever. We performed a systemic examination, but autoimmune diseases and malignancy were not demonstrated. She had a positive tuberculin test 20 years ago. In addition, contrast-enhanced CT revealed calcification of right supraclavicular lymph node. Tuberculosis infection was strongly suspected, and then T-SPOT was positive. We performed additional examinations with sputum culture and biopsy of her lymph node and skin, but we could not demonstrate definitive pathological findings suggesting active TB infection. Finally, she was diagnosed with LTBI, daily treatment was initiated with isoniazid 300 mg for a planned duration of six months. After that, her symptoms were dramatically improved. At follow-up one year later after that treatment, there were no new erythema nodosum lesions. We report the case with a review of the literature.

## P1-068

**Bloodstream infection with Helicobacter equorum (H. equorum)-like Bacterium in systemic lupus erythematosus (SLE)**

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Conflict of interest: None

[Case] The patient was a 74-year-old woman with SLE, which was diagnosed at age 33 and treated with prednisolone (PSL). She developed fever and back pain. Blood cultures revealed the presence of Gram-negative spiral bacilli, which led to her hospitalization. We considered bacteremia caused by *Campylobacter* spp. or *Helicobacter* spp. and started administration of meropenem (MEPM). MRI of the lumbar spine showed pyogenic vertebral osteomyelitis and discitis. Due to low bacterial abundance, mass spectrometry failed to identify the bacterial species. However, 16S rRNA sequencing revealed *H. equorum*-like bacterium. Based on drug susceptibility test (DST), antibiotics were de-escalated from MEPM to ciprofloxacin and minocycline. She had resolution of fever and CRP was normalized. [Discussion] Human infection with *H. equorum*-like bacterium has been reported only in a patient with X-linked agammaglobulinemia presenting with pleurisy. Our case was an immunocompromised host due to a decrease in CD4+ T cell in blood resulting from prolonged treatment with PSL. Given the susceptibility of patients on long-term immunosuppressive therapy with PSL to rare bacterial infections, it is crucial to identify bacterial species by 16S rRNA sequencing and conduct DST for proper antibiotic selection.

## P1-069

**A case of SLE-TMA treated with high-dose steroids, rituximab, and plasma exchange developed Stenotrophomonas maltophilia pneumonia and pulmonary hemorrhage during therapy**

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Conflict of interest: None

A 61-year-old female was diagnosed with SLE in 1989 and started on 30 mg PSL. She was referred in 2018 taking 5 mg PSL. As joint pain worsened with PSL tapering, tacrolimus 1 mg was added in 2020. PSL was reduced to 3.5 mg in August 2022 but pericardial effusion increased from April 2023. It did not improve despite increasing PSL and tacrolimus, so she was hospitalized in July. On day 1, Hb was 9.4g/dL, schistocytes 1+, platelets 65,000, LDH 897 U/L, Cr 1.28 mg/dL, suggesting TMA. Findings were leg edema without fever, impaired consciousness, or diarrhea. Drug-induced TMA by tacrolimus was considered so it was stopped and treatment with mPSL60 mg, FFP, and RTX started. Cr increased to 2.1 mg/dL, plasma exchange begun renal function did not improve. Renal biopsy showed TMA and LN class V. On day 25, Hb dropped to 5 g/dL, CHDF started, intubated. Lavage revealed alveolar hemorrhage. *S. maltophilia* grew in lavage and blood culture. After antibiotics blood cultures negative but TMA did not improve. She died on day 47. This is a case of alveolar hemorrhage during treatment for SLE-TMA. *S. maltophilia* suggests possible pneumonia. However, TMA symptoms including hemorrhage cannot be ruled out. Infectious causes should be considered when hemorrhage occurs during immunosuppressive therapy.

## P1-070

**A case of severe PCP developed due to immune reconstitution following the improvement of pancytopenia induced by MTX. Another case of PCP developed while using SRM, but continuing SRM prevented severe PCP**

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Conflict of interest: None

[Background] Pneumocystis pneumonia (PCP) is more severe in RA than in AIDS due to an immune overreaction. [Case 1] A 75-year-old woman with RA, who had been taking MTX, was admitted to our hospital with cough and dyspnea on exertion for one month, and pancytopenia without any findings on a chest CT scan. The replacement of folic acid was started. On the morning of the third day of admission, her WBC count was elevated. However, in the evening, she suddenly developed respiratory failure. She was treated with mPSL pulse, TAC, and ST drugs, but her condition worsened at night with SpO2 of 88% on 10 L/min oxygen. After initiating TCZ treatment, she recovered and was diagnosed with PCP. [Case 2] An 80-year-old woman with RA who had stopped therapy due to herpes zoster was in remission; however, her arthritis flared up and she started SRM. One month later, the patient developed PCP. SRM was not discontinued and PSL was reduced more rapidly than the usual protocol. Oxygen demand was 4L/min at admission, but she could discontinue oxygen promptly. [Clinical Significance] We present two cases valuable for considering PCP treatment strategies: one of rapid PCP exacerbation following the improvement in MTX-induced pancytopenia, and another of continuous use of SRM without worsening of PCP.

## P1-071

**A case of VEXAS syndrome with Vibrio vulnificus sepsis during tocilizumab treatment**

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University Hospital

Conflict of interest: None

A 76-year-old man presented with fever, left ear swelling, left cervical lymphadenopathy, macrocytic anemia, high CRP and IgG levels, multiple pulmonary granular shadows in X-4 years. Lymph node biopsy suggested IgG4-RD, and moderate-dose PSL was initiated with improvement symptoms except for anemia. However, during the tapering of PSL, his signs and symptoms recurred, and clinically idiopathic multicentric Castleman disease was suspected. The addition of tocilizumab (TCZ) improved his condition. Subsequently, myelodysplastic syndrome became to be prominent, and the diagnosis of VEXAS syndrome was confirmed with UBA1 gene mosaic mutation. He was managed with TCZ, low dose PSL, and transfusions. In July, X year, he developed fever, chills, and vomiting, with a high WBC count and qSOFA was positive for 3 items. Sepsis was suspected, and TCZ was discontinued. Tazobactam piperacillin led to improvement. Vibrio vulnificus was detected by blood culture. Vibrio vulnificus infection has a high mortality, and he was at high risk for Vibrio vulnificus infection because of his clinical status. In case of VEXAS syndrome, it is important to consider the possibility of Vibrio vulnificus infections, and select appropriate antibiotics when sepsis is suspected.

## P1-072

**Clock controlled gene Tef regulates proliferation of RA-FLS via Cell Cycle regulators**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA), characterized by tumor-like proliferation of RA fibroblast like synoviocyte (RA-FLS), has various symptoms related to circadian rhythms. However, the central role of clock genes on the joint destruction of RA remains unclear. The aim of this study is to examine the roles of clock genes on RA-FLSs. [Methods] After transfected siRNA *Tef*, RA-FLS was stimulated with or without IL-6/sIL-6R (100 ng/ml) or TNF-α (10 ng/ml) to examine the cell viabilities by WST-8 assay. Total protein was extracted from RA-FLSs to analyze the expression of Cyclin D, Cyclin E, p21 by western blot. Mouse embryonic fibroblasts (MEFs) were isolated from of *Tef*-/- or wild-type mouse embryos to measure cell viabilities by WST-8 assay and Foci-formation assay. RNA was collected from *Tef*-/- or wild-type mouse livers and analyzed by RNA-seq. [Results] Under silencing *Tef,* stimulation of IL-6/sIL-6R and TNF-α increased the cellular viabilities and expression of Cyclin D, Cyclin E, while those of p21 were decreased with IL-6. Cellular viabilities was increased in *Tef*-/- MEFs. RNAseq analysis showed that E2F7 was decreased in liver from in *Tef*-/- mouse. [Conclusions] The results suggest that *Tef* is involved in the cell proliferative activity of RA by regulating cycle regulators via E2F7.

## P1-073

**CD146mid cells derived from pannus cause ankylosis as they differentiate into osteogenic cells via hypertrophic chondrocytes**

Yoko Miura, Satoshi Kanazawa
Department of Neurodevelopmental Disorder Genetics, Nagoya City University Graduate School of Medical Sciences, Aichi, Japan

Conflict of interest: None

[Objective] Rheumatoid arthritis is characterized by pannus formation, progressive bone destruction, and ankylosis. The bone pathology during this disease progression remains unclear. In this study, we investigated ectopic bone differentiation using an arthritis model. [Methods] D1BC mice were immunized low-dose bovine type II collagen. We performed *in situ* hybridization and immunohistochemical staining on inflamed and ankylosed joints. Synovial fibroblasts were isolated, and cell populations were sorted by flow cytometry. Bone differentiation populations were identified via RNA-seq analysis and qPCR. [Results] During joint inflammation, synovial fibroblasts expressed bone differentiation markers *Runx2, Sox9*, and *Col10a1*. As inflammation resolved, we observed ectopic Collagen X-positive hypertrophic chondrocytes co-expressing *Runx2* and *Sox9*. Flow cytometry revealed abundant *Runx2*, *Sox9*, and *Col10a1*, triple positive cells in the CD146 middle-positive population. [Conclusions] It is suggesting that CD146 middle-positive population differentiates into osteocytes via hypertrophic chondrocytes in the pannus, leading to osteoarthritic ankylosis.

## P1-074

**Generation of inhibitory anti-human TLR7 monoclonal antibody**

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Conflict of interest: Yes

[Objective] Toll-like receptor 7 (TLR7) is a pathogen sensor that recognizes single-stranded RNA and guanosine derivatives, and is known to induce inflammation by recognizing host-derived nucleic acids. Our anti-mouse TLR7 monoclonal antibody can alleviated the phenotype when administered to mouse disease models, such as autoimmune hepatitis and lupus nephritis. Therefore, we aimed to establish an inhibitory anti-human TLR7 for application to TLR7-dependent inflammatory diseases. [Methods] BALB/c mice were immunized with human TLR7 overexpressing cell line, and hybridomas were obtained by fusion of splenocytes and myeloma partners. Clones recognizing human TLR7 were selected by flow-cytometry using culture supernatant. Antibodies were purified from the clones and used for experiments. [Results] Of the approximately 30 clones obtained, inhibitory activity was observed in 12 clones. These antibodies recognize monkey TLR7 but not recognize mouse TLR7 of human TLR8. Furthermore, when the inhibitory antibody was administered to our human TLR7 transgenic mice, cytokine production in response to the TLR7 ligand was suppressed. [Conclusions] These results suggest that human TLR7 inhibitory antibodies are promising for the control of TLR7-dependent inflammatory diseases.

## P1-075

**Proposition of the Castleman disease (iMCD-NOS) as Tph cell immunological disorder**

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[1]SANKEN, Osaka University, [2]Nagasaki University

Conflict of interest: None

[Objective] iMCD-NOS was an unknown cause of disease excepted for IL-6 production. Therefore, it is required to find the essential pathogenesis of this disease. [Methods] To establish the iMCD-model mouse, the lymph node cells of the patient were transplanted into the immunodeficient NSG mouse. After 3-4 weeks the mouse had gradually moved slowly, decreased body weight with hair fall. On the examination, it appeared inflammatory status with anemia, hypoalbuminemia, and increasing human IgG, IgA and IgE. This observation suggested that the mouse seemed to be the iMCD-model mouse, then the immunological analysis is performed. [Results] When $CD3^+$T cells were removed from whole cells of lymph mode, the abnormal findings did not observed, suggesting that this model mouse might be an immunological disorder. To analyze the lymphocytes from the patient's lymph mode in NSG, $CD4^+PD\text{-}1^{high}CXCR5^-CCR2^+$Tph cells presenting CXCL13 were infiltrated in spleen. When a CXCL13 antibody was inoculated into NSG mice after transplantation of the patient lymph node cells, the abnormal findings were immerged. [Conclusions] This iMCD-model mice showed the immune abnormality with activation of Tph cell, indicating that iMCD-NOS might be a immunological disrober with activation of Tph-CXCL13-B cell axis.

## P1-076

**The role of integrins in rheumatoid arthritis**

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Conflict of interest: None

[Objective] Integrins were originally identified as receptors for extracellular matrix (ECM) and cellsurface molecules (e.g., VCAM-1 and ICAM-1). Later, we discovered that many soluble growth factors/cytokines bind to integrins and play a critical role in growth factor/cytokine signaling. Several growth factor/cytokines activated integrins by binding to the allosteric sitein the integrin headpiece (site 2), which is distinct from the classical ligand (RGD)-binding site (site 1). We showed that several inflammatory factors (CX3CL1, CXCL12, CCL5, sPLA2-IIA) bind to site 2 and activate integrins. Also, we developed the site 2 derived integrin peptides, which inhibit integrin activation by cytokines. [Methods] In this studies, we evaluated the role of integrins and the effect of the site 2 derived integrin peptides in rheumatoid arthritis. [Results] Integrins were activated in PBMCs from patients with RA. Integrins in PBMCs from patients with RA were down-regulated after treatment with corticosteroids and immunosuppressants. Site 2 peptides suppressed arthritis in CAIA model mice. [Conclusions] We propose that site 2 is involved in the pro-inflammatory action of these proteins and a potential therapeutic target.

## P1-077

**Olfactory bulb granule cell lineage-specific prokr2 knockout reduces the severity of anti-collagen antibody-induced arthritis**

Kazuhiro Otani, Masayuki Yoshiga, Daitaro Kurosaka
The Jikei University School of Medicine

Conflict of interest: None

[Objective] We reported that prokineticin2 (PK2) receptor antagonist reduced the severity of arthritis in a mouse model and that IL-6 is expressed in the olfactory bulb (OB) before the onset of arthritis and is associated with decreased food intake. Prokr2, a PK2 receptor, forms a feed-forward loop with JAK-STAT signaling. Prokr2 signaling is involved in neurogenesis in the granule cell layer of the OB. Therefore, we analyzed the relationship between the severity of arthritis and food intake in OB granule cell lineage-specific prokr2 knockout (KO) mice. [Methods] We induced anti-collagen-induced arthritis in GFAP-specific prokr2 KO mice and compared the severity of arthritis with wild-type mice. Changes in cytokine expression in the brain, peripheral tissues, and serum, as well as dietary intake, were compared after LPS administration. [Results] The severity of arthritis was decreased in knockout mice. Cytokine expression in the brain was suppressed, while peripheral tissue and serum cytokine expression was unchanged. The decrease in food intake was mild in the KO mouse. [Conclusions] In OB granule cell lineage-specific prokr2 KO mice, there may be a mechanism to suppress arthritis and peripheral symptoms that is not mediated by inflammatory cytokine expression in peripheral tissues.

## P1-078

**Investigation of the effects of neutrophil extracellular traps (NETs) on lung fibroblasts**

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Conflict of interest: None

[Objective] Neutrophil extracellular traps (NETs) are released by the binding of antineutrophil cytoplasmic antibody (ANCA) to neutrophils and are known to be a pathogenic mechanism of vasculitis. On the other hand, its direct involvement in the pathogenesis of interstitial pneumonia has not been fully investigated. In this study, we investigated the cytokine-mediated effects of NETs on lung fibroblasts (NHLF). [Methods] NETs released from neutrophil cells obtained by inducing differentiation of promyelocytic cells derived from HL-60 cells, which are acute promyelocytic leukemia cells, with all-trans retinoic acid (ATRA) were generated. The expression of inflammatory cytokines and metalloproteinases were measured by qPCR in (1) NETs co-cultured with NHLF, (2) HL60 co-cultured with NHLF before induction, and (3) NHLF without co-culture (control). [Results] NETs obtained from HL-60 cells induced to differentiate by ATRA were confirmed by optical microscopy. The expression of IL-6, TNF-α, IL-8/CXCL8, and ADAM-17 mRNA in NETs co-cultured NHLFs were significantly increased compared to HL-60 cocultured NHLFs. [Conclusions] NETs are involved in cytokine production from NHLF. These cytokines are also known to be generally expressed in patients with interstitial pneumonia.

## P1-079

**Vaccines against endogenous peptides using T/B epitope**

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Conflict of interest: None

Therapeutic vaccines against diseases other than infectious diseases have been developed in recent years for a variety of conditions, and clinical development is underway. Many of these existing vaccines targeting endogenous proteins have been synthesized by binding antigens to macromolecules. Although these macromolecules have high immunogenicity and facilitate antibody production, they are complex to synthesize and can easily induce unexpected immune responses: side effects and weakened efficacy. Whereas our peptide epitope vaccine has a simple structure that conjugates T cell epitope inducing Naïve T cells to become follicular helper T cells and B cell epitope that is the target antigen. This vaccine is simple to synthesize in formulation and can be induce antibodies when administered with an adjuvant. Furthermore, we found that the T epitope identified from the spike protein of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) functioned as the antibody inducer in the peptide vaccine; the vaccine conjugating the T epitope with angiotensin II (Ang II) induced antibodies against Ang II and suppressed hypertension in a mouse hypertension model. This T epitope is expected to be one of the tools for developing peptide vaccines for immune diversity.

## P1-080

**Information Extraction from Medical Record Summaries Using Japanese Large Language Models for Automated Statistics**

Ryuichi Nakahara[1], Keiichiro Nishida[1], Yoshihisa Nasu[1], Ryozo Harada[2], Shuichi Naniwa[1], Noriyuki Shimizu[1], Chinatsu Ichikawa[1], Yasushi Takahashi[3], Toshifumi Ozaki[1]
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Conflict of interest: Yes

[Objective] Collecting clinical data is costly. We developed a system for auto-collecting time-series medication and test data from rheumatoid arthritis patients' summaries. Challenges arose due to varying conversion rules across facilities. Using Large Language Models (LLM), we explored rule-based conversions through text prompts. We also examined cloud-based models like GPT-4, which require external data transmission, versus local Japanese LLMs. [Methods] Using rheumatoid arthritis records, we created fictional summaries for 100 patients. We investigated conversion capacities by defining rules via prompts and compared GPT-4 with the local model, Elyza. [Results] Without conversion rules in prompts, both models failed. With rules, GPT-4 had an 85% success rate in 100 cases, while Elyza had 30%. GPT-4 required less rule clarification. [Conclusions] While cloud-based LLMs performed better, local LLMs offer in-hospital use, making them a promising option for future development.

## P1-081

**Stabilization of type 2 ryanodine receptor reduces pathologic autoantibodies**

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Conflict of interest: None

[Objective] We investigated the effect of stabilization of type 2 ryanodine receptor (RyR2) on ovalbumin (OVA) immunization mice. [Methods] We compared the serum levels of OVA IgG in (1) wild type mice, (2) wild type mice treated with dantrolene (stabilizer of RyR1, 2, 3), and (3) V3599K KI mice which show stabilization of RyR2. [Results] Serum levels of OVA IgG were significantly lower in the both dantrolene group and V3599K KI mice group than those in the control group ($p < 0.05$). [Conclusions] These results suggest that stabilization of RyR2 reduces pathologic autoantibodies.

## P1-082

**LipoxinA4 in synovial fluid enable to discriminate between rheumatoid arthritis and osteoarthritis**

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Conflict of interest: None

[Background] In some clinical case, it's difficult to diagnosis RA and OA. I wondered if there is a new biomarker to distinguish between RA and OA. Many lipid mediators, such as prostaglandins have been reported to induce inflammation. But in recently, lipid mediators that reduce inflammation have been reported, one of which are Lipoxin $A_4$ ($LXA_4$). Therefore, we focus on $LXA_4$ in RA. [Purpose] To investigate the difference in $LXA_4$ concentration in synovial fluid of patients with RA and OA. [Subjects and Methods] We enroll 18 RA patients and 26 OA patients who underwent total knee arthroplasty, and collect knee joint synovial fluid. After enzyme treatment, we measure $LXA_4$ concentration, using liquid chromatography tandem mass spectrometry/mass spectrometry. After that, we compare $LXA_4$ concentrations RA and OA. [Results] $LXA_4$ concentration (pmol/ml) is significantly higher in RA group than in OA group. We perform ROC curve analysis. it is revealed that, the cut off is 2.47 (pmol/ml), the sensitivity is 61.1 (%), the specificity is 100 (%), the positive likelihood ratio is Infinity, and the negative likelihood ratio is 0.38. [Conclusion] This results indicate that $LXA_4$ would be a new biomarker to distinguish between RA and OA.

## P1-083

**Mast cells contribute to progressive fibrosing interstitial lung disease via inducing myofibroblast differentiation**

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Conflict of interest: None

[Objective] We have previously reported that number of mast cells (MC) are increased in progressive fibrosing interstitial lung disease (ILD). We examined whether MCs induced pulmonary fibroblasts to differentiate into myofibroblasts. [Methods] The co-culture of the human mast cell line (HMC-1) with pulmonary fibroblasts was performed. Fibroblasts were treated with HMC-1-conditioned medium for 24 hours. ACTA2 mRNA synthesis in the fibroblasts was evaluated by RT-qPCR. Neutralization antibodies for human TGF-β1 were used during the fibroblast culture with HMC-1-conditioned or standard culture media. [Results] In the co-culture experiment, the ACTA2 mRNA level significantly increased compared to that in the control fibroblast monoculture. Furthermore, the ACTA2 mRNA was significantly upregulated in fibroblasts cultured with HMC-1-conditioned medium compared to that in fibroblasts cultured in a standard medium. In addition, the neutralization of TGF-β1 abolished the ACTA2 mRNA upregulation in fibroblasts cultured in the HMC-1-conditioned medium, thereby suggesting that HMC-1-derived TGF-β1 contributes to myofibroblast differentiation. [Conclusions] The findings suggest a novel role for MCs in the development of ILD via TGF-β1 production-induced myofibroblast differentiation.

## P1-084

**Suppression of cytokine signaling in peripheral blood immune cells from patients with rheumatoid arthritis on Jak inhibitors**

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Conflict of interest: None

[Objective] We investigated the effects of Jak inhibitors on Stat phosphorylation in peripheral blood immune cells from patients with RA. [Methods] Cytokines were added to whole blood from RA patients with low disease activity or clinical remission under treatment with methotrexate (MTX), golimumab, baricitinib or upadacitinib, and healthy controls (HC). The mean fluorescence intensity (MFI) of pStat1, 3, 4 and 5 in each immune cell was measured by flow cytometry. MFI ratio before and after cytokine stimulation was calculated. Median MFI ratio (MFI treatment group/MFI HC group) of each pStat of 0.4 and less than 0.4, and $p<0.05$ for a comparison between the two groups was defined as significant inhibition of Stat phosphorylation. [Results] In Jak inhibitor group, pStat1, 3 and 5 in CD4, CD8, and CD14 positive cells, pStat3 and 5 in CD19 and CD123 positive cells, and pStat3 in CD16/56 positive cells following IFN-α stimulation and also pStat1 in CD14 and CD19 positive cells following IFN-γ stimulation was significantly suppressed. No significant suppression was observed in MTX or golimumab group. [Conclusions] Significant suppression of Stat phosphorylation in response to multiple cytokine stimulation was observed in peripheral blood immune cells of patients with RA on Jak inhibitors.

## P1-085

**Differential control of RB phosphorylation by antirheumatic drugs in TNF alpha-induced synovial fibroblast proliferation**

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Conflict of interest: None

[Objective] The mechanisms regulating cell cycle progression of synovial fibroblast (RASF) in rheumatoid arthritis are not fully understood. CDK6 is a cell cycle regulator at G1 phase, and we have previously reported its expression inhibitor (C6I) attenuated TNFα-induced RASF proliferation without suppressing CDK4 expression and significantly inhibited RB phosphorylation. This study aims to compare the effect of existing drugs, Palbociclib (PAL) and MTX on TNFα-induced cell proliferation in vitro with the antiproliferative effect of C6I. [Methods] Inhibitors (C6I, PAL, MTX) were added to TNFα-stimulated RASF and viable cells were measured after 72 h using a CCK8. The mRNA expressions were quantified by qPCR. The phosphorylation levels of RB were analyzed by Western blotting. [Results] Cell viability was significantly suppressed with C6I or PAL addition, but not with MTX. CDK6 mRNA levels suppressed only by C6I. TNFα-induced RB phosphorylation was significantly inhibited by C6I or PAL to the same extent but not altered by MTX. [Conclusions] As previously reported, MTX did not affect proliferation of RASF. C6I and PAL demonstrated similar inhibitory effects on proliferation and RB phosphorylation in RASF, although mechanisms involved in the regulation of CDK6 were different.

## P1-086

**Mice with macrophage-specific deficiency of the dsRNA editing enzyme ADAR1 develop fulminant pneumonia with positive anti-MDA5 antibodies**

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Conflict of interest: None

<Background> The double-stranded RNA editing enzyme ADAR1 is known to function in an MDA5 pathway-dependent manner, but its association with the pathogenesis of anti-MDA5 antibody (Ab)-positive fulminant interstitial pneumonia is unknown. To clarify the role of ADAR1 in the innate immune pathogenesis of fulminant lung inflammation, we analyzed macrophage-specific ADAR1-conditional knockout mice (Lys-ADA1-cKO) in a model of antigen-induced airway inflammation. <Methods> OVA was intratracheally administered to OVA/Alum sensitized mice. Following the challenge, histopathological analysis was performed. Intrapulmonary cell populations were analyzed by flow cytometry and RNA sequencing analysis. Various Ab titers were measured on sera. <Results> Compared to wild-type (Wt) mice, the lungs of cKO mice showed increased cellular infiltration by T cells, neutrophils, and macrophages and vasculitis with marked alveolar hemorrhage. Surprisingly, not only OVA-specific IgE Abs but also MDA5-specific IgG Abs were higher in cKO mice than in Wt mice. cKO macrophages expressed various inflammation- and immunity-related genes compared to Wt. <Conclusion> The perturbation of ADAR1 functions in macrophages may be implicated in the pathogenesis of *anti-MDA5* Ab-positive fulminant interstitial pneumonia.

## P1-087

**Alteration of microbial composition in the skin and blood in vasculitis**

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Conflict of interest: None

[Objective] Various microorganisms have been associated with the pathogenesis of vasculitis. However, the causal microbial agents and underlying mechanisms are not fully understood. In the present study, we characterized the microbiome profile of patients with cutaneous vasculitis using metagenome shotgun sequencing. [Methods] Blood and skin tissue samples were collected from 18 patients with vasculitis [cutaneous arteritis (n=4), IgA vasculitis (n=12), microscopic polyangiitis (n=1), cryoglobulinemic vasculitis (n=1)] and comprehensive analysis of microbial genes was performed and compared with samples from 14 healthy donors. [Results] The number of SEN virus reads was increased in serum and skin from vasculitis patients compared to healthy donors. In particular, the number of SEN virus reads was increased in sera from patients with cutaneous arteritis. We also analyzed serum bacterial taxa using LDA effect size to detect differences between patients with vasculitis and HD. The bacterial read that was remarkably elevated in the vasculitis serum was from *Corynebacteriales*. [Conclusions] These findings demonstrate that vasculitis is associated with considerable alteration of the microbiome in the blood and skin and suggest a role for the infectious trigger in vasculitis.

## P1-088

**Clinical investigation of ADAM-17 in collagen disease related interstitial lung disease**

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Conflict of interest: None

[Objective] To elucidate the pathogenesis of interstitial lung disease (ILD) by examining clinical data, imaging findings, and serum cytokines in collagen disease related interstitial lung disease (CTD-ILD). [Methods] We analyzed serum ADAM-17, fractalkine/CX3CL1, and CXCL16 of 69 patients with inflammatory muscle diseases (10 patients with CADM, 34 patients with DM, 25 patients with PM), 22 patients with RA, 42 patients with SSc, and 12 patients with MCTD) by ELISA. We also examined the correlation with clinical data. We divided into 6 patterns of ILD and 5 groups of extent of lesions on CT images, and investigated the correlation with clinical data. [Results] We found that ADAM-17 in serum in rheumatic disease was significantly higher compared with in healthy controls. KL-6, SP-D, and ADAM-17 were significantly higher in patients with than without ILD. KL-6, SP-D, ADAM-17, fractalkine/CX3CL1, and CXCL16 showed significant differences in each disease group. SP-D and fractalkine/CX3CL1 were correlated with ADAM-17, respectively. Finally, we investigated that ADAM-17 showed no significant differences in imaging findings. [Conclusions] The expression of cytokines in CTD-ILD differed depending on the disease group and the degree of pattern and extent of lesions.

## P1-089

**Evaluation of the functions of ITIH4 and its citrullinated form in two experimental arthritis models**

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Conflict of interest: None

[Background] Inter-alpha-trypsin inhibitor heavy chain 4 (ITIH4) is a plasma protein that inhibits neutrophil migration and increases at the onset of rheumatoid arthritis (RA). In contrast, citrullinated ITIH4 (cit-ITIH4) induces neutrophil migration in vitro and is specifically expressed in RA blood and joints. However, its function in arthritis remains unclear. [Methods] We examined ITIH4 and cit-ITIH4 expression in blood of K/BxN serum transfer arthritis (STA) and collagen-induced arthritis (CIA), and also investigated citrullinated protein expression in CIA joints and lungs. The severity of STA and CIA were compared between wild-type mice (WT) and ITIH4 deficient mice (KO). [Results] In STA and CIA, serum ITIH4 and cit-ITIH4 increased from the onset of arthritis, and cit-ITIH4 increased most during the extreme arthritis phase. Citrullinated protein was observed in CIA joints, but not in the lungs. There was no significant difference in the severity of STA or CIA and infiltrating cells to joints in CIA between KO and WT. However, neutrophil infiltration to the CIA lungs significantly increased in KO. [Conclusions] ITIH4 may inhibit neutrophil infiltration in arthritis model, but cit-ITIH4 is deficient in KO joints and its function in arthritis could not be determined.

## P1-090

**Anti-rheumatic potential of PLK inhibitory therapy in a rheumatoid arthritis model**

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Conflict of interest: None

[Objective] Polo-like kinase (PLK) family has a pivotal role in cell cycle progression. A recent study has shown that the inhibition of PLK1 and PLK2 has a therapeutic effect on rheumatoid arthritis (RA) and osteoarthritis (OA) by inducing apoptosis in synovial cells. The purpose of this study is to investigate the anti-rheumatic potential of PLK inhibitors in an RA mouse model. [Methods] BI2356, a PLK inhibitor, was administered to zymosan-treated SKG mice. The therapeutic effect was evaluated through clinical, histological, and bone morphological assessment. The expression levels of cytokines and PLKs in joints and serum were measured with quantitative PCR and ELISA. The anti-proliferative effect of PLK inhibition was investigated using fibroblast-like synoviocyte (FLS) cell lines. [Results] BI2356 treatment ameliorated arthritis in both clinical and histological assessment of SKG mice. Furthermore, the treatment suppressed the loss of bone mineral density. As a mechanism of action, BI2356 attenuated the expression levels of inflammatory cytokines and PLK2 in joints and serum. In addition, BI2356 demonstrated a tendency to

suppress the proliferation of FLS in vitro. [Conclusions] These results suggest that PLK inhibitory therapy may have potential as a novel strategy to overcome RA.

## P1-092

**The coronary arteritis induced by Candida albicans water soluble fraction (CAWS) was exacerbated in NOD1 knockout mice**

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Conflict of interest: None

[Objective] The administration of NOD1 ligand, FK565, induces coronary arteritis like Kawasaki disease in mice. Similarly, *Candida albicans* water soluble fractions (CAWS) also induces coronary arteritis. We evaluated the role of NOD1 in CAWS induced coronary arteritis model. [Methods] CAWS was administered to NOD1 knockout (NOD1-KO) and wild type (WT) mice for 5 days, and they were sacrificed at day 28. In pathological evaluation the severity of inflammation was graded on a four-point scale. Furthermore, BMDCs were stimulated with CAWS and/or ATP, and the production of cytokines were measured. [Results] The incidence rates were 70% in WT (n = 10) and 100% in NOD1-KO (n = 7). The severity scores were 1.7±1.3 in WT and 3.0±0.0 in NOD1-KO (p = 0.0088). The area of inflammation were 1.17±1.34 $mm^2$ in WT and 2.72±0.59 $mm^2$ in NOD1-KO (p = 0.032). The secretion of IL-1β from BMDCs was significantly higher in NOD1-KO. The increasing of IL-1β was attenuated by addition of an ASK1 inhibitor. [Conclusions] The induction of coronary arteritis by CAWS was not dependent on NOD1. On the contrary, the deficiency of NOD1 aggravated the coronary arteritis in mice. The possibility that ASK1, one of MAPKKKs, was associated with the exacerbated inflammation in NOD1-KO was indicated.

## P1-093

**TNFalpha-induced adipose-related protein (TIARP) suppresses the pathogenesis of bleomycin-induced pulmonary fibrosis**

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Conflict of interest: None

[Objective] TIARP (STEAP4 as a human orthologue) is a six-transmembrane protein induced by inflammatory cytokines such as TNFα. We previously reported that TIARP-/- mice exhibited an exacerbation of arthritis, which was associated with enhanced cytokine/chemokine production from CD11b+ cells and synovial fibroblasts. In this study, we aimed to investigate the role of TIARP in bleomycin (BLM)-induced pulmonary fibrosis. [Methods] 1) Analysis of TIARP expression in mouse lungs 2) Histological analysis and flow cytometry (FACS) analysis of BLM-induced pulmonary fibrosis in TIARP-/- mice 3) Functional analysis of human lung fibroblasts (HLF) with STEAP4 knockdown [Results] 1) TIARP expression was increased in fibrotic portions of the interstitium in mouse lungs after BLM treatment. 2) TIARP-/- mice showed enhanced lung fibrosis and inflammatory cell infiltration, especially of macrophage subsets. (3) STEAP4 expression was increased by TNFα in HLF. STEAP4 knockdown resulted in increased cell proliferation and IL-6 expression after TNFα stimulation. Inhibition of IL-6 signaling limited cell proliferation in STEAP4 knockdown HLF. [Conclusions] TIARP may contribute to the pathogenesis of pulmonary fibrosis by regulating IL-6 production and cell proliferation of macrophages and fibroblasts.

## P1-094

**Effect on the gut microbiome when treated with prebiotics or anti-gut microbiome/LPS antibodies by methotrexate in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective and Methods] It has been reported that high-dose methotrexate (MTX) decreases Bacteroides, commonly referred to as healthy bacteria, in rheumatoid arthritis (RA) and MTX responsiveness was influenced by the baseline gut mycobacterial composition. In this study, we demonstrated that csDMARDs IR RA patients treated with milk antibodies (anti-gut microbiome/Lipopolysaccharide (LPS) antibodies) and prebiotics exhibited good clinical efficacy and changes in mycobacterial composition, as previously reported. However, approximately 60% of the 87 patients had previously taken MTX (2-14 mg/week). In this study, we analyzed the effect of MTX on gut microbiome composition and clinical outcomes [Results] **1)** The MTX-treated group showed greater effectiveness in DAS28-ESR compared to the MTX-untreated group in all three groups.**2)** MTX reduced gut mycobacteria and increased E. coli (indicating dysbiosis).**3)** Milk antibodies augmented the reduction of IL-6 and TNF production by MTX. **4)** Milk antibodies influenced an increase in fecal LPS, possibly originating from healthy bacteria like Bacteroides and Petrella, but MTX did not. [Conclusions] MTX affects clinical efficacy and mycobacterial composition changes when patients are treated with prebiotics or anti-gut microbiome/LPS antibodies.

## P1-095

**Anemia as a comorbidity of rheumatoid arthritis is independent one**

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Conflict of interest: None

[Objective] The reason for anemia due to rheumatoid arthritis (RA) was tried to identify. [Methods] Patients with RA since August 2010 were picked. Their clinical data at the first consult were extracted. Mean values of patient's age, gender proportion (Gender), disease duration of RA, anti-citrullinated polypeptide antibodies, rheumatoid factor, hemoglobin (HGB), albumin (ALB), lymphocyte count (LYMPH), serum iron, total bilirubin, cystatin-C-based estimated glomerular filtration rate (eGFR), clinical disease activity index, C-reactive protein (CRP), number of comorbidities were calculated, and these values were evaluated with HGB as dependent and the other variables as independent factors. As a control, patients who consulted other diseases than RA (nRA) were also picked up and compared to the RA group. RA and nRA were paralleled using propensity score matching (PSM) to adjust significantly different factors between the two groups. [Results] A total of 463 for RA and 345 for nRA were picked up. Gender, ALB, LYMPH, and eGFR correlated significantly with HGB in both groups and CRP in the RA group with the crude dataset. After PSM, HGB in the RA and nRA was significantly different (RA < nRA). [Conclusions] The anemia in the RA patient is suggested as an independent one.

## P1-096

**Biomarker exploration of EGPA and ANCA-associated vasculitis using novel proteomics**

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Conflict of interest: Yes

ANCA-associated vasculitis (AAV) is a refractory disease with a poor prognosis, and a diagnostic biomarker (BM) is required. At the same time, BM that reflects disease activity is also important because relapses are frequent. EGPA, accompanied by eosinophilic inflammation, has a distinct pathogenesis compared to MPA and GPA, making its diagnosis and treatment particularly challenging. To explore these BMs, we performed exploratory proteomics on serum samples from 12 patients with AAV including EGPA, 19 patients with other diseases including bronchial asthma and

rheumatoid arthritis, and 5 healthy controls. For validation, additional proteomics was performed on serum samples from 12 patients with EGPA pre- and post-treatment, 10 patients with bronchial asthma, and 10 healthy controls. As a result, a total of 7289 proteins were identified from both proteomics, respectively. Further statistical examination identified both EGPA-specific and general AAV BMs that accurately diagnose these diseases and indicate disease activity. Moreover, by integrating proteomic data with the associated clinical information, we gained insights into the significance of these proteins in the pathogenesis of both EGPA and AAV.

## P1-097

**Changes in M2BPGi and FIB-4 index during administration of IL-6R antibody in rheumatoid arthritis**

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Conflict of interest: None

[Objective] TO investigate liver fibrosis when IL-6R antibody administered to RA patients. [Methods] We conducted a retrospective chart review of the changes in FIB-4 index and M2BPGi before and after administration of IL-6R antibody in RA. [Results] FIB-4 index and M2BPGi were measured simultaneously before and after administration of IL-6R antibody in 73 cases, a total of 227 times. Administration period 1.5 yrs, 74.0% female, age 73.0 years, HBV carrier 2.7%, past infection 34.2%, HCV 1.4%, usage rate and amount of each drug; PSL 13.7%, PSL dose 4.1 mg, SASP 41.1%, bucillamine 34.2%, iguratimod 19.2%, mizoribine 20.5%, CyA 1.4%, MTX 9.6%, MTX dose 6.0 mg, leflunomide 2.7%, IL-6R antibody SAR 21.9%, TCZ 78.1%, pre-administration M2BPGi 0.95, FIB-4 index 1.57, platelet count 264,000, AST 18, ALT. The values of each parameter after administration were M2BPGi 1.05, FIB-4 index 1.81, platelet count 226,000, AST 20, ALT 15. Testing the changes in each parameter before and after administration, FIB-4 index ($p< 0.0001$), platelet count ($p<0.0001$), AST ($p=0.0408$), and ALT ($p<0.0001$), but no significant change was observed in M2BPGi ($p=0.1123$). [Conclusions] If the FIB-4 index increases during administration of IL-6R antibody in RA, careful interpretation is required using other parameters.

## P1-098

**Consideration of cases of rheumatoid arthritis diagnosed following a preoperative examination for knee surgery**

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Conflict of interest: None

[Objective] We examined cases diagnosed with rheumatoid arthritis (RA) as a result of a preoperative test for knee surgery. [Methods] We included cases that were found abnormal values in preoperative blood tests for surgery of knee osteoarthritis (OA) during from April 2018 to October 2023. Among these, we reviewed the clinical findings and outcomes of 14 cases diagnosed with RA. [Results] The mean age was 64.8 (21-79) years, 71.4% were female, the mean RF value was 84.5 (0-359) IU/ml, 57.1% positive rate, the mean anti-CCP antibody titer was 128.8 (0-470) U/ml, 64.3% positive rate, the mean CRP value was 5.2 (0.5-12.4) mg/dl, and 100% positive rate. 3 cases (21.4%) had arthritis only in knee joints, and 11 cases (78.6%) had arthritis also in hand/finger joints. 7 cases (50%) underwent surgery after medical treatment for RA, 2 cases (14.3%) started medical treatment after surgery, and 5 cases (35.7%) avoided surgery because the condition improved with medical treatment. [Conclusions] Among patients treated for knee OA, RA complications were sometimes observed, and in some cases, medical treatment for RA improved the condition and surgery was avoided. Even in patients with symptoms mainly in knees, checking other joint symptoms and blood tests may be useful for early detection of RA.

## P1-099

**A case of polyarthritis complicated with diabetes mellitus**

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Conflict of interest: None

[Background] Patients with diabetes mellitus (DM) often present with musculoskeletal symptoms such as diabetic cheiroarthropathy, palmar flexor tendonitis, and carpal tunnel syndrome. Rheumatoid arthritis (RA) is characterized by tenosynovitis in the initial stages. When patients with DM develop joint symptoms, further investigation is required to differentiate musculoskeletal symptoms of DM, autoimmune diseases such as RA, and paraneoplastic syndromes. We report a case of a patient with DM revealed tenosynovitis and synovitis. [Case] A 70-year-old woman with type 1 DM presented with polyarthralgia visited an orthopedist. She was diagnosed as diabetic neuropathy and treated, but her condition did not improve and she was referred to our hospital. After the examination, the possibility of diabetic neuropathy was ruled out. Although RF, anti-CCP antibody, and CRP were all negative in blood tests, ultrasonography and contrast-enhanced MRI showed symmetrical synovitis and tenosynovitis in the fingers and wrist joints. She was diagnosed with RA based on the imaging findings, and treated with methotrexate. [Discussion] Musculoskeletal symptoms associated with DM have various pathologies, and it is difficult to distinguish from RA. The imaging examination may be useful in the diagnosis.

## P1-100

**The Evaluation of relative factors associated with maintaining long-term structural remission of Rheumatoid Arthritis (RA) patients: A single-center retrospective analysis by means of Modified total Sharp Score**

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Conflict of interest: None

[Objective] To elucidate the factors associated with maintaining Xp structural remission in RA patients in our institution. [Methods] We conducted a retrospective analysis of fifty-three RA patients between April 2016 and March 2022. Modified total Sharp Scores (mTSS) were measured by at least two Rheumatologists for 3 years or more. Logistic regression analysis was performed to analyze the factors associated with maintaining structural remission in RA patients. Maintaining structural remission was defined as preserving $\Delta mTSS \leqq 0.5$/year for at least 3 years. [Results] Fifty-three RA patients (mean age; 66.3 years, female; 64.1%, RA-Stage at baseline; I, n=17; II, n=18; III, n=6; IV, n=12) were enrolled. Twenty-six patients (49.6%) achieved maintaining structural remission. Multivariate analysis revealed "RA-Stage at the first visit" (odds ratio [OR] 3.45, 95% confidence interval [CI] 1.22-9.74) as an only independent factor associated with maintaining structural remission with statistical significance ($p<0.05$). [Conclusions] In our institution, 49.6% of RA patients could achieve strict structural remission. RA-Stage at the first visit could be associated with maintaining long-term structural remission.

## P1-101

**Utility of screening patients with pain sensitivity in rheumatoid arthritis by physical examination of 18 tender point sites, according to ACR 1990 criteria for the classification of fibromyalgia (FMS)**

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Conflict of interest: None

[Objective] To assess the screening methods of RA patients with sensitivity to pain, using physical examination of the 18 tender point sites, according to ACR 1990 criteria for the classification of FMS. [Methods] 149 patients with rheumatoid arthritis (51: male, 98: female, all under the age of 80) were divided into two groups based on the presence of (group B: 10 patients) or absence of (group A: 139 patients) tenderness at the 18 tender point sites described above. We examined the difference between group A and B, regarding age, gender ratio, history of RA, stage, class, HAQ-DI, tender joint count, swollen joint count, RF, ACPA, CRP, ESR,

PS-VAS, PGA, EGA, DAS28CRP, DAS28ESR, CDAI, and SDAI. [Results] Significant differences were observed in age (A: 66 years old, B: 73 years old), class, HAQ-DI (A: 0.23, B: 1.01)), tender joint count (A: 1.0, B: 12.8), 18 tender point sites count (A: 0, B: 5.8), PS-VAS (A: 19.7, B: 41.2), and PGA (A: 20.1, B: 42.9). Significant differences were also observed in DAS28CRP (A: 1.97, B: 3.37), DAS28ESR (A: 2.48, B: 4.00), CDAI (A: 4.12, B: 14.0), and SDAI (A: 4.49, B: 14.4). [Conclusions] Screening patients with pain sensitivity in RA by physical examination of the 18 tender point sites, according to ACR 1990 criteria for the classification of FMS, was useful.

## P1-102

**A novel disease activity classification of rheumatoid arthritis for Joint Index Vector method**

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Conflict of interest: None

Objective: Joint Index Vector method (JIV) is a novel quantitative indicator of joint involvement for patients with rheumatoid arthritis (RA). We tried to classify the JIV as a disease activity classification. Methods: All joint findings and disease activity in RA patients have been monitored since July 2014. Associations between JIV and CDAI, and JIV and mHAQ statistically. Results: A total of 21,936 times of measurement was picked up. Vxy of the JIV significantly correlated with CDAI, and the remission (REM) in CDAI was equivalent to Vxy ≦ 0.1. The LDA was equivalent to Vxy ≦ 0.4. In contrast, REM, LDA, MDA, and HDA mixed in the groups of Vxy > 0.4. In the Vxy > 0.4, the mHAQ score differed significantly among the REM, LDA/MDA, and HDA. The REM and the other disease activity groups could be classified with Vz > 0.05 of the cut-off index (COI), and the HDA and the other groups could be classified with Vz > 0.625 of the COI. Thus, the remission of JIV as Vxt ≦ 0.1, the LDA as Vxy ≦ 0.4, or Vxy > 0.4 and Vz ≦ 0.05, the MDA as Vxy > 0.4 and Vz > 0.05 and Vz ≦ 0.625, and HDA as Vxy > 0.4 and Vz > 0.625 were determined. Conclusions: JIV is an available indicator for joint involvement and its utility increases when the level of disease activity is included.

## P1-103

**Evaluating add-on effect of molecular-targeted drugs by joint index vector**

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Conflict of interest: None

[Objective] According to treatment guideline for RA, b/tsDMARDs (b/tD) are recommended when the therapeutic target is not achieved by MTX. Our aim is to assess the add-on effects of b/tD using joint index vector (J Big Data 2018;5:37). [Methods] From *NinJa* '19 to '21, 4145 patients, treated with MTX for 3 years and not with b/tD for the first two years, were extracted. Transform matrix for predicting next-year vectors in MTX users was obtained from mean vectors of '19 and '20. The difference between predicted and actual X, Y, Z, and scaler V: dX, dY, dZ, and dV were compared in patients with (+) or without (-) b/tD. [Results] In the third year, b/tD were used in 104 patients. Median [IQR] of dX, dY, dZ, and dV were 0.00 [-0.01, 0.05] (-) vs. 0.00 [-0.18, 0.03] (+) ($p<0.01$), 0.00 [-0.04, 1.87] (-) vs. -0.03 [-0.12, 0.94] (+) ($p<0.001$), 0.00 [-0.05, 0.03] (-) vs. 0.00 [-0.13, 0.09] (+) ($p=0.18$), 0.00 [-0.02, 0.06] (-) vs. -0.02 [-0.20, 0.10] (+) ($p<0.001$), respectively. Predicted vectors in patients without b/tD were roughly in accordance with actual ones, and the difference between them in patients with b/tD reflected the add-on effects of the drugs. [Conclusions] Combination use of b/tD and MTX made vector scalers shorter than predicted ones and had add-on effects of decreasing disease activities.

## P1-104

**Analysis of Risk Factors for 5-Year Renal Function Decline in Patients with Rheumatoid Arthritis in Our Hospital**

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Conflict of interest: None

[Objective] Renal function is one of the most important factors in drug selection in patients with rheumatoid arthritis (RA). The purpose of this study was to analyze risk factors for renal function decline over a 5-year period in patients with rheumatoid arthritis at our hospital. [Methods] Patients who attended our department for 5 years from April 2018 to March 2022 were included. One hundred and forty-five patients (39 males and 106 females) were included, excluding those who introduced or discontinued MTX during the period. Mean age 67.7 years. 108 MTX users, mean MTX use 7.7 mg. 51 biologics users, 5 JAK inhibitor users. The mean annual decline in eGFR (0.5 mL/min/1.73m2/year) in a healthy population was compared by groupwise Univariate and multivariate analyses were performed between the over declined (group A: 57 subjects) and normal (group B: 88 subjects) groups. [Results] Multivariate logistic regression analysis was performed using age, MTX use, RF factors, CCP antibody, and ESR as explanatory variables. The results showed that age was the only independent factor associated with above-average eGFR decline ($p<0.05$). [Discussion and Conclusions] It is known that the rate of decline of renal function accelerates with age, and the results of this study are consistent with this.

## P1-105

**Serum Mac-2 binding protein glycosylation isomer levels correlate with disease activity in patients with rheumatoid arthritis, a disease associated with type 1 interferonopathy**

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Conflict of interest: None

[Objective] The aim of this study is to evaluate the utility of serum M2BPGi levels in patients with RA. [Methods] This was a cross-sectional study. A total of 135 eligible RA patients were included in this study in our department's database from January to April 2020, excluding patients with neither RA disease activity nor laboratory data including Mac2BPGi. [Results] The median age of patients was 67.0 (IQR: 57.0-73.0) years, and the median disease duration was 13.0 (9.0-6.5) years. The median SDAI was 2.02 (1.16-5.11). Median serum M2BPGi levels were 0.85 cut-off index (C.O.I.) (0.63-1.18). M2BPGi was significantly correlated with SDAI and DAS28-CRP ($r=0.230$ and $r=0.238$, respectively). Serum M2BPGi levels were significantly lower in the DAS28-CRP remission group compared to the non-remission group (0.80 vs. 1.07, $p<0.02$). Multiple regression analysis of serum M2BPGi identified age and SDAI as independent factors. [Conclusions] The study showed that serum M2BPGi levels correlate with disease activity in rheumatoid arthritis as an independent factor. It has been suggested that serum M2BPGi may be a marker for the assessment of disease activity in RA.

## P1-106

**Examination of the predictive factor of the D2TRA in our hospital**

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Conflict of interest: None

[Objective] Recently, biological and targeted synthetic disease modifying anti-rheumatic drugs (b/ts DMARDs) are expected to be more effective in patients with rheumatoid arthritis (RA). However, some patients are resistant to multi-drug therapy, and the term of "difficult-to-treat RA (D2TRA)" is widely recognized. The aim of this study was to investigate the clinical feature, the predictors of D2TRA in Y clinic specialized in

collagen disease. [Methods] Total of 413 cases who were administered first b/ts DMARDs in Y clinic from February 2008 to February 2022 and were followed for at least 1 year was enrolled. D2TRA was defined as failure of two or more b/ts DMARDs with different mechanisms of action. Logistic regression analysis was used to identify the predictors of D2TRA. [Results] Female, positive anti-CCP antibodies, high disease activity, interstitial lung disease, history of malignancy, and history of autoimmune disease were identified as the predictors of D2TRA. [Conclusions] Female, high disease activity, interstitial lung disease, positive anti-CCP antibody, history of malignancy, and history of autoimmune disease were found as candidates of D2TRA predictor. Further studies will be required to clarify the strategy for treatment of patients with RA.

## P1-108

**Change in tartrate-resistant acidic phosphatase 5b titers reflects joint damage in rheumatoid arthritis**

Takayoshi Owada[1], Takayuki Kobayashi[1], Ayae Tanaka[2], Hideyuki Satoh[1], Masamitsu Tatewaki[1], Kei Ikeda[2], Hirokuni Hirata[1], Masafumi Arima[2], Kazuhiro Kurasawa[2], Yasutsugu Fukushima[1]
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Conflict of interest: None

[Object] To clarify the relationship between serum tartrate-resistant acidic phosphatase (sTRACP)-5b and joint damage in rheumatoid arthritis (RA). [Methods] The subjects were men (≦55 yo) and premenopausal women with RA and underwent both sTRACP-5b measurements and assessments by mTSS at enrollment and 1 year later. Reduction of minimal significant change (MSC) in sTRACP-5b levels was defined as significant decrease. Radiographic remission (RR) was defined as yearly progression <0.5 by mTSS. [Results] Objects were 50 RA patients (40 women, age 46 years, 39 seropositive, CDAI 6, mTTS 5), 6 before treatment and 44 during treatment. sTRACP-5b levels tended to be higher in mTTS only in pretreatment RA. Decrease of TRACP-5b above MSC was observed in 11 of 44 patients, whose progression of joint damage was less than that of non-decrease (p=0.01). In addition, the rate of structural remission was 81.8% for sTRACP-5b reduction of MSC or greater, compared with 39.4% for no reduction (p=0.03). sTRACP-5b change was a factor associated with RR (unit OR; 0.978 [0.961-0.991], p=0.0002). [Conclusion] sTRACP-5b levels were associated with joint damege. In the absence of a significant decrease in sTRACP-5b, about 60 of patients would be expected to progress to joint damage.

## P1-109

**Positive antinuclear antibodies pose a risk of persistent fatigue in patients with RA who have attained remission ~from SETOUCHI-RA registry~**

Akiko Nagasu[1], Kazuhisa Nakano[1], Shunichi Fujita[1], Sumie Asano[1], Takahiko Akagi[1], Shoko Tsuji[1], Hiroyasu Hirano[2], Yoshitaka Morita[1]
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Conflict of interest: None

[Objective] To elucidate the characteristics of patients with rheumatoid arthritis (RA) experiencing lingering fatigue during remission. [Methods] A single-center retrospective study (SETOUCHI-RA registry). Out of 872 adult RA patients in our care between August and December 2022, 315 achieved CDAI remission. We defined fatigue VAS scores of ≧20 mm as "persisting fatigue." The multivariable logistic analysis yielded the following outcomes. [Results] Among the 81 patients who continued to experience fatigue after achieving CDAI remission, 66 were women, with an average age of 64 years, a disease duration of 10 years, and RF/ACPA positivity of 70%/69%. There were no discernible differences in complications or the use of csDMARD, b/tsDMARD, or corticosteroids based on the presence or absence of persisting fatigue. Multivariable logistic analysis identified antinuclear antibody (ANA) levels exceeding 40 times as an independent risk factor. [Conclusions] Previous studies have demonstrated that ANA positivity is associated with persistent fatigue, even in the absence of clinical signs of collagen disease. In patients with RA in remission, ANA positivity is also a risk factor for persistent fatigue, suggesting that ANA positivity may serve as a reference for selecting therapeutic agents.

## P1-110

**Investigation of lumbar spine lesions in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] We examined the prevalence of lumbar scoliosis and spondylolisthesis in rheumatoid arthritis (RA) patients. [Methods] We studied 82 RA patients with or without low back pain aged 50+ (16 males, 66 females) excluding those on dialysis or with lumbar spondylolysis. Lumbar lesions with a Cobb angle >10 degrees were classified as scoliosis and displacements >3 mm as spondylolisthesis. Logistic regression used age, gender, RF, and ACPA titers to analyze these outcomes. [Results] 48.7% had scoliosis, 45.1% had spondylolisthesis, and 24.4% had both. No significant factors were found for individual conditions, but the ACPA titer was significant when analyzing both. [Conclusions] Nearly half of the RA patients showed lumbar spine abnormalities, potentially higher than the general population's past rates. It was also suggested that more severe structural changes may be associated with ACPA titer.

## P1-111

**Anti-CCP Antibody Positive Rheumatoid Arthritis Presenting with Synovitis of the Sternoclavicular Joint, Intermetatarsal Bursitis, and Retrocalcaneal Bursitis in the Absence of Peripheral Arthritis**

Yuji Miyoshi, Nanae Okimoto, Keisuke Hirobe, Yuki Terashima, Kei Karakida, Sayuri Mizumoto, Issei Takahashi, Tomoko Sano, Tomohiro Kato, Takaaki Ito, Akane Ito, Yoshitaka Ueda, Nanase Honda, Eisuke Takamasu, Kae Onishi, Masako Utsunomiya, Yoshiki Nagai, Naoto Yokogawa, Kota Shimada
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Conflict of interest: None

Introduction: Rheumatoid arthritis (RA) is an autoimmune disease primarily characterized by chronic destructive polyarthritis. We report an atypical case of seropositive RA-positive absent of peripheral arthritis. Case Presentation: A woman in her fifties developed right toe pain, which, within a year, extended to her upper chest and heel, prompting her visit to our rheumatology department in December of year X. Musculoskeletal ultrasound demonstrated active synovitis in the right sternoclavicular joint, enthesitis at the Achilles tendon, right retrocalcaneal bursitis with accompanying bone erosion, and intermetatarsal bursitis. No synovial hypertrophy was identified by ultrasound in the peripheral joints. The patient's anti-CCP antibodies were >500 U/mL. Diagnosed with anti-CCP-positive RA; she commenced methotrexate (MTX) treatment in December of year X. Due to minimal symptom improvement, subcutaneous abatacept was introduced in April of year X+1. By September, pain had ceased, and ultrasound confirmed the therapeutic response. Clinical Significance: This case underscores intermetatarsal bursitis as a useful clinical finding suggestive of RA and highlights the presence of atypical RA absent peripheral arthritis.

## P1-112

**Effectiveness of subcutaneous methotrexate in our department**

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Conflict of interest: None

[Objective and methods] Methotrexate (MTX) have become the anchor drug for rheumatoid arthritis, but gastrointestinal (GI) side effects of oral route may restrict its use in most of the patients. An alternative to oral MTX (MTX OR) is the parenteral MTX administration. Although parenteral formulations of MTX have been available worldwide, it was not available in Japan until recently. On September 2022, a subcutaneous injection method of MTX was approved in Japan. We examined the 6 months follow up of 7 patients who switched from MTX OR to subcutaneous MTX (MTX SC) at our department. [Results] The mean weekly dose of MTX OR was 8.0 mg/week before the switch to MTX SC. The reasons for discontinuation of MTX OR were GI 100%, hepatotoxicity 28.5%, and fatigue / diarrhea 14.2%. After MTX SC was started, 28.5% discontinued due to GI. After 6 months, the weekly dose of MTX SC was 7.5 mg in 28.5%, 10.0 mg in 14.2%, and 12.5 mg in 28.5%. 42.8% was able to discontinue glucocorticoids (GC) and csDMARDs due to improvement in disease activity. [Conclusions] MTX SC may improve disease activity and reduce the use of GC and csDMARDs when MTX OR is inadequate due to side effects. MTX SC has the potential to delay or avoid the need for switching to much more expensive biological drugs or tsDMARDs.

## P1-113

**Gastrointestinal Symptoms of Subcutaneous Methotrexate**

Tatsuo Watanabe[1], Daisuke Kihira[1], Yoichiro Haji[2], Mizuki Kato[2], Mitsuru Watanabe[2], Takanori Ito[2], Yui Amari[2], Yukina Yokoyama[2], Mirai Hozumi[2], Sho Higuri[2]
[1]Department of Orthopedic Surgery, Daido Hospital, [2]Department of Rheumatology, Daido Hospital

Conflict of interest: None

[Objective] Methotrexate (MTX) is an anchor drug in the treatment of rheumatoid arthritis. In particular, gastrointestinal symptoms are relatively common among MTX adverse events. In Japan, a subcutaneous formulation of MTX became available in November 2022. Therefore, we investigated gastrointestinal symptoms in patients who switched from oral MTX to MTX subcutaneous injection. [Methods] Among rheumatoid arthritis patients in our hospital, 4 patients who were switched from oral MTX to MTX subcutaneous injection (MTXsc) and whose gastrointestinal symptoms could be evaluated before and after the switch were included in the study. Gastrointestinal symptoms were evaluated using the Gastrointestinal Symptom Rating Scale. [Results] One patient was treated with upadacitinib, and the other three patients were treated with MTX alone. NSAIDs were used in all 4 patients, proton pump inhibitors in 1 patient, and acetaminophen in 1 patient. The most improved item was nausea, which improved from a mean of 5.5±1.9 to 2.8±2.2. No significant improvement was observed in the other parameters. All patients were able to continue MTXsc for more than 12 weeks. [Conclusion]: All 4 patients who were treated with MTX and then MTXsc continued for at least 12 weeks. Nausea" improved the most.

## P1-114

**Adverse effects and efficacy of switching from oral methotrexate to subcutaneous injection in patients with rheumatoid arthritis**

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Department of Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: None

Objective: To compare the side effects and efficacy of subcutaneous methotrexate (MTX) with those of oral MTX in rheumatoid arthritis (RA) patients with nausea and fatigue caused by MTX use. Methods: Patients who had been treated with MTX for at least 12 weeks and who had nausea and fatigue with foliamin 10 mg/w or 15 mg/w or 1 mg/day were included in the study. The primary endpoint was the change in nausea VAS from week 0 to week 13. MTX and foliamin were administered at the same dose for at least 2 weeks before consent was obtained and for 13 weeks after the start of the study. Results: The study was initiated in December 2022, and 30 patients (20 in the change group and 10 in the continuation group) who were available for analysis to date were compared. Patient backgrounds were not significantly different between the two groups in age, gender, duration of disease, MTX dose, and CDAI, but the foliamin dose and DAS28-ESR were higher in the modified group. ΔNausea VAS (-28.00 vs 11.50, $p<0.001$) and ΔMalaise VAS (-11.00 vs 15.00, $p= 0.046$) were significantly improved in the change group. There were no significant differences in Δanorexia VAS, CDAI, and DAS28-ESR between the two groups. Conclusion: MTX subcutaneous injection can improve nausea and anorexia.

## P1-115

**Usefulness of subcutaneous MTX formulation for patients with difficulty in increasing oral MTX dose or insufficient response**

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Miyashita Rheumatology Clinic

Conflict of interest: None

[Purpose] To clarify the efficacy and safety of a subcutaneous MTX (MTXsc) preparation for patients who have difficulty increasing their oral MTX (MTXpo) dose or have insufficient effects. [Methods] 56 RA patients who had difficulty increasing the dose of MTXpo or had insufficient effects due to AEs were changed from MTXpo to MTXsc in a retrospective study. [Results] Among the 56 patients, there were 37 cases in which dose increase was difficult and 19 cases in which the effect was insufficient. The reasons for difficulty in increasing the dose were gastrointestinal symptoms (nausea and epigastric symptoms) in 18 cases, systemic symptoms such as fatigue in 6 cases, elevated liver enzymes in 8 cases, and decreased white blood cells in 3 cases. The average MTX dose was 7.7 mg/week, and 81.1% of patients started with MTXsc 7.5 mg. In cases of GI symptoms/fatigue, cases of elevated liver enzymes, and cases of decreased WBCs, the average MTX oral doses were 9.1, 6.3, and 9.3 mg/week, respectively, and increased to an average of 10, 9.1, and 10.8 mg/week at 8 weeks after changing MTXsc. [Conclusion] By switching to a subcutaneous MTX formulation, it may be possible to increase the dose and reduce disease activity in cases where dose increase is difficult or the effect is insufficient.

## P1-116

**Four Cases of Rheumatoid Arthritis Switched to Subcutaneous Injection due to Ineffectiveness/Intolerance of Oral Methotrexate**

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Meiyo Immunology & Rheumatology Clinic

Conflict of interest: None

[Objective] MTX (oMTX) may be reduced or discontinued if there is intolerance to oMTX, and other csDMARDs or bDMARDs may be added if the effect of oMTX is inadequate. In this study, I report on the effects of switching to subcutaneous MTX (scMTX) in RA patients in these situations. [Cases] Case 1: A 69-year-old woman with inadequate response to oMTX 12 mg/wk and development of hepatic impairment was switched to scMTX 12.5 mg/wk. Hepatic impairment resolved and RA activity decreased with scMTX 15 mg/wk. Case 2: A 45-year-old woman on oMTX 12 mg/wk had persistent monoarthritis of right 5$^{th}$ MTP. oMTX was increased to 16 mg/wk, but was not responsive. Monoarthritis resolved after switching to scMTX 15 mg/wk. Case 3: A 44-year-old woman with alopecia on oMTX 12 mg/wk was switched to scMTX 10 mg/wk, so alopecia disappeared and arthritis activity decreased. Case 4: A 49-year-old man with poor response to oMTX 16 mg/wk was changed to scMTX 15 mg/wk. Arthritis activity decreased from the first week of the change to scMTX. [Clinical Significance] ScMTX was at last approved in Japan in 2022. When oMTX is ineffective or intolerant, there is a clinical struggle to decide whether to add a bDMARD or a csDMARD to reduce RA activity. ScMTX may overcome these situations and avoid concomitant use of bDMARD.

## P1-117

**Experience with the Use of Subcutaneous Methotrexate in Established Rheumatoid Arthritis**

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Department of Orthopaedic Surgery, Nihon University

Conflict of interest: None

[Objective] In 2022, subcutaneous methotrexate (MTX S.C.) became available for treating rheumatoid arthritis (RA) in Japan. MTX S.C. has been reported to be effective and has fewer gastrointestinal symptoms. This report presents our experience with the use of MTX S.C. [Methods] We focused on 9 RA patients who initiated MTX S.C. 8 out of 9 were on oral MTX with an average dosage of 9.3 mg per week. Steroids (PSL) were used by 4 out of the 9 patients with an average daily dosage of 2.9 mg. 4 cases exhibited liver function impairment due to oral MTX. [Results] SDAI showed improvement in 5 out of 9 patients. The PSL dosage decreased from an average of 2.9 mg per day before treatment to an average of 1.6 mg per day at the final assessment. Liver function impairment improved in 1 case, and gastrointestinal symptoms were not observed. There were 3 cases classified as challenging, with 1 case itching and 2 cases reporting fatigue. The average initial dose of MTX S.C. was 8.5 mg per week, and the dosage at the final assessment was 10 mg per week. [Conclusions] For cases MTX S.C. could be continued, disease activity improved, and PSL dosage could be reduced. MTX S.C. is effective for cases where the escalation of MTX is challenging due to gastrointestinal symptoms or liver function impairment.

## P1-118

**Utility and continuation rate of subcutaneous methotrexate for patients with rheumatoid arthritis**

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Conflict of interest: Yes

[Purpose] Oral (o) MTX can`t be continued in many cases due to gastrointestinal (GI) side effects. After approval of subcutaneous (sc) MTX, we investigated its utility and continuation rate. [Method] Among 43 cases with scMTX, 38 (60.2 ± 10.7 years, 73.7% female) followed up to 3 months were investigated for reasons for introduction, adverse events, changes in disease activity, and continuation rate. [Results] The oMTX dose at baseline was 8.0 [IQR; 0, 12] mg/w, and DAS28-ESR was 3.23 [2.92, 4.35]. The reasons were 68.4% for GI symptoms, 13.2 for enhancing effects, 13.2 for switching from leflunomide (REF), and 5.2 for MTX-naive patients. Of the 26 cases with GI symptoms, symptoms disappeared in 24 (92.3%). In each reason for starting scMTX, the changes in disease activity, liver function, and blood cell counts did not show significant changes. The continuation rate was 73.7%, which was the lowest in the group switching from LEF (40%). The most common reason was feeling unwell (50%), followed by refusal to accept injections (33.3%). [Conclusion] Switching to scMTX markedly improved GI adverse events by oMTX. However, no improvement in disease activity was observed, and the continuation rate was unexpectedly low, so care must be taken in selecting suitable patients.

## P1-119

**Effect of switching from oral to subcutaneous injection of methotrexate on disease activity in rheumatoid arthritis**

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Conflict of interest: None

[Objective] MTX is an anchor drug for RA, but many patients are unable to take sufficient doses due to gastrointestinal (GI) symptoms. We investigated the RA patients treated with subcutaneous MTX (MTX-SC) in our hospital. [Methods] Of 1476 RA patients in our department, those who received MTX-SC were extracted. Reasons for MTX-SC introduction, patient background, and disease activity (DAS28-ESR and CDAI) were extracted retrospectively from the electronic medical records. [Results] MTX-SC was used in 30 patients. Mean age was 55.5±13.8 years, 28 (93.3%) were female, median disease duration was 8.3 years [range 0.5-38]. Oral MTX dose was 8.0 mg [0-14] and MTX-SC dose was 7.5 mg [7.5-15]. DAS28-ESR was 3.10±1.35, 2.66±1.22, 3.03±0.89, and 2.51±0.94 (p=0.028) at 0, 4, 8, and 12 weeks, respectively. CDAI was 11.54±8.90, 6.61±5.58, 7.24±3.57, and 5.22±2.94 (p=0.003), respectively. The reasons for switching to MTX-SC were nausea (60%), stomatitis (13.3%), intensified treatment (13.3%) and liver abnormalities (10%). Of the 18 patients who switched to MTX-SC for nausea, 16 (88.9%) were able to continue the MTX-SC. [Conclusions] At 12 weeks after switching to MTX-SC, DAS28-ESR and CDAI were decreased. MTX-SC also showed a good retention rate in patients with GI symptoms on oral MTX.

## P1-120

**The Actual Situation of Oral Methotrexate Use Based on Patient Questionnaire and the Indication of Subcutaneous Injection Formulation to be Examined through the Use of Subcutaneous Injection of Methotrexate at our Hospital**

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[1]Kindai University Nara Hospital, [2]Kindai University Hospital

Conflict of interest: None

[Objectives] Methotrexate (MTX) is mainly used in oral form in Japan, but there are some cases in which patients are unable to continue taking MTX. In this study, we conducted a questionnaire survey on the actual conditions of patients taking oral MTX and examined the indications for subcutaneous injection of MTX through actual cases of use of the subcutaneous injection formulation. [Methods] A questionnaire was sent to 118 rheumatoid arthritis patients attending our hospital who were taking MTX. Three patients were using subcutaneous injections, and the reasons for their use of subcutaneous injections were investigated. [Results] As many as 17% of the survey respondents said they did not understand how to take MTX, and more than 30% said they had leftover medication. In addition, more than 40% of patients experienced side effects. Regarding the cases using the subcutaneous injection formulation, there were two cases who switched to the oral formulation due to gastrointestinal symptoms, and the remaining one case had high disease activity, so we expected rapid onset of effects. [Conclusion] The results suggest that a subcutaneous injection formulation may be an active indication when MTX oral administration is expected to be unstable or when a stable effect is expected.

## P1-121

**Results of a questionnaire on nausea and vomiting in patients taking oral MTX and cases switching to MTX subcutaneous injection**

Shigenori Tamaki[1], Takashi Kato[2], Takashi Kida[3], Motokazu Kai[4], Kunikazu Ogawa[4], Yusuke Suzuki[1], Hidenao Imada[1], Hitomi Nagasaka[1], Yutaka Kawahito[3], Hisaji Oshima[5], Ikuko Tanaka[1]
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Conflict of interest: None

[Purpose and Methods] Nausea caused by oral MTX (poMTX) occurs in about 20% of patients taking the drug. The MTX subcutaneous injection (scMTX) is expected to reduce nausea. We conducted a questionnaire survey on the presence and degree of nausea and switching to scMTX in 406 patients taking poMTX. [Results] The frequency of nausea was almost non-existent (77%), several times in a few months (7%), two or three times in a month (8%) and almost every time (8%). Among those who wanted to switch to scMTX in the existing group, 49% did not want to change, 8% wanted to change, 27% were undecided but would like to hear

from them, and 23% were willing to wait and see. When asked why they did not want to switch to scMTX (open-ended), financial reasons, such as the high price, were the most common reason (36%), followed by concerns about self-injection (18%). 16 patients switched to scMTX, and 2 patients wanted to increase MTX and discontinue Bio. We introduced scMTX in three patients who had previously discontinued poMTX due to nausea. Nausea after starting scMTX improved from a pre-start VAS of 100 to almost 0 ~ 20. [Conclusions] Switching from poMTX to scMTX was effective as a measure against nausea, but economic reasons were a barrier to switching.

## P1-122

**Short-term results of MTX subcutaneous injection formulation for rheumatoid arthritis (RA)**

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Conflict of interest: None

[purpose] MTX subcutaneous injection formulation (hereinafter referred to as MTX SC) We conducted questionnaires and ultrasound examinations on cases treated at our clinic to examine efficacy and safety. [Method] 42 patients who transitioned from oral MTX to MTX SC. The investigation period is R5.1 to R5.9. Age ranged from 17 to 83 years, disease duration ranged from 1 to 58 years, stage I-8/II-20/III-10/IV-4/, class 1-19/ 2-23. CDAI was also observed over time. The degree of improvement in PD was examined in 27 cases in which US could be examined 1 month after administration. [Result] The self-injection procedure was easy for 28 patients, and half of the patients, 21, had no pain during injection. The average injection pain VAS was 1.5 cm. The turning point of side effects when taking MTX disappeared in 20 patients. There were few side effects with MTX SC administration, and 55% felt the effects after 1M (significant response: 45% in 19 patients, effective: 10% in 4 patients). The average CDAI improved to 8.6 before administration. Of the 19 cases that improved, 16 cases (84%) improved to PD Grade 0-1. [Conclusion] MTX SC is easy to administer, can be used relatively safely even in cases where oral MTX administration is difficult, and has a tendency to be highly effective.

## P1-123

**Usage status of Metoject at our hospital**

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Conflict of interest: None

[Purpose] The effectiveness and safety of the MTX injection Metject (MET). [Objective] MET has been used for 24 patients. The breakdown is: MET was introduced from the beginning: 4, side effects of oral medication: 13, the patient was elderly and it was difficult to take the medication stably: 3s, strengthening treatment: 3. [Results] Average age: 57.2 years, average disease duration: approximately 3 years, history of receiving biologics/JAK inhibitors: 3 patients, mean DAS28-CRP before introduction: 3.58, 2.59 after 2 months. HAQ was 0.92 and 0.68. From oral agents, the average oral MTX dose could be increased from 7.6 mg to 11.07. No side effects such as abnormal liver function or stomatitis were observed even in using MET, 15 mg. [Conclusions] In the literature, MET is superior to oral agents in terms of fewer gastrointestinal symptoms and a higher proportion of long-chain MTX-PG, which correlates with improved disease activity, than oral agents at the same dose. Among early adopters of MTX, the continuation rate is higher for injection than for oral. However, some patients are hesitant because they are self-injected and are a little more expensive than oral drugs, it is possible that injectable preparations will be used at the same level as oral drugs.

## P1-124

**Study of the Efficacy of Ozoralizumab Therapy in Patients with D2TRA**

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Conflict of interest: None

[Objective] To assess the efficacy of ozoralizumab (OZR) in patients with D2TRA. [Methods] Among the patients who initiated OZR treatment at our institution from the drug's launch to October 2023, this study included 18 patients who initiated OZR for the treatment of D2TRA. Before the OZR therapy initiation, the mean number of Bio/JAK i used was 5.6, and all the patients had received TCZ. We assessed the efficacy of OZR using patient VAS, CDAI, SDAI, and morning stiffness (MST) immediately before treatment initiation, 2- and 4-weeks after treatment initiation, and every 4 weeks thereafter. [Results] Efficacy evaluation of OZR was possible 2 weeks after treatment initiation. In 14 patients, the patient VAS, CDAI, SDAI, and MST improved at 2 weeks post-treatment initiation, and these end points improved further or remained improved thereafter. The remaining 4 patients discontinued the treatment due to worsening of their VAS, CDAI, SDAI, and MST or an inadequate response at 2 weeks post-treatment initiation. [Conclusion] In this study, we assessed the efficacy of OZR after treatment initiation in patients with D2TRA. Efficacy evaluation of OZR was possible as early as 2 weeks post-treatment initiation, suggesting that OZR can be a therapeutic option in patients with D2TRA.

## P1-125

**Safety and retention rate for 21 patients treated with ozoralizumab**

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Conflict of interest: None

[Objective] We initiated this study to evaluate the safety and retention rate of ozoralizumab in clinical practice. [Methods] The subjects were 21 RA patients who were started on ozoralizumab between December 2022 and September 2023 and were able to be followed for at least 16 weeks after administration. We reviewed subsequent progress in the electronic medical record to assess safety and continuation rates of ozolalizumab. We also evaluated other newly administered TNF inhibitors during the same time period. [Results] During the observation period, 4 adverse events occurred in 21 patients treated with ozolalizumab. One of them was allergic symptoms (facial flushing) after the first dose, and the drug was subsequently discontinued. Safety data for the 40 patients treated with other TNF inhibitors showed 11 adverse events, 5 of which resulted in discontinuation. There was no significant difference in retention rates between ozolalizumab and other TNF inhibitors ($p$=0.289). [Conclusions] Ozoralizumab showed comparable safety and retention rate compared to other TNF inhibitors. We will continue to provide appropriate information and follow-up for patients to assess long-term safety.

## P1-126

**Golimumab dosage for patients with rheumatoid arthritis**

Tetsu Itami, Hirotaka Yamazawa, Kaori Ishimura, Chisato Ashida, Hiroki Akazawa, Daisuke Tomita, Toshihiko Shiga, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita, Itaru Matsumura
Kindai University

Conflict of interest: None

[Objective] To compare golimumab 100 mg and 50 mg efficacy in rheumatoid arthritis patients. [Methods] Fifty-three rheumatoid arthritis patients treated with golimumab at the Department of Rheumatology, Kinki University Hospital were included in the study. The patients had to meet ACR/EULAR classification criteria. We divided the patients into two groups: golimumab 50 mg and golimumab 100 mg. We compared disease activity, persistence rates, and ultrasound synovitis at 24 and 52 weeks in

these two groups. Disease activity was assessed by DAS28, and ultrasound was assessed by B-mode grayscale/power Doppler imaging at the hand, wrist, elbow, shoulder, and knee joints. [Results] There were no differences in patient characteristics such as age, number of previously used biologics, and disease activity in the golimumab 50 mg (n=17) and golimumab 100 mg (n=36) groups. Both groups showed no difference in disease activity and persistence rates of DAS28CRP and ESR at 24 and 52 weeks; golimumab 100 mg with MTX showed superior improvement in ultrasound gray scale compared to golimumab 50 mg with MTX. [Conclusions] We observed a predominant improvement in grayscale in the group using 100 mg golimumab with MTX.

## P1-127

**Efficacy of ozoralizumab in real world clinical level in patients with rheumatoid arthritis**

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[1]Nippori Orthopaedics and Rheumatic Clinic, [2]Department of Orthopaedic Surgery, Toho University, Omori Medical Center

Conflict of interest: Yes

[Objective] In order to clarify the efficacy of ozoralizumab in RA at 24 weeks of real world clinical level. [Methods] 58 RA patients treated with ozoralizumab in our clinic from 2023.12. including 11 male, 47 female with mean age of 60.9 years, mean disease duration of 10.6 years were analyzed the efficacy by using DAS28 (CRP), CDAI, SDAI. The continuation rate and adverse events were also investigated at 24 weeks. [Results] DAS28 (CRP), CDAI and SDAI at baseline were 4.42, 19.9 and 20.5 improved to 2.51, 5.17 and 6.08. The remission rate of DAS28 (CRP) was 55.2% at 24 weeks. The continuation rate was 70.7%. Tolerations was 14 patients, skin rash was 2 patients and pharyngitis was 1 patient. [Conclusions] The sufficient efficacy of ozoralizumab at 24 weeks in real world clinical level was recognized. csDMARD was used in case with toleration of ozoralizumab.

## P1-128

**Short-term Results of Ozoralizumab for Rheumatoid Arthritis with a High Risk of Progression of Joint Destruction**

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Conflict of interest: None

[Objectiv] We report on the effectiveness of Ozoralizumab in 22 cases with treatment duration of 3 months or more, with a focus on its efficacy. [Methods] Disease activity at 1 month and 3 months after Ozoralizumab administration was assessed. [Results] All cases were female, with an average age of 76 years. Eleven cases were treated with BIO or JAK inhibitors, and 12 cases were treated with MTX. Imaging examinations revealed bone marrow edema in small or medium-large joints in 14 cases. In these cases, the DAS28-CRP decreased significantly from 3.83 at the start of treatment to 3.29 ($P<0.01$) at 1 month and 3.25 ($P<0.01$) at 3 months. SDAI decreased from 19.9 to 14.8 ($P=0.01$) and 12.8 ($P<0.01$). Swollen joints decreased from 4.73 to 2.76 ($P<0.01$) and 2.20 ($P<0.01$). Ozoralizumab was effective not only in cases resistant to DMARDs but also in cases resistant to BIO and JAK inhibitors, as well as in cases with involvement of medium-large joints, not just small joints, especially showing remarkable efficacy in refractory joint effusion. [Conclusions] The efficacy of Ozoralizumab was recognized for rheumatoid arthritis with a high risk of progression of joint destruction.

## P1-129

**Short-term Results of Adalimumab Biosimilar Subcutaneous Injection**

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Conflict of interest: None

[Objective] We report on the efficacy of two types of Adalimumab Biosimilar Subcutaneous Injection (ADA-BS) administered for over 6 months at our institution, focusing on 13 cases of company A's product (GA) and13 cases of company V's product (GV). [Methods] For the evaluation of efficacy, we examined the ADA-DAS28-CRP scores and patient VAS values at the start of treatment, and at 4, 12, and 24 weeks for both GA and GV. For cases with rapid joint destruction observed in X-rays, the improvement degree of bone marrow edema on MRI was investigated. [Results] The average ages, disease duration for GA and GV were 64.8 years and 62.1 years and 81.7 months and 125.5 months, respectively. At baseline, 4, 12, and 24 weeks, the DAS28-CRP scores were 3.7, 2.8, 2.6, 2.7 for GA, and 3.9, 3.1, 3.3, 2.9 for GV, respectively. Similarly, patient VAS values were 41.9, 29.1, 25.4, 23.1 for GA and 35.5, 34.6, 25, 24.1 for GV. In GA, there were 2 cases of effective discontinuation and 2 cases of ineffective discontinuation, while in GV there was 1 case of ineffective discontinuation. In cases of joint destruction progression, widespread bone marrow edema as observed by MRI was notably improved after ADA administration. [Conclusions] ADA-BS was shown to be useful for MTX-IR cases in both GA and G V.

## P1-130

**Efficacy in patients with rheumatoid arthritis treated ozoralizumab in daily clinical practice**

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Conflict of interest: None

[Objective] We investigate efficacy in patients with rheumatoid arthritis (RA) treated ozoralizumab (OZR) in daily clinical practice. [Methods] We conducted a retrospective survey of the medical records of 8 patients with RA who started OZR from February 2023, and examined the patient characteristics, disease activity, retention rates, and safety at the baseline, 4, 12 weeks. [Results] There were 8 patients (7 females), with an average age of 75.1±3.7 years, disease duration of 16.6±3.8 years, 75.0% receiving methotrexate, with dose at 6.0±1.3 mg, 50% using steroids, 4 were biologic-naive, and 3 had prior exposure to ≧3 biologics. The mean DAS28 was 4.18±0.54, SDAI was 17.9±3.9, mHAQ was 0.61±0.21, and treatment duration was 3.5±0.8 months. At 4 and 12 weeks, 25% and 80% of patients achieved low disease activity (LDA) by DAS28 and SDAI, respectively. The 12-week treatment persistence rate was 62.5%. One patient discontinued treatment due to a urinary tract infection, and one patient showed no response. [Discussion] Limited bio-naïve cases and inclusion of patients with multiple prior treatment failures may have contributed to lower rates of achieving LDA. Given the relatively short observation period, more cases need to be accumulated for a comprehensive assessment.

## P1-131

**Experience with Oloralizumab in the Treatment of Rheumatoid Arthritis at our Institution**

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Conflict of interest: None

Objective: This report presents our experience with Oloralizumab, a next-generation TNF antibody, in treating rheumatoid arthritis patients. Methods: Five patients (1 male and 4 females) with an average age of 74 years (range: 61-83) were observed for an average duration of 14.4 weeks (range: 12-17). The treatment history of biologics included one naive case,

three cases as the second drug, and one as the fifth. Of the three patients switching from Golimumab, one switched from a 50 mg+MTX regimen, two from a 100 mg monotherapy, and one from Abatacept due to decreased pain efficacy. The average 100mmVAS scores at the time of administration, 4 weeks, and 12 weeks were 25 mm, 15 mm, and 10 mm, respectively, showing improvement. Case Study: An 83-year-old male with EO-RA-induced left hand synovitis (Echo: GS3, PD3) showed no response to 50 mg Golimumab+6 mg MTX. Following a synovial biopsy revealing a diffuse myeloid type, he was switched to Oloralizumab 30 mg+MTX 6 mg. Four weeks post-administration, echo remission was achieved. Conclusion: Although this is based on short-term experience, three out of five patients demonstrated early improvement in VAS and DAS28 (CRP). As a once every 4-week subcutaneous TNF inhibiting formulation, Oloralizumab appears to offer potential efficacy in early stages.

## P1-132

**A case of rheumatoid arthritis with acute heart failure with reduced ejection fraction developed after introduction of ozoralizumab**

Takaaki Ito, Yuji Miyoshi, Hiroto Tomoda, Nanae Okimoto, Kei Karakida, Yuki Terashima, Keisuke Hirobe, Sayuri Mizumoto, Issei Takahashi, Tomohiro Kato, Tomoko Sano, Akane Ito, Yoshitaka Ueda, Nanase Honda, Eisuke Takamasu, Kae Onishi, Masako Utsunomiya, Yoshiki Nagai, Naoto Yokogawa, Kota Shimada
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Conflict of interest: None

[Introduction] TNF inhibitors can increase the risk of cardiovascular adverse events, and their use is contraindicated in congestive heart failure patients. Ozoralizumab (OZR) has not been tested on these patients, and it's currently unclear whether it raises the risk of cardiovascular adverse events. [Case] An 81-year-old woman had rheumatoid arthritis for 14 years. She was doing well with her medicines until her symptoms flared up around January. In July, OZR was commenced, and 23 days after one dose, she developed acute heart failure. Her cardiac function dropped from 60% in March to 30% in July. Detailed examination did not show any coronary disease or signs of ischemia. After medications for heart failure were started, her symptoms ameliorated. A month after stopping OZR, her cardiac function improved. Antirheumatic therapy henceforth must be carefully adjusted according to the course of heart failure. [Clinical Significance] This is the first reported case of heart failure occurring after OZR administration. In this case, new heart failure with reduced ejection fraction occurred after initiating OZR, and her cardiac function improved after discontinuing OZR, suggesting the possibility that OZR induced heart failure.

## P1-133

**The short-term efficacy and safety of switching to ozolarizumab in elderly patients with rheumatoid arthritis who have not responded adequately to abatacept treatment**

Gen Kuroyanagi[1,2,3], Naoki Okayama[3], Hiroaki Sakai[1], Yohei Kawaguchi[1], Ayaka Takahashi[1,4], Atsushi Imamura[1,4]
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Conflict of interest: None

[Objective] Abatacept is commonly used in older patients with rheumatoid arthritis. However, considering the risk of infection, even if abatacept alone or in combination with methotrexate is not effective, steroids or csDMARDs are only added to control disease activity in some patients. We used ozolarizumab in bio-naïve patients and confirmed its efficacy. However, the effectiveness of ozolarizumab in elderly patients with rheumatoid arthritis who do not respond to abatacept has not been reported. [Methods] This study investigated the short-term efficacy and safety of ozolarizumab in 72, 74, and 83-years patients who had an inadequate response to abatacept. [Results] The average disease duration was 18.7 years. One patient used methotrexate. Another patient used steroids. There was no history of use of bDMARDs other than abatacept. Before ozolarizumab treatment, mean DAS28-CRP, CDAI, and CRP were 3.77, 27.67, and 1.3 mg/dl, respectively. One and three months after administration, mean DAS28-CRP, CDAI, and CRP were 2.30, 16.00, and 0.2 mg/ml (1M), and 2.09, 10.00, and 0.1 mg/ml (3M), respectively. No side effects were observed. [Conclusion] Ozolarizumab treatment could be effective and safe in elderly patients with rheumatoid arthritis who had an inadequate response to abatacept.

## P1-134

**Three patients with RA showed early improvement after treatment with ozoralizumab**

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Komagamine Rheumatoid Orthopaedic Clinic

Conflict of interest: None

It is characterized by its high transferability to inflammatory tissues and is expected to have an early clinical effect. Case 1] A female in her 60s (Stage 4, Class 1). PtGA also improved from 4 on the first day to 2 on the third day and remained at 3 thereafter. The PtGA also improved from 4 on the first day to 2 on the third day, and remained at 3 thereafter. Arthroscopic findings in PD were Grade 3 on the day of treatment, Grade 2 after 3 days, and Grade 2 after 28 days, and GS decreased from GS Grade 3 on the first day to Grade 2 after 7 days. Case 2] A woman in her 30s (Stage 4, Class 1) who had been treated with MTX 6 mg/w and Bio1, her right elbow joint pain improved 2 days after OZR administration. Case 3] A woman in her 60s (Stage 4, Class 2) with 58 years of illness and multiple drug use. She had right knee and elbow joint pain, but the pain disappeared after 4 days of OZR administration, and ROM of the right knee also improved. Clinical Significance: OZR showed a rapid improvement in joint echocardiographic findings. Clinical findings and subjective symptoms also improved at an early stage, suggesting that the drug is a drug with a rapid onset of effect.

## P1-135

**Efficacy of ozoralizumab in elderly rheumatoid arthritis patients**

Daiki Nakagomi[1,2], Moe Watanabe[1,2], Nakako Mabuchi[1,2], Soichiro Kubota[1,2], Ryosuke Ito[1,2], Yoshiaki Kobayashi[1,2], Shunichiro Hanai[1,2]
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Conflict of interest: Yes

Ozorarizumab is the newest BIO-DMARDS, launched in December 2022. It has a trimeric structure in which two anti-human TNFα Nanobody® molecules and one anti-human serum albumin Nanobody® molecule are fused. It is only available in Japan and its efficacy has been confirmed in domestic clinical trials in the OHZORA and NATSUZORA studies, but its effectiveness in actual clinical practice is unknown. The number of elderly rheumatoid arthritis (RA) patients is increasing, especially in Japan, and the proportion of difficult-to-treat RA is high in terms of various complications. Therefore, we will report the background, efficacy and adverse events of 18 elderly RA patients treated with ozoralizumab at our institution. For some patients, we also report imaging evaluation using ultrasound.

## P1-136

**Current status of rheumatoid arthritis cases treated with biosimilars in our hospital**

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Conflict of interest: None

[Purpose] We investigated the cases of rheumatoid arthritis (RA) treated with biosimilars. [Subjects] Eighteen outpatients with RA who had received BS during the past 4 years were included in the study. [Results]

Four of the patients were male and 14 were female, ranging in age from 36 to 80 years. By drug, infliximab (IFX)-BS was used in 7 cases, etanercept (ETA)-BS in 8 cases, and adalimumab (ADA)-BS in 3 cases. The details are as follows: 6 patients changed from IFX to IFX-BS, 1 patient naively received IFX-BS, 4 patients changed from ETA to ETA-BS, 4 patients naively received ETA-BS, 1 patient naively received ADA-BS, 1 patient had used IFX-BS before and now received ADA-BS, and 1 patient changed from ADA to ADA-BS. The reason for choosing ADA-BS was financial reasons in the remaining 16 patients, while 2 patients who paid 0% of the total cost wanted to help reduce the national health care cost. Many of the patients were anxious about the BS, but were reassured by the physician that "the effect will probably be the same. [Discussion] Although a certain percentage of patients are uneasy about the term "follow-up product," we believe that the number of patients who choose BS will increase in the future due to explanations from attending physicians, nurses, and pharmacists.

## P1-137

**Effects of Ozoralizumab in Patients with D2T RA**

Miho Karube[1,2], Hiroki Matsuno[1,2], Hayato Tose[1,2], Satoshi Hayakawa[1], Mitsumasa Kishimoto[2], Yoshinori Komagata[2]
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Conflict of interest: None

[Objective] We investigated the efficacy and safety of ozolarizumab in difficult-to-treat RA (D2T RA). [Methods] Subjects were 5 patients with D2T RA who attended our hospital and were using 2 or more types of BIO or JAK preparations, and who were difficult to treat. With consent, subcutaneous injections of ozolarizumab were administered at 4-week intervals for 12 days. The drug was administered weekly. Efficacy was evaluated by ACR50/70 achievement rate and CDAI. Safety was judged by the presence or absence of side effects. [Results] All cases were female and the median age was 53 years. The median disease duration was 7 years. MTX was used in 2 cases. BIO and JAK were used in 2 cases of 4 types, 1 case of 3 types, and 2 cases. The ACR50 achievement rate after 12 weeks was 80% (4/5), but the ACR70 achievement rate was 60% (3/5). A high change in CDAI was observed from the 4th week. MMP-3 and CRP levels similarly decreased from the 4th week, but one patient experienced a relapse after 8 weeks due to GC reduction. There were no obvious side effects and the continuation rate was 100%. [Conclusions] Even in D2T RA patients, ozolarizumab tends to have a rapid onset of effects, and may improve social life, work ability, and QOL.

## P1-138

**A case of a man with "true" ankylosing spondylitis complicated by seropositive rheumatoid arthritis**

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Center for Rheumatic Diseases, Matsuyama Red Cross Hospital, Ehime, Japan

Conflict of interest: Yes

[Case] A 59-year-old man. He was diagnosed with ankylosing spondylitis (AS) in his 20s. He had polyarthritis since the fall of X-1, and a left pleural effusion was observed. In March X, blood tests were positive for RF and anti-CCP antibody, and thoracentesis revealed exudative pleural effusion, leading to the diagnosis of rheumatoid arthritis (RA) and rheumatoid pleurisy, and he was referred to our hospital in April. At the initial visit, SDAI 36.7, DAS28 (CRP) 5.6, limbs X-rays showed bone erosions, and he was considered to have high disease activity. X-ray showed bamboo spine, and pelvic CT showed fusion of sacroiliac joint. He had HLA-B27, so he was diagnosed with "true" AS complicated with seropositive RA. On the other hand, he had HBV-DNA, so with the diagnosis of asymptomatic HBV carrier, and he began taking tenofovir in June. For RA, he was started on salazosulfapyridine. It was effective, but inadequate. In July, he started subcutaneous injection of ozoralizumab, which was successful, and his RA in remission. [Discussion] There are reports of AS and RA combined, but they are rare. And it's often questionable whether the diagnosis is true or not. Our case is considered to be a valuable example of a patient with "true" AS and RA who achieved remission with a TNF-α inhibitor.

## P1-139

**Efficacy of Etanercept Biosimilar Switching from Etanercept Reference Product, using Ultrasound and Clinical Data in Outcomes of Real World Therapy (ESCORT-NGSK Study)**

Remi Sumiyoshi[1], Shin-ya Kawashiri[1], Mizuna Otsuka[1], Yoshika Tsuji[1], Toshimasa Shimizu[1], Tomohiro Koga[1], Naoki Iwamoto[1], Takahisa Suzuki[2], Yukitaka Ueki[3], Masahiko Tsuboi[4], Toshihiko Hidaka[5], Hirokazu Takaoka[6], Yoshifumi Tada[7], Atsushi Kawakami[1]
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Conflict of interest: None

[Objective] To evaluate the change in disease activity of patients with rheumatoid arthritis who have maintained clinical remission or low disease activity (LDA) with etanercept reference product when switched to etanercept BS "MA", using not only clinical measures but also joint ultrasound. [Methods] Patients who had maintained clinical remission or LDA for at least 24 weeks under etanercept were switched to etanercept BS "MA" at the same dosage and its efficacy was prospectively evaluated. Clinical and ultrasound assessments were performed every 12 weeks. In addition, 38 cytokines/chemokines were measured at the baseline, at 24 weeks, at 36 weeks, and at 52 weeks. [Results] Twenty patients were enrolled, 5 in the 25 mg/week group and 15 in the 50 mg/week group. 4 of the 20 patients discontinued during the course of the study. Of the 11 patients who started at 24 weeks on a reduced dose, all completed the study up to 52 weeks. [Conclusions] This is the first study to prospectively evaluate the effect of switching from a etanercept to a subsequent product using not only a clinical measures but also joint ultrasound. Another strength of this study is that it evaluated the efficacy of drug dose reduction after switching to a subsequent product.

## P1-140

**Efficacy and Safety of Ozoralizumab in Rheumatoid Arthritis Patients in Practice**

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Conflict of interest: None

[Objective] OZR is the sixth anti-TNFα agent approved in Japan for rheumatoid arthritis (RA) in September 2022. In this study, we report on the efficacy and safety of 14 post-marketing cases. [Methods] Safety and efficacy were evaluated up to 6 months after the start of OZR. Efficacy was evaluated by DAS28-ESR, DAS28-CRP, SDAI, and CDAI at 1, 2, 3, and 6 months after the start of OZR, and safety was evaluated by the incidence of adverse events. [Results] The mean age was 72.2 years, and the mean duration of RA disease was 16.2 years. 64.3% (9/14) of patients continued to use MTX at 6 months, 6 patients used MTX, and 10 patients had a history of bio/ts DMARDs. Safety: Adverse events (skin rash in 1 case, psoriasis in 1 case) were observed in 2 of the 14 patients. Efficacy of OZR showed a reduction in disease activity at 1, 2, 3, and 6 months after the start of treatment, and there was no difference in efficacy between patients receiving MTX and those not. [Conclusions] OZR showed a reduction in disease activity as early as 1 month after the start of treatment, and the effect of OZR appeared early.

## P1-141

**Short-term efficacy and safety of Ozoralizumab in rheumatoid arthritis patients at our hospital**

Tomoyo Miki[1], Takaaki Komiya[1], Yosuke Kunishita[2], Taketoshi Watanabe[1], Yuji Uzawa[1], Toshihisa Igarashi[1], Shohei Nagaoka[1]
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wa, Japan, [2]Inflammatory Disease Section, National Human Genome Research Institute, National Institutes of Health, USA

Conflict of interest: None

[Objective] In this study, we evaluated the efficacy and safety of Ozoralizumab (OZR) in rheumatoid arthritis (RA). [Methods] RA patients attending our hospital, those who received OZR between February and August 2023 were included in the study. Patient background, examination results and findings after the start of OZR were collected retrospectively from medical records from the start of OZR until October 2023 or until the discontinuation of OZR. [Results] Twelve patients were included in the study, with a mean age of 72.8±7.18 years and mean disease duration of 11.6±9.9 years at the start of OZR. Nine patients had a history of biologic agents and JAK inhibitors, and 4 patients had a history of malignancy, of which no one was in tumor-bearing status. Disease activity was significantly reduced ($p < 0.001$) from 4 weeks after initiation, with a persistence rate of 83.3% at 16 weeks after OZR initiation. Two patients discontinued OZR during the observation period, one due to adverse events (skin rash) and one due to inadequate response. [Conclusions] In our clinical practice, OZR was introduced to elderly patients in whom the choice of concomitant medications and complications were problematic, and showed a certain level of short-term efficacy and safety.

## P1-142

**Experience of ozoralizumab treatment in patients with rheumatoid arthritis at Tama-Hokubu Medical Center**

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Conflict of interest: None

[Objective] Ozoralizumab (OZR) is the first humanized nanobody® biological DMARD in Japan and was launched in December 2022. We treated RA patients with OZR, switched from another TNFα inhibitor, or for the first biologics, and here we report the efficacy analysis. [Methods] We introduced OZR to RA patients with inadequately controlled disease activity with existing therapy. Disease activity at week four after DAS28-CRP evaluated OZR introduction. [Results] Seven patients were included during the period from August 2023 to October 2023. The mean age was 77.7±6.8 years old. The mean disease duration was 28.4±46.4 months, and the mean DAS28-CRP was 4.6±1.6 at the baseline: most patients had intermediate to high disease activity. Before OZR, patients were treated with golimumab in 4 cases (3 with MTX) and MTX in 3 cases. OZR was selected because most of the patients were too old to self-inject. At four weeks of induction, the mean DAS28-CRP improved to 2.1±1.2, and two patients achieved DAS28-CRP remission. [Conclusion] OZR may be an option for subcutaneous injection administered every four weeks. We will report the results of this study, including the progress.

## P1-143

**Comparative study of continuation rate and safety in patients with rheumatoid arthritis treated with JAK Inhibitors or abatacept**

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Conflict of interest: Yes

[Objective] Safety concerns of JAK inhibitors (JAKi) have been reported for malignancy, herpes zoster, and major cardiovascular events (MACE). We compared the safety of JAKi with abatacept (ABT) in rheumatoid arthritis (RA) patients. [Methods] The continuation rate and safety data of 179 patients with RA, who received JAKi or ABT and were observed for more than one year, were compared retrospectively. [Results] When comparing the patient backgrounds of the JAKi group (n=104) and the ABT group (n=75), the one-year continuation rate was significantly higher in the ABT group (55%/81%, $p<0.001$). The rate of discontinuation within one year due to adverse events was significantly higher in the JAKi group (22%/9%, $p=0.026$). The mean age of patients who discontinued due to adverse events in the JAKi group was 71 years, which was higher in patients who continued for more than one year (63 years, $p=0.005$). The discontinuation rates within one year due to infections (4%/4%), malignancies (2%/1%), Herpes Zoster (1%/0%), and MACE (2%/0%) showed no significant differences between the two groups. [Conclusion] The safety of JAKi compared to ABT suggested that adverse events were more frequent in the elderly, but comparable for discontinuation due to infection, malignancy, herpes zoster, and MACE.

## P1-144

**Therapeutic effects of JAK inhibitors with or without methotrexate in the treatment of rheumatoid arthritis**

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Conflict of interest: None

[Objective] We compared the therapeutic efficacy of JAK inhibitors with and without concomitant MTX. [Methods] We investigated the respective continuation rates at 52 weeks in patients treated with JAK inhibitors with and without concomitant MTX. The 149 RA patients treated with JAK inhibitors for 52 weeks were classified into 87 patients in the MTX group and 62 patients in the MTX-naive group, and their efficacy was examined. [Results] The continuation rate of JAK inhibitors up to 24, 52 weeks was 75.4, 65.2% in the MTX group and 76.6, 59.7% in the MTX-naive group. The MTX-naive group was older (69.5 vs 61.0 years, $p<0.01$) and had lower renal function (eGFR: 61.1 vs 75.2, $p<0.01$). The DAS-28ESR at 0, 4, 12, 24, 36 and 54 weeks was 4.8, 3.9, 3.6, 3.6, 3.5 and 3.6 in the MTX group and 5.1, 4.3, 4.1, 4.0, 4.1 and 4.3 in the MTX-naive group. It was significantly lower at 12 ($p=0.014$), 36 ($p=0.015$) and 52 weeks ($p<0.01$) in the MTX group. CDAI was 19.7, 12.4, 9.0, 9.4, 9.1 and 9.1 in the MTX group and 22.0, 15.0, 13.0, 11.9, 12.5 and 14.2 in the MTX-naive group. The MTX group was significantly lower at 12 ($p < 0.01$), 36 ($p = 0.034$) and 52 weeks ($p < 0.01$). [Conclusions] The results suggest that MTX combination may increase the continuation rate and therapeutic efficacy of JAK inhibitors.

## P1-145

**Effectiveness of Cycling JAKi in Patients Who Failed a JAKi**

Takahito Kojima[1], Yutaro Yamada[1], Tadashi Okano[1], Kenji Mamoto[1], Shohei Anno[2], Kazuki Orita[2], Masahiro Tada[3], Kentaro Inui[4], Tatsuya Koike[5], Hiroaki Nakamura[1]
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Conflict of interest: None

[Background] With the advent of different types of JAK inhibitors (JAK), patients with rheumatoid arthritis (RA) may now have another type of JAK as an option as the next treatment when treatment with the first JAK is failed. [Purpose] The purpose of this study was to examine the continuation rate and efficacy of RA patients who received JAK cycling. [Method] At our hospital and related facilities, we investigated the clinical effects over a 52-week period in patients who cycled to other JAKs after using JAK. [Results] Out of a total of 65 patients who were cycled from

JAK to JAK, 35 were able to continue for 52 weeks. In the 35 cases that continued for 52 weeks, DAS28-CRP was 4.12, 3.35, 3.11, 3.24, and 3.35 at weeks 0, 4, 12, 24, and 52, showing improvement after 4 weeks. In addition, MMP-3 (ng/ml) was 168.0, 112.8, 118.6, 88.8, and 87.9, which rapidly improved after 4 weeks. Furthermore, among the 27 cases of JAK cycled to UPA, 20 cases were able to continue treatment for 52 weeks, showing a high continuation rate. [Conclusion] JAK Cycling is effective, with a high continuation rate and improvement in disease activity.

## P1-146

**Investigation of switching between JAK inhibitors in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate the therapeutic outcome of switching between JAK inhibitors in patients with rheumatoid arthritis. [Methods] Among 21 patients who switched between JAK inhibitors at our hospital after 2018, 17 patients who were available for follow-up for at least 52 weeks were included, excluding 2 patients who switched due to adverse events and 2 patients who switched from tofacinitib in remission. Improvement in disease activity and the presence of adverse events were examined. [Methods] 8 patients used baricitinib, 5 patients used upadacitinib, and 4 patients used filgotinib. There were 1 male and 16 female patients with a mean age of 69.6 ± 13.5 years and a mean disease duration of 6.7 ± 6.1 years. The average number of biologics and JAK inhibitors used was 3.0 ± 1.9. Twelve patients were treated with methotrexate and five with prednisolone; two patients discontinued due to adverse events and four patients discontinued due to inadequate response. The mean DAS28-CRP was 3.80±1.41 at the start of the study, but improved from the start: 3.23±1.62 after 4 weeks, 2.39±01.11 after 12 weeks, 2.04±1.17 after 24 weeks, and 1.73±0.91 after 52 weeks. [Conclusions] Switching between JAK inhibitors in inadequate response is useful.

## P1-147

**Long-term efficacy and utility of remission-induction of JAK-inhibitors and glucocorticoid therapy for elderly-onset seronegative rheumatoid arthritis**

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Conflict of interest: None

[Purpose] To investigate the long-term efficacy and safety of remission-induction therapy using JAK inhibitors and prednisolone (PSL) for elderly-onset seronegative rheumatoid arthritis (seronegative EORA). [Method] Ten patients diagnosed with seronegative EORA at Niigata Rinko Hospital and Niigata Bandai Hospital after April 2019, were treated for remission-induction with JAK inhibitors and PSL, and followed up to 52 weeks after the initiation of the therapy. [Results] DAS28 (3)-CRP at RA diagnosis averaged 4.58±0.99, the mean mHAQ was 1.69±0.73, the mean serum CRP was 8.9±4.3 mg/dl, and the mean dosage of PSL was 9.6±6.7 mg/day, respectively. Two weeks after the start of JAK inhibitors, data were improved dramatically as the mean DAS28 (3)-CRP1.41±0.35, the mean mHAQ0.22±0.24, and the mean serum CRP 0.08±0.08 mg/dl. PSL was discontinued in 2 patients 24 weeks after, and 6 patients 52 weeks after the initiation of the therapy. [Conclusion] Remission-induction therapy with JAK inhibitors and PSL can improve RA disease activity immediately, reduce the dosage of PSL, and maintain a remission state in patients with seronegative EORA.

## P1-148

**Real-world study comparing the efficacy of Janus kinase inhibitors in patients with difficult-to-treat rheumatoid arthritis**

Shinya Hayashi
Kobe University Graduate School of Medicine

Conflict of interest: None

**Objective:** This study aimed to analyze the clinical efficacy of JAK [A1] inhibitors in these patients and evaluate the factors influencing their efficacy using real-world data. **Method:** 159 JAK inhibitor-treated patients with rheumatoid arthritis were categorized into D2TRA and non-D2TRA groups. Data including the Clinical Disease Activity Index (CDAI) at initiation and 6 months after drug administration, drug retention months, and reason for discontinuation due to toxic adverse events were collected. **Results:** The retention rates significantly differed ($p$=0.030) at 6 months between the D2TRA and non-D2TRA groups. CDAI-LDA rates differed significantly between the two groups ($p$<0.001). CDAI-LDA achievement 6 months after drug introduction was significantly associated with the number of previous uses of biologic and/or targeted synthetic disease-modifying anti-rheumatic drugs and CDAI at baseline in all cases. However, no predictive factors were identified for patients with D2TRA. **Conclusion:** Compared to non-D2TRA patients, D2TRA patients demonstrated significantly lower drug retention rates, CDAI-LDA achievement rates, and safety of JAK inhibitors. No significant predictive factor for CDAI-LDA achievement 6 months after drug introduction was detected in D2TRA patients.

## P1-149

**Effect of Janus kinase inhibitors (JAKi) on lung disease (LD) in patients with rheumatoid arthritis (RA)**

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Conflict of interest: None

<Objective> To clarify effect of JAKi on LD in RA. <Methods> RA patients who started JAKi between Aug 2013 and Sep 2023 and underwent chest CT before and after initiation of JAKi were enrolled. We examined 1) patients' background, 2) CT imaging before initiation of JAKi, 3) change in first CT imaging after initiation of JAKi, retrospectively. <Results> 1) We enrolled 8 female patients whose age was 55.43±12.09 years old, disease duration was 22.14±11.91 years, and 2 cases had smoking history. Baricitinib, filgotinib, and tofacitinib were administered in 5, 2, and 1 cases, respectively. All cases received PSL, 4 received csDMARDs, and 7 had previously treated with biologics. The CRP was 1.25±2.23 mg/dl. 2) 3 cases had no LD, 4 had interstitial LD (ILD), and 1 had airway disease (AD) before initiation of JAKi. 3) The first CT were performed at 46.57±37.37 weeks after initiation of JAKi. 2 cases without LD and 4 cases with ILD before initiation of JAKi showed no deterioration nor new lesion. One case without LD while who had history of drug-induced LD (DILD) showed newly onset ILD, and one case showed exacerbation of preexisting AD. <Conclusion> JAKi might relate with exacerbation of preexisting AD, and newly onset ILD in cases with previous DILD, while little effect on preexisting ILD.

## P1-150

**Examination of the retention rate of JAK inhibitors in rheumatoid arthritis complicated by interstitial lung disease -Analysis using Kansai multicenter ANSWER cohort -**

Hideyuki Shiba[1,2], Takuya Kotani[1], Wataru Yamamoto[3], Yuri Hiramatsu[1], Ayaka Yoshikawa[1], Koji Nagai[1], Kenichiro Hata[1], Keisuke Nishimura[4], Akira Onishi[5], Motomu Hashimoto[6], Yuichi Maeda[7], Yuji Nozaki[8], Chisato Ashida[8], Yonsu Son[9], Hideki Amuro[9], Hidehiko Makino[9], Ryota Hara[10], Masaki Katayama[11], Tohru Takeuchi[1]
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Conflict of interest: None

Objective: This study assessed how ILD affects JAK inhibitor efficacy in rheumatoid arthritis (RA) and its impact on medication discontinuation. Methods: The study analyzed 458 RA patients with known ILD status and JAK inhibitor treatment. Researchers used a Cox proportional hazards model to assess ILD's influence on JAK inhibitor discontinuation. Kaplan-Meier analysis compared discontinuation rates between ILD-positive and ILD-negative patients. In the ILD-positive group, discontinuation rates were compared based on JAK inhibitor selectivity. Medication persistence was tracked for 24 months. Results: The study included patients with median values of 19.2% male, age 65, disease duration 110 months, CDAI score 13.9, and 17.2% had ILD. ILD-positive patients, notably older, with longer disease durations, less MTX use, more PSL use, and higher KL-6 levels. JAK inhibitor discontinuation rates didn't significantly differ based on ILD presence. In ILD-positive cases, no significant differences in discontinuation rates were observed among JAK1,3, JAK1,2, and JAK1 inhibitors. Conclusion: This study found no significant impact of ILD on JAK inhibitor discontinuation in RA patients. Also, in ILD-positive cases, JAK inhibitor selectivity didn't significantly affect discontinuation rates.

## P1-151

**Examination of the efficacy and effects on lung lesions of Janus kinase inhibitors in rheumatoid arthritis patients at our hospital**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients with interstitial pneumonia (IP) or airway lesions require appropriate drug selection and careful follow-up. Since there are few reports on the effects of Janus kinase inhibitors (JAKi) on lung lesions, we investigated them at our hospital. [Methods] We conducted a retrospective observational study of 39 patients treated with JAKi (12 with tofacitinib, 10 with baricitinib, 6 with peficitinib, 7 with upadacitinib, and 4 with filgotinib). We evaluated efficacy using DAS response and CDAI, and confirmed the presence of IP and chronic airway inflammation using chest HRCT. [Results] There were 10 cases with IP complications and 14 cases with chronic airway inflammation (4 of them had both). One patient treated with tofacitinib had a high KL-6 level of 1123 U/mL before administration and died from acute exacerbation of IP 2.5 years later. The remaining 9 cases had no significant change in IP. Airway inflammation improved in 1 case, mildly changed in 3 cases, and had no significant change in 10 cases. Regardless of lung lesions, DAS28-ESR and CDAI significantly decreased after 1 year. [Conclusions] Although JAKi are considered to be effective and relatively safe for lung lesions, caution should be taken when using IP with high KL-6 levels.

## P1-152

**Continuation rate of JAK inhibitors in RA patients with lymphopenia caused by JAK inhibitors**

Kenji Saito[1], Haruki Matsumoto[1], Yuya Sumichika[1], Shuhei Yoshida[1], Yuya Fujita[1], Jumpei Temmoku[1], Naoki Matsuoka[1], Tomoyuki Asano[1], Shuzo Sato[1], Eiji Suzuki[2], Hiroshi Watanabe[1], Masayuki Miyata[3], Kiyoshi Migita[1]
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Conflict of interest: None

[Objective] JAK inhibitors are known to cause adverse events (AEs) in some cases, and lymphopenia is known to be involved in AEs such as infections and malignant tumors, but there have been few reports examining the association of lymphopenia with the rate of continuation of JAK inhibitors. This study investigated the drug continuation rate according to the lymphocyte count after administration of JAK inhibitors in RA patients. [Methods] Patients with RA who had been treated with tofacitinib (TOF) (n=38) or baricitinib (BARI) (n=74) were included. We retrospectively analyzed whether lymphocyte counts reflected JAK inhibitors' discontinuation rate due to AEs. [Results] One-quarter of RA patients treated with JAK inhibitors had lymphopenia. Drug retention rates for JAK inhibitors were significantly lower in patients with lymphopenia than those without. A decrease in the drug continuation rate was observed in the TOF group due to lymphopenia, but no decrease in the drug continuation rate was observed in the BARI group. Reasons for discontinuation included infection and malignant tumors, which were more prominent in the lymphopenia group. [Conclusions] Lymphopenia due to TOF may predict the risk of AEs in RA patients.

## P1-153

**Comparison of incidence rates of infections in RA patients treated with JAK or IL-6 inhibitors: a multicenter cohort study**

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Conflict of interest: None

[Objective] This study aimed to compare the incidence rates (IRs) of infections, including herpes zoster (HZ), in RA patients treated with JAKis or IL-6 inhibitors (IL-6is). [Methods] We retrospectively analyzed 427 RA patients treated using IL-6is (n = 273) or JAKis (n = 154). After adjusting for clinical characteristic imbalances by propensity score matching (PSM), we compared the IRs of infections including HZ between the JAKi and IL-6i groups. [Results] Observational period: 1247.65 patient-years (PY); median observational period: 2.46 years. After PSM, IRRs comparing JAKi with IL-6i were 3.37 (95% CI: 1.32-9.76) for serious infections other than HZ (SI) indicating that the JAKi-treated group was more likely to develop SI than the IL-6i-treated group. Multivariate Cox regression analyses revealed that the use of prednisolone > 2.5 mg/day and coexisting interstitial lung disease (ILD) were independent risk factors for SI. The IRs of HZ were not significantly different between the JAKi and IL-6i groups before and after PSM analysis. [Conclusions] Our study showed increased IRs of SI in RA patients treated with JAKis compared with those treated with IL-6is. The presence of ILD and the use of GC were found to be independent risk factors for SI in RA patients treated using JAKis.

## P1-154

**Survey on inactivated herpes zoster vaccination rates and herpes zoster incidence in patients using JAK inhibitors**

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Conflict of interest: None

[Objective] Patients using JAK inhibitors (JAKI) could be at a higher risk of herpes zoster (HZ) than those using other biological drugs. At Kameda Clinic, pharmacists provide information about inactivated herpes zoster vaccine (VC) to patients starting JAKI therapy. Here we investigated the VC vaccination rates of patients using JAKI and the subsequent incidence of HZ. [Methods] Patients with rheumatic diseases who began using JAKI, including tofacitinib (Tofa), upadacitinib (Upa), baricitinib (Bari), and filgotinib (FIL), between August 2017 and February 2023 were eligible for inclusion. If the JAKI was switched, it was considered a new case and evaluated for up to 52 weeks. We evaluated various parameters including VC vaccination rates, the incidence of HZ, and the continuation of JAKI. [Results] Among the 249 enrolled patients (13 Tofa users, 61 Upa users, 170 Bari users, and 5 FIL users), 29 (11.6%) received VC. The incidence of HZ at week 52 was 11 (4.4%), including 6 Upa users (9.8%) and 5 Bari users (2.9%). There was a statistically significant difference in the incidence of HZ between the Upa and Bari cohorts ($p < 0.05$). [Conclusions] Although the incidence of HZ was similar to that of previous studies, our findings suggest that incidence differs among JAKI.

## P1-155

**Relationship between spinal ankylosis and spinal mobility in ankylosing spondylitis: Tsurumai ankylosing spondylitis in musculoskeletal study (T-ASK study)**

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Conflict of interest: None

[Background] This study is aimed to examine the relationship between the degree and location of spinal ankylosis and spinal mobility in patients with ankylosing spondylitis (AS). [Methods] Spinal mobility was assessed using the Bath Ankylosing Spondylitis Metrology Index (BASMI). The degree of spinal ankylosis was defined as the number of intervertebral fusions in the cervical, thoracic, and lumbar spine. The correlation between the five items of BASMI and the number of intervertebral fusions in the whole spine, cervical spine, thoracic spine, and lumbar spine was investigated. Of 81 AS patients enrolled in the T-ASK study, 27 patients in which CT was evaluated the 25 intervertebral fusions from C1/2 to L5/S and BASMI was measurable were included. [Results] A strong positive correlation was found between BASMI and the number of whole spinal intervertebral fusion ($r=0.81$, $p<0.01$). The tragus to wall distance was strongly associated with the number of lumbar intervertebral fusions, lumbar anteversion with the number of thoracic intervertebral fusions, and cervical rotation with the number of cervical intervertebral fusions. [Conclusions] There was a relationship between the degree of spinal ankylosis and spinal mobility in AS.

## P1-156

**Characteristics of low back pain in patients with ankylosing spondylitis: Tsurumai ankylosing spondylitis in musculoskeletal study (T-ASK study)**

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Conflict of interest: None

[Background] The characteristics of low back pain in ankylosing spondylitis (AS) is not yet well understood in Japan. [Objective] To investigate the characteristics of low back pain in patients with AS. [Methods] Of 81 AS patients enrolled in the T-ASK study, 26 patients who responded to a questionnaire survey on low back pain were included. The questionnaire surveyed the presence or absence of back or buttock pain, age at onset of low back pain, change in pain during exercise, change in pain at rest, presence or absence of nocturnal pain, effect of analgesics, and mode of onset of pain. [Results] 96.2% of patients experienced low back or buttock pain. The mean age of onset of low back pain was 24.9 years old. 56% reported that low back pain decreased during exercise, and 32% reported that it worsened. 44% reported that low back pain worsened at rest, and 24% reported that it decreased. 80% experienced nocturnal pain. 80% reported that analgesics were effective. 28% reported that the pain appeared suddenly. [Conclusions] In a questionnaire survey of low back pain in patients with AS, a certain number of patients had characteristics different from inflammatory low back pain.

## P1-157

**Differences in physical function between ankylosing spondylitis and rheumatoid arthritis from the T-ASK study**

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Conflict of interest: None

[Objective] Ankylosing spondylitis (AS) produces physical dysfunction, including limitation of movement. The aim of this study was to compare physical function in patients with AS with that of patients with rheumatoid arthritis (RA). [Methods] 23 AS patients (T-ASK study) and 328 RA patients (Fairy study) who participated in a study on frailty were included in the study. Two groups were evaluated after PS adjusted for age at study entry: the AS group (10 patients) and the RA group (50 patients). [Results] Patient background after PS was age 53 / 53 years, male 80 / 10%, disease duration 13 / 13 years. As for physical function, there were no significant differences in 2-step test value (1.35 vs. 1.25) or gait speed (1.42 vs. 1.34 sec.). As patient subjective assessment, there was a significant difference only in the 25-question Geriatric Locomotive Function Scale (GLFS-25) (24 vs. 12 points) ($P=0.003$). As for muscle mass, there were significant differences in both limb skeletal muscle mass index (7.87 vs. 6.64) and trunk muscle mass (25.6 vs. 20.3 kg) ($P<0.001$). [Discussion] Muscle mass was significantly higher in the AS group, which had more male patients, due to the greater influence of gender, suggesting that AS patients have higher GLFS-25 than RA patients.

## P1-158

**Case Series and Literature Review: Exploring the Correlation between Tietze's Syndrome and Rheumatic Diseases, with Special Reference to Spondyloarthritis (SpA)**

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Conflict of interest: None

**Objective:** The aim is to clarify the correlation between Tietze's syndrome, characterized by tender, non-suppurative swelling in the anterior chest wall, and rheumatic diseases, particularly SpA. **Cases: No 1.** 44-year-old male presented with swelling of the sternoclavicular (SC) joint and digital involvement, without back pain, abnormal MRI findings in the sacroiliac joint nor the serum autoantibodies. **No 2.** 46-year-old male exhibited sternal angle pain, along with pustules on the palms. Chest wall MRI disclosed abnormal signals around the lesion. The diagnosis was pustulotic arthro-osteitis (PAO), effectively managed with Guselkumab. **No 3.** 27-year-old male presented with SC pain. Enthesitis of the extremities recurred, leading to the diagnosis of peripheral SpA. **Discussion:** Tietze's syndrome manifests as a painful swelling in the upper thoracic costochondral (CC) or SC joints. In contrast, rheumatic diseases, such as SAPHO syndrome, PAO, gout and SpA, often involve the CC or SC joints, potentially masquerading as Tietze's syndrome. In accordance with the ASAS classification criteria, SpA is a term encompassing a various rheumatic diseases. Consequently, it is imperative to differentiate SpA from

Tietze's syndrome over an expended period, even after an initial diagnosis.

## P1-159

**The study of spinal ankylosing factors in patients with axial spondyloarthritis**

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Conflict of interest: None

[Objective] To analyze factors associated with the progression of spinal ankylosis in Japanese ax-SpA patients. [Methods] The 60 patients who were diagnosed with spondyloarthritis and met the ax-SpA classification criteria of ASAS in our department were selected. The 14 cases were excluded, and the remaining 46 cases were included. Spinal lesions were measured using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at baseline and baseline+2 years. Univariate analysis and multiple regression analysis were performed using age, sex, disease duration, disease status, NSAIDs and csDMARDs, biologic use, ESR, CRP, VAS, HAQ, mSASSS score at baseline, and New York Criteria score. [Results] When comparing the two groups, HAQ ($p=0.045$) and mSASSS at baseline ($p=0.049$) were significantly higher in the advanced group. On univariate analysis, only mSASSS at baseline was significantly correlated ($p=0.012$) with the difference in mSASSS over 2 years. Multiple regression analysis showed a significant correlation between HAQ ($p=0.049$) and mSASSS at baseline ($p=0.013$). [Conclusions] In this study, baseline mSASSS and HAQ influenced the progression of spinal ankylosis. Patient-reported self-assessment may be important in the treatment of ax-SpA to inhibit spinal ankylosis.

## P1-160

**A treatment result of inflammatory back pain: IBP of Spondyloarthritis**

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Conflict of interest: None

[Purpose] Inflammatory low back pain is a symptom from the spine to the sacroiliac joints in spondyloarthritis (SpA), and is often observed in axial spondyloarthritis (Axial SpA), but it can also be seen in peripheral spondyloarthritis (pSpA). We report on the treatment results of patients presenting with inflammatory low back pain in our department. [Conclusion] In many cases of r-ax SpA, ankylosing spine has been already observed, and pain relief can often be obtained with Nsaids. In nr-ax SpA, there were many cases with active inflammation and cases where MTX and bDMARDs were used. MTX is effective in many cases of PsA, but when the effect is insufficient, bDMARDs and IL-17 inhibitors are also effective.

## P1-161

**Analysis of the impact of dactylitis on the achievement of minimal disease activity (MDA) in psoriatic arthritis (PsA)**

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Conflict of interest: None

[Objective] Several methods have been proposed to evaluate disease activity in psoriatic arthritis (PsA), and minimal disease activity (MDA) is used as a Treat to Target (T2T) remission index. In this study, we analyzed the effect of dactylitis on MDA with PsA patietnts. [Methods] We evaluated the relationship between the presence or absence of dactylitis and the achievement of MDA in PsA patients whose MDA could be evaluated. Dactylitis was observed at least in finger in all patients. The mean age was 56±5 years, and the male-to-female ratio was 6:3. Two patients were treated with MTX (one with MTX alone), six with biologic agents (five with TNF inhibitors and one with IL-17 inhibitor), and two with no treatment. [Results] The $\chi^2$ test showed a significant correlation ($p<0.05$) between dactylitis and MDA achievement, suggesting that the presence of dactylitis was associated with non-achievement of MDA. [Conclusions] The presence of dactylitis could make it more difficult to achieve MDA. In particular, the presence of residual dactylitis in fingers could be an important predictor for achieving MDA, and therefore, it is necessary to reconsider treatment.

## P1-162

**Investigation of the usefulness of CT scan in the diagnosis of axial spondyloarthritis**

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Conflict of interest: None

[Objective] Axial spondyloarthritis (axSpA) is a potentially disabling inflammatory arthritis of the spine, usually presenting as chronic back pain, typically before the age of 45. MRI is recommended for axSpA diagnosis. Here, we assessed the value of CT scans for 16 patients at our hospital. [Methods] We reviewed axSpA cases at our hospital from April 2018 to August 2023. [Results] The average age at diagnosis was 62.5 years, with an average delay of 16 years. The sacroiliac joint imaging included X-rays in 100%, CT in 81%, and MRI in 100%. Spine imaging included X-rays in 100%, CT in 81%, and MRI in 87%. Sacroiliitis was seen in X-rays for 31%, CT for 76%, and MRI for 75% of patients. MRI showed vertebritis or enthesitis in 57%. X-rays revealed ossification or vertebral deformity in 31%, CT in 92%, and MRI in 57%. Specific breakdown: cervical lesions were in 30% of CT scans and 20% of MRIs, thoracic lesions in 77% of CT scans and 60% of MRIs, and lumbar lesions in 69% of CT scans and 20% of MRIs. [Conclusions] CT scans had high sensitivity in detecting ossification and vertebral deformities and were comparable to MRI in identifying sacroiliac joint issues. CT scans appear useful for diagnosing axSpA.

## P1-163

**Clinical findings of HLA-B61 homozygote, HLA-B54 homozygote, and HLA-B (54, 61) heterozygous patients diagnosed with axial spondyloarthritis (SpA) or SAPHO syndrome at our hospital**

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Conflict of interest: None

[Objective] In patients diagnosed with axial SpA or SAPHO syndrome and subjected to H LA-B typing, HLA-B61 and B54 were significantly more frequent than in ordinary Japanese. Therefore, we investigated the clinical findings of HLA-B61 or B54 homozygous patients and HLA-B (54,61) heterozygous patients. [Methods] Nine HLA-B61 homozygous patients (I group), two HLA-B54 homozygous patients (II group), and 13 HLA-B (54,61) heterozygous patients (III) were compared with environmental risk factors, pain site, X-ray findings. [Results] Five patients in group I, one in group II, ten in group III classified as PsA, three in group I, one in group II, and three in group III classified as SAPHO. In all three groups, weight gain and excessive carbohydrate intake were the most common environmental risk factors, and the most common symptoms were systemic pain. X-ray findings of sacroiliitis were rated at least 3 degrees unilateral or 2 degrees bilateral in the mNY grade in almost all cases. Severe spinal lesions were observed in 2 patients in group II and 4 in group III. [Conclusions] Comparison of the pathophysiology of the three groups suggests that HLA-B61 and B54 are involved in the progression of sacroiliac joint lesions, and B54 may be a risk factor in the progression of spinal lesions.

## P1-164

**Clinical features of SAPHO syndrome in our hospital**

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Conflict of interest: None

[Objective] This study aimed to identify clinical features of SAPHO syndrome. [Methods] Patients with SAPHO syndrome diagnosed at our department between December 2017 to July 2023 were retrospectively analyzed. [Results] Twenty-four patients (male/female: 8/16, mean age at the time of diagnoses: 50.25±14.6 years) were included. Eleven patients were positive for CRP, 2 for MMP-3, 4 for RF, and 2 for ACPA. Cutaneous manifestations occurred in 11 patients (44%), 10 with palmoplantar pustulosis and 1 with acne. Osteoarticular lesions included sternoclavicular arthritis in 21 patients, spondylitis in 8, sacroiliac arthritis in 9, and peripheral arthritis in 4. MRI was performed in 18 patients and bone scintigraphy in 21. Treatment included NSAIDs monotherapy in 2 patients, methotrexate in 22, and sulfasalazine in 3. Glucocorticoid were used in 14 patients, with a median initial dose of 5 mg (2.5-30 mg), and 9 patients terminated GC during the course of the study. TNF-α inhibitors were used in 4 patients, and anti-IL-23p19 antibody were used in 1 patient. [Conclusions] Most patients were well controlled with existing treatment. We report on the selection of treatment for SAPHO syndrome and the course of treatment at our hospital.

## P1-165

**SPARKLE-J, a New Registry for Spondyloarthritis, Pustular arthro-osteitis and SAPHO syndrome**

Shigeyoshi Tsuji[1,2], Kiyoshi Matsui[2,3], Yoshinori Taniguchi[2,4], Yukari Okubo[2,5], Yuko Kaneko[2,6], Naoto Tamura[2,7], Hideto Kameda[2,8], Mitsumasa Kishimoto[2,9], Hiroaki Dobashi[2,10], Atsushi Kawakami[2,11], Tatsuya Atsumi[2,12], Nami Okamoto[2,13], Ryo Oda[2,14], Yuho Kadono[2,15], Yuya Takakubo[2,16], Ayako Nakajima[2,17], Yasuharu Nakashima[2,18], Keishi Fujio[2,19], Manabu Fujimoto[2], Hiroaki Matsuno[2], Yuri Matsubara[2], Ippei Miyagawa[2], Masaaki Mori[2], Akimichi Morita[2], Masahiro Yamamura[2], Rei Watanabe[2], Taiki Nozaki[2], Masashi Tamaki[2], Tetsuya Tomita[2,20]
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Conflict of interest: None

[Objective] In a large scale, multi-center research group for improving medical standards and patient QOL in spondyloarthritis and related diseases represented by ankylosing spondylitis, funded by the Ministry of Health, Labour and Welfare of Japan, A disease registry was developed for spondyloarthritis, pustular arthro-osteitis, and SAPHO syndrome. [Methods] The registry was named SPARKLE-J (**S**pondyloarthritis, **P**AO (pustulotic arthro-osteitis), and S**A**PHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome **R**egistry lin**K**ed to the nationa**L** databas**E** of **J**APAN. The study group consists of members from 29 facilities and departments. [Results] The total number of cases registered in SPARKLE-J by FY2022 was 461. The breakdown by disease was 265 cases of psoriatic arthritis, 57 cases of ankylosing spondylitis, 5 cases of non-radiographic axial spondyloarthritis, 3 cases of IBD-related spondyloarthritis, and 2 cases of reactive arthritis, 87 cases of PAO and 42 cases of SAPHO syndrome. [Conclusions] In the future, our research group plans to collect and analyze the registry data of SPARKLE-J every year to clarify the actual status of spondyloarthritis, PAO, and SAPHO syndrome in Japan.

## P1-166

**Clinical Features of Psoriatic Arthritis in SPARKLE-J, a New Registry for Spondyloarthritis, Pustular arthro-osteitis and SAPHO syndrome**

Shigeyoshi Tsuji[1], Hideto Kameda[2], Mitsumasa Kishimoto[3], Tatsuya Atsumi[4], Yukari Okubo[5], Nami Okamoto[6], Atsushi Kawakami[7], Manabu Fujimoto[8], Ippei Miyagawa[9], Masaaki Mori[10], Akimichi Morita[11], Rei Watanabe[8], Tetsuya Tomita[12]
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Conflict of interest: None

A large multicenter research group, the Ministry of Health, Labour and Welfare of Japan Research Grant for Intractable Diseases, has established a new registry for spondyloarthritis, pustulotic arthro-osteitis, and SAPHO syndrome. The primary objective of this registry is to improve the standard of care and patient quality of life for individuals suffering from spondyloarthritis and related diseases, including ankylosing spondylitis. Its name is SPARKLE-J (Spondyloarthritis, PAO, and SAPHO syndrome Registry linKed to the nationaL databasE of JAPAN. A total of 265 psoriatic arthritis cases were registered in SPARKLE-J in FY2022. They were 56.9 ± 12.8 years of age, 7.7 ± 6.0 years of psoriatic arthritis duration, 48.7 ± 13.2 years of age at onset, BMI 24.8 ± 11.0, and smoking rate 25.5%, ASDAS 1.8±1.1, and low disease activity & remission was 68.0% in total, serum CRP 0.7±1.8 mg/dl, CRP positivity 40.4%, ACPA positivity 5.5%, RF positivity 11.4%, and HLA B27 positivity 0.53%. mHAQ was 0.2±0.4 on average as QoL evaluation. NSAIDs were used in 45.3% of patients, steroids in 2.0%, MTX in 37.2%, and biologic agents in 23.0%. Our research group plans to annually collect and analyze the registry data of SPARKLE-J to better understand the status of psoriatic arthritis in Japan.

## P1-167

**Development of IL17A Vaccine Targeting Axial Spondyloarthritis**

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Conflict of interest: Yes

[Objective] Antibody targeting IL17A has become an effective treatment option for axial spondyloarthritis because the IL23/IL17A pathway is involved in the pathogenesis. We evaluated the efficacy of the IL17A vaccine in a rat model of spondylitis, and found that the vaccine was effective in treating arthritis and spondylitis. In this study, we conducted a phase I study in healthy adults and examined the safety of the IL17A vaccine in humans. [Methods] The study was a single-center, randomized, placebo-controlled, double-blind study of healthy adults aged 20-65 years. The actual drug group was divided into two groups, low-dose and high-dose, each with 8 subjects, and administered three times every 4 weeks. Each group had a placebo group of 2 subjects. The patients were followed up for 20 weeks after the first injecion, and the safety and antibody titer increase were examined. [Results] 100% of patients in the vaccine group had adverse events. Almost all were injection site reactions. No serious adverse events were observed in all patients. Antibody titers increased after 4 weeks and were maintained from 8 to 20 weeks. [Conclusions] The IL17A vaccine was found to be safe and increase antibody titer in humans.

## P1-168

**Efficacy of granulocyte and monocyte adsorption apheresis (GMA/GCAP) for psoriatic arthritis refractory to bio/ts-DMARDs**

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Conflict of interest: None

[Objective] Psoriatic arthritis (PsA) has a wide range of treatment options, such as bio-DMARDs and ts-DMARDs. Recently the concept of Difficult-to-Treat (D2T) PsA has been proposed. Granulocyte and monocyte adsorption apheresis (GMA/GCAP) is an extracorporeal therapy controlling inflammatory processes through their cellular functions. In this study, we evaluated the efficacy of GMA/GCAP in 45 patients with PsA who had an inadequate response to bio/ts-DMARDs at our institution. [Methods] Between February 2021 and July 2023, forty-five PsA patients with inadequate response to bio/ts-DMARDs. These 45 PsA patients underwent of GMA/GCAP (once/w, 10 w), and the efficacy was evaluated using a composite index of disease activity (DAPSA, ASDAS, BASDAI) before and after the GMA/GCAP. [Results] There was a significant improvement in sPGA, DAPSA, ASDAS, and BASDAI from the end of the both 5th and 10th session ($p<0.01$), The proportion of patients with REM+LDA in DAPSA improved from 28.9% to 51.1%, and the proportion of patients with REM+LDA in ASDAS improved from 50% to 62.2%. [Conclusions] Despite the limitation of a single-center, 45-patient, 10-week observational study, GMA/GCAP is a useful treatment for patients with PsA refractory to bio/ts-DMARDs.

## P1-169

**Ixekizumab treatment exhibits favorable outcomes for disease activity and patient-reported outcomes in biological naïve patients with radiographic axial spondyloarthritis achieving clinically important pain at night reduction**

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Conflict of interest: Yes

**Objectives** To assess the association of spinal pain at night (SP-N) improvement in patients treated with Ixekizumab (IXE) up to week (W) 52 with other efficacy parameters. **Methods** The Phase 3 trial COAST-V investigated the efficacy of IXE in 341 biologic-naïve patients with radiographic axial spondyloarthritis (r-axSpA). Patients were randomised to IXE, adalimumab, or placebo (PBO). Only IXE-approved dose (every 4W) data are presented here. Associations of SP-N improvement with efficacy and patient-reported outcomes (PROs), including ASDAS <2.1 and morning stiffness, were analyzed. **Results** A greater proportion of patients achieved ≧3 improvement in SP-N with IXE treatment compared to PBO at W16 (63.0% vs 32.2%, $p<0.001$) and improvement was sustained up to W52. In the patients achieving ≧3 improvement in SP-N at W16 and those not achieving, ASDAS <2.1 was 58.8% vs 16.7% ($p<0.001$) at W16, 66.7% vs 33.3% ($p<0.01$) at W52, and change from baseline in intensity / duration of morning stiffness using a numeric rating scale was -4.5 vs -1.6 ($p<0.001$) / -3.8 vs -1.5 ($p<0.001$) at W16, -4.7 vs -2.3 ($p<0.001$) / -4.1 vs -1.5 ($p<0.001$) at W52, respectively. **Conclusion** IXE improved SP-N for patients with r-axSpA. Improvements in SP-N were associated with improvements in disease activity and PROs.

## P1-170

**Development of Extra-musculoskeletal Manifestations in Upadacitinib-treated Patients With Psoriatic Arthritis, Ankylosing Spondylitis, or Non-radiographic Axial Spondyloarthritis (Encore)**

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Conflict of interest: Yes

[Objective] To assess the development of Extra-musculoskeletal manifestations (EMMs) among patients (pts) with PsA, AS, or nr-axSpA treated with UPA 15 mg (UPA) or placebo (PBO) in the SELECT clinical trial program. [Methods] This analysis includes safety data from UPA trials in PsA (2 trials), AS (2 trials), and nr-axSpA (1 trial). Treatment-emergent adverse events of EMMs, including uveitis, inflammatory bowel disease (IBD), and psoriasis, were assessed. EMMs are reported as exposure-adjusted event rates (events/100 patient years [E/100 PY]). [Results] The majority of pts across PsA, AS, and nr-axSpA did not have a prior history of EMMs at baseline. In PsA, development of uveitis and IBD were low regardless of treatment. In AS, development of uveitis was numerically higher (E/100 PY [95% CI]) in pts treated with PBO (7.5 [2.7, 16.3]) vs UPA (2.8 [1.8, 4.1]); occurrence of IBD and psoriasis were low. In nr-axSpA, development of uveitis was numerically higher in pts treated with PBO (2.1 [0.4, 6.3]) vs UPA (0.9 [0.2, 2.7]); occurrence of IBD and psoriasis were low or absent. [Conclusions] Data from this post-hoc analysis describe adverse events of EMMs and should be interpretated with caution. Development of EMMs in pts treated with UPA was generally low across PsA, AS, and nr-axSpA.

## P1-171

**Achievement of Disease Control in PsA Patients Treated With Upadacitinib at Week 152: Post Hoc Analysis of the Long-term Extensions of Two Phase 3 Trials (Encore)**

Shigeyoshi Tsuji[1], Arthur Kavanaugh[2], Kristi V Mizelle[3], Oliver Fitzgerald[4], Enrique R Soriano[5], Peter Nash[6], Sandra Ciecinski[7], Limei Zhou[8], Arathi Setty[7], Laure Gossec[9]

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Conflict of interest: Yes

[Objective] To assess the achievement of goals according to composite measures in pts with PsA following long-term treatment with upadacitinib (UPA). [Methods] Post hoc analysis of pts from the SELECT-PsA 1 (N=1704) and SELECT-PsA 2 (N=641) studies was performed. Proportions of pts achieving with Minimal Disease Activity (MDA)/Very Low Disease Activity (VLDA), achievement of low disease activity (LDA) or remission (REM) using the Disease Activity index for PsA (DAPSA), PsA Disease Activity Score (PASDAS), and Routine Assessment of Patient Index Data 3 (RAPID3) were assessed. [Results] At 3 years, ~50-70% of pts remained in the studies. In SELECT-PsA 1, similar proportions of pts treated with UPA15, PBO switched to UPA15, or ADA achieved MDA (range: 50-55%) or VLDA (range: 19-24%) at wk 152. In SELECT-PsA 2, similar response rates were observed for MDA (range: 41-44%) and VLDA (range: 9-12%) amongst pts receiving UPA15 or PBO switched to UPA15. The proportions of pts achieving LDA or REM for DAPSA, PASDAS, and RAPID3 were similar between UPA15, PBO switched to UPA15, and ADA. [Conclusions] High rates of LDA and REM were reported in pts treated with UPA15, which were similar to PBO switched to UPA15 and ADA, across several measures of disease activity irrespective of prior DMARD exposure.

## P1-172

**Direct and Indirect Effects of Upadacitinib or Adalimumab on Pain in Psoriatic Arthritis: Results from a Randomized Phase 3 Study (Encore)**

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Conflict of interest: Yes

Objective: The objective of this analysis was to assess the direct and indirect (ie, by changes in inflammation surrogates) effects of treatment with upadacitinib (UPA) or adalimumab (ADA) vs placebo (PBO) on pain in patients (pts) with PsA. Methods: SELECT-PsA1 was a randomized, double-blind phase 3 study in pts with PsA. As observed analysis was used for change from baseline (BL) to wk 16 in Patient's Global Assessment of pain (PtGA) or tender joint count (TJC28) and observed case multiple mediation analysis for effect of UPA/ADA vs PBO. Indirect effect on pain was assessed based on itch, total enthesitis, Leeds *Enthesitis* Index, and CRP. Results: 1281 pts were included in this analysis (UPA n=429, ADA n=429, PBO n=423). PtGA improved with UPA vs PBO from BL to wk 16 (-25.0 vs -11.0; $P<0.05$). Total effects (15.1 and 12.4) and direct effects (9.8 and 8.3) on improvement in PtGA were greater with both UPA vs PBO and ADA vs PBO at wk 16 (all $P<0.001$). Direct and indirect effects on pain assessed as improvement in PtGA were numerically greater with UPA vs ADA. Improvement in elicited pain assessed as TJC28 was also greater with UPA and ADA vs PBO (all $P<0.05$). Conclusions: UPA and ADA produced higher mean improvements in pain via inflammatory or non-inflammatory mechanisms vs PBO in PsA pts.

## P1-173

**Long-Term Efficacy and Safety of Risankizumab for csDMARD-IR Patients with Active Psoriatic Arthritis: 148-Week Results from the KEEPsAKE 1 Trial (Encore Presentation)**

Hideto Kameda[1], Lars Erik Kristensen[2], Mauro Keiserman[3], Kim Papp[4], Leslie Mccasland[5], Douglas White[6], Vassilis Stakias[7], Thomas Iyile[7], Kyle Carter[7], Ahmed M Soliman[7], Leonidas Drogaris[7], Michael M Chen[7], Byron Padilla[7], Frank Behrens[8]

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Conflict of interest: Yes

**Objectives**: We report the efficacy and safety of Risankizumab (RZB) in PsA patients (pts) through week (wk) 148. **Methods**: KEEPsAKE 1 is an ongoing phase 3 global clinical trial to evaluate the efficacy and safety of RZB vs placebo (PBO) in PsA patients (pts) with an inadequate response, intolerance or contraindication to ≧1 csDMARD (csDMARD-IR). Pts were randomized 1:1 to receive RZB 150 mg or PBO at wk0, 4 and 16. Pts randomized to RZB and PBO received blinded PBO and RZB at wk24, respectively. Starting at wk28, all pts receive open-label RZB150 mg every 12wks until wk316. Efficacy and safety were assessed in all pts who received ≧1 doses of the study drug. **Results**: Overall efficacy results at wk52 and 100 were maintained at wk148 [ACR50, MDA, PASI90, improvement of mNAPSI, PGA-F, HAQ-DI, SF-36 PCS and FACIT-F and increase in PSA-mTSS from baseline (BL), and the rate of pts with no radiographic progression]. Resolution of enthesitis and dactylitis was in RZB and PBO/RZB. The overall rates of treatment-emergent adverse events (TEAEs), serious TEAEs and AEs leading to discontinuation of study drug were comparable to PBO-controlled period. **Conclusion**: Treatment with RZB showed durable efficacy in csDMARD-IR PsA pts through 148wks. RZB was well-tolerated, with no new safety signals.

## P1-174

**Long-Term Efficacy and Safety of Risankizumab for Active Psoriatic Arthritis: 148-Week Results from the KEEPsAKE 2 Trial (Encore Presentation)**

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Conflict of interest: None

**Objectives**: We report the efficacy and safety of Risankizumab (RZB) in PsA patients (pts) through week (wk) 148. **Methods**: KEEPsAKE 2 is an ongoing phase 3 global clinical trial evaluating the efficacy and safety of RZB vs placebo (PBO) in PsA pts with previous inadequate response or intolerance to 1 or 2 biologics and/or ≧1 csDMARD. Pts were randomized 1:1 to receive double-blinded treatment with RZB 150 mg or PBO for

24wks at wk0, 4 and 16. Starting at wk24, all pts receive open-label RZB 150 mg every 12wks through wk316. Efficacy and safety were assessed in all pts who received ≧1 doses of the study drug. Treatment emergent adverse events (TEAEs) are summarized. **Results**: Pts (RZB N=224; PBO/RZB N=219) maintained similar efficacy at wk148 to those at wk52 and 100, including ACR50, PASI90, change from baseline (BL) in HAQ-DI, SF-36 PCS and FACIT-F and MDA. Resolution of enthesitis and dactylitis was observed for pts with enthesitis and dactylitis at BL, respectively, in RZB and PBO/RZB at wk148. The overall rates of TEAEs, serious TEAEs and AEs leading to discontinuation of study drug remained stable and was consistent with those for the PBO-controlled period. **Conclusion**: Treatment with RZB 150 mg shows durable efficacy in pts with PsA through 148wks, with no new safety signals.

## P1-175

**Guselkumab Provides Clinically Meaningful Improvents in Patient-Reported Outcomes in Patients with Active Psoriatic Arthritis Who Are Inadequate Responders to Tumour Necrosis Factor Inhibitors: Results Through One Year of a Phase 3b, Randomized, Controlled study (COSMOS)**

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Conflict of interest: Yes

[Objective] To investigate guselkumab effect on achievement of clinically important improvements in patient-reported outcomes through week 48 in psoriatic arthritis patients inadequate response to TNF inhibitors from the COSMOS trial. [Methods] Early GUS response was evaluated by achieving minimal clinically important improvements (MCII, 15-point increase) in Pt Pain, PtGA PsO, PtGA Arthritis, PtGA PsO/Arthritis, and DLQI MCII (≧5-point improvement). More rigorous criteria included FACIT-Fatigue (≧4-point improvement), HAQ-DI (≧0.35-point improvement), DLQI 0/1, and SF-36 PCS (≧5-point improvement). [Results] The post hoc analysis involved 285 randomized pts (GUS Q8W: n=189; Placebo: n=96). GUS exhibited higher PRO response rates (MCII in PtGA PsO, PtGA Arthritis, PtGA PsO/Arthritis, Pt Pain, DLQI) than Placebo from W8 to W24, with responses in FACIT-Fatigue, HAQ-DI, DLQI 0/1, and SF-36 PCS. Response rates continued to rise through W48 with GUS, maintaining consistency upon PBO to GUS crossover. [Conclusions] In TNFi-IR PsA pts, GUS was associated with rapid effect for achievement of MCIIs and sustained response across PROs, including skin and joint symptoms, pain, fatigue, functional status, and skin-specific and physical function-related QoL, with increasing response through W48.

## P1-176

**Domains impacting minimal disease activity non-achievement in guselkumab-treated patients with psoriatic arthritis and inadequate response to TNFi (COSMOS)**

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Conflict of interest: Yes

[Objective] To identify domains and factors contributing to the minimal disease activity (MDA) non-achievement at Week (W) 48 for guselkumab (GUS)-treated patients (pts) with PsA and inadequate response to TNF inhibitors from the COSMOS trial. [Methods] MDA achievement was evaluated in randomized GUS Q8W pts (n=189). Time to achieving each domain was assessed with Kaplan-Meier analyses. Scores were normalized to SJC (0-66) scale to account for differences in scales and domain strictness. Predictors for time to achievement and W48 MDA achievement were analyzed. [Results] GUS improved all MDA domains through W48. Achieving minimal scores for LEI, SJC and PASI were faster than for PtGA, HAQ-DI, pt pain and TJC. Predictors of time to achievement for 1) HAQ-DI ≦0.5, 2) pt pain ≦15, 3) PtGA ≦20, and 4) TJC ≦1: 1) higher HAQ-DI, worse fatigue; 2) worse pt pain, fatigue; 3) worse fatigue; 4) higher TJC, MTX use, no fibromyalgia. Similar factors including older age were associated with W48 non-achievement. [Conclusions] GUS provided sustainable improvement in all MDA domains. Physician-reported domains (LEI, PASI, SJC) were achieved faster than pt-driven domains (PtGA, HAQ-DI, pt pain, TJC). Baseline domain scores, worse fatigue and MTX use were inversely correlated in the refractory domains.

## P1-177

**Efficacy and safety outcomes of TAK-279, a selective oral tyrosine kinase 2 (TYK2) inhibitor, from a randomized, double-blind, placebo-controlled phase 2b trial in patients with active psoriatic arthritis (PsA): Encore presentation at ACR 2024**

Nahoko Tanikoshi Tanaka[1], Alan Kivitz[2], Elena Muensterman[3], Arthur Kavanaugh[4], Désirée van der Heijde[5], Piotr A Klimiuk[6], Valenzuela Guillermo[7], Dokoupilova Eva[8], Poirier Gabrielle[9], Srivastava Bhaskar[9], Dasen Sue[9], Zhang Xinyan[9], Mona Trivedi[3], Holly Weng Haoling[10], Hong Ting[3], Peter Pothula[3], Xenofon Baraliakos[11]

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Conflict of interest: Yes

[Objective] TAK-279 is a highly selective, oral, allosteric TYK2 inhibitor, shown to be effective with safety profile in a phase 2b PsO study. This study evaluated efficacy and safety of TAK-279 in active PsA patients treated over 12 weeks. [Methods] This phase 2b randomized, multicenter, double-blind, placebo (PBO)-controlled, dose-ranging study (NCT05153148) was conducted at 45 sites in North America and Europe. Eligible patients were ≧18 years, with PsA ≧6 months, met CASPAR criteria, and had ≧3 TJC and SJC at enrolment despite prior other treatments. Patients were randomized 1:1:1:1 to receive TAK-279 5 mg, 15 mg, or 30 mg, or PBO, once daily. Primary endpoint: proportion of patients achieving ACR 20 response at Week 12. [Results] In total, 290 patients were treated; 245 completed. The primary endpoint was met with a significantly greater proportion of patients achieving ACR 20 with TAK-

279 vs PBO (53.3% and 54.2% vs 29.2%, both p=0.002). Safety outcomes are similar rate in the TAK-279 and PBO groups; no deaths occurred. [Conclusions] TAK-279 was well tolerated and demonstrated superior dose-dependent efficacy to PBO over 12 weeks of treatment in patients with active PsA. Its safety profile was consistent with that observed in the phase 2b PsO study.

## P1-178

**Real-World Switching and Discontinuation Patterns for Biologic Disease-Modifying Antirheumatic Drugs in Patients with Active Psoriatic Arthritis in Japan (Encore Presentation)**

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Conflict of interest: Yes

**Objectives:** Real-world treatment (Tx) switching (TS) and discontinuation (TD) rates for PsA patients (pts) initiating bDMARDs over 24 months (MOs) were quantified. **Methods:** In JMDC Database (Jan. 2005 - Aug. 2022) pts with ≧1 PsA claim before a bDMARD claim were included. TS and TD were assessed up to 24 MOs past Tx initiation (TI) of bDMARD and rates were evaluated. **Results**: 779 pts met inclusion criteria [adalimumab (AD: 264), bimekizumab (5), brodalumab (BR: 53), certolizumab pegol (CZ: 108), guselkumab (GU: 115), ixekizumab (IX: 156), risankizumab (RZ: 74), secukinumab (SE: 188), tildrakizumab (5), ustekinumab (US: 53)]. At 12/24 MOs after TI, TD and TS rate of bDMARD was 37.5/49.0% and 22.2/31.2%, respectively. TS rates at 12/24 MOs varied across bDMARDs (18.9-30.3/26.3-36.6%). TD rates at 12/24 MOs were lowest for RZ (21.6/31.8%), followed by US (24.2/35.8%), IX (31.2/38.2%), GU (37.4/48.6%), SE (36.1/53.2%), BR (48.0/53.3%), CZ (34.7/55.6%) and AD (49.0/59.1%). HRs of TS or TD over 24 MOs were higher among CZ, SE, AD, BR and GU vs RZ ($p<0.05$). **Conclusion:** TS and TD were common in the 1st 24 MOs of Tx with bDMARDs. While TS rates varied across bDMARDs, TD rates were lowest for RZ. HRs of TS or TD vs RZ were higher across most bDMARDs, indicating higher Tx persistence for RZ.

## P1-179

**Experience treating HLA B27-negative AS**

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Conflict of interest: None

[Objective] This study aimed to investigate the clinical course of HLA B27-negative ankylosing spondylitis cases. [Methods] We included 102 patients (86 males and 16 females) who underwent HLA testing for suspected spondyloarthritis in our outpatient department from 2003 to 2023. The examiners and several rheumatologists discussed the results and classified them according to the Assessment of SpondyloArthritis International Society (ASAS) classification criteria. Age at onset, age at diagnosis, initial symptoms, presence or absence of inflammatory back pain, plain radiographic findings of sacroiliac joints (grade), findings of spinal tonicity, presence or absence of introduction of biological agents, and CRP at last observation were investigated. [Results] There were four HLA-B27-negative AS cases in which the differential disease could be completely excluded retrospectively, one of which was difficult to diagnose due to the absence of inflammatory lumbar back pain. [Conclusions] HLA-B27-negative AS is rare, and a rigorous diagnosis is essential. In addition, there are cases in which symptoms improve with the administration of biologic agents, but progression of tonicity is seen on imaging, leaving room for further investigation regarding the choice of therapeutic agents.

## P1-180

**Clinical features and response to therapy of SAPHO syndrome/palmoplantar pustulosis osteoarthritis (PAO) in our hospital**

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Conflict of interest: None

Objective: SAPHO syndrome is an osteoarticular lesion associated with palmoplantar pustulosis (PPP), pustular psoriasis, and severe acne. Methods: We retrospectively reviewed the medical records and imaging findings of 21 Japanese patients (female/male: 16/5, mean age at onset: 55 years) who met the criteria for SAPHO syndrome proposed by Kahn from 2018 to 2023 at our hospital. Results: Eighteen of the 21 patients had skin symptoms such as palmoplantar pustulosis, acne, and psoriasis, and 3 patients did not present with skin symptoms. Skin symptoms preceded pustulosis in 52% of patients, and no patient had both symptoms at the same time. The most frequent patient symptoms were anterior chest wall pain and peripheral joint pain (50% each), followed by back pain (19%) and sacroiliac joint pain (19%). CRP was negative in all but one case. Tonsillectomy was performed in 2 patients, and BPs were administered in 10 patients. Nonsteroidal anti-inflammatory drugs were used in 20 patients. Conventional synthetic disease-modifying anti-rheumatic drugs were used in 17 patients and biological DMARDs in 13 patients. [Conclusion] In conclusion, we report on the characteristics of patients with SAPHO syndrome diagnosed in our clinic and their response to treatment, with a literature comparison.

## P1-181

**Post-development validation of vertebral compression fracture detection AI**

Ryozo Harada[1], Ryuichi Nakahara[2], Wataru Yamamoto[3], Hiroshi Hagino[4], Koji Takasugi[5], Kazuhiko Ezawa[5], Shinichiro Fujita[6], Kie Inoue[6], Rumi Inoue[7], Sakiko Shinmyo[8], Yoshihisa Nasu[2], Keiichiro Nishida[2,9]
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Conflict of interest: None

[Objective] To evaluate whether the semi-quantitative method (SQ method) for the diagnosis and qualitative evaluation of vertebral fractures can be performed automatically by using AI to detect vertebral fractures from simple X-rays. [Methods] Fifty patients who underwent osteoporosis treatment evaluation at our hospital between 2022 and 2023 were randomly selected, and thoracic and lumbar spine simple X-ray lateral images were extracted. The AI-based analysis using DICOM data was performed by LPIXEL. [Results] SQ grade0: 626, grade1: 74, grade2: 39, grade3: 45 vertebrae were extracted. AI was able to detect vertebrae with a specificity of 98%. Fracture determination had a sensitivity of 80% and specificity of 85%, and SQ Grade0: 85%, grade1: 60%, grade2: 97%, grade3 100% correct. [Conclusions] The vertebral body detection rate and grade correct response rate of the pilot algorithm seemed to be high. The detection of minor differences between SQ grade 0 and 1 may be a problem of algorithm adjustment in addition to the above problems. In the future, we would like to develop software that enables more accurate vertebral fracture detection and qualitative evaluation, which will contribute to the treatment of osteoporosis.

## P1-182

**The Digital Image Processing method is useful for diagnosing osteoporosis in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Osteoporosis is one of the major complications in patients with rheumatoid arthritis (RA). However, the treatment rate is low because few medical institutions have device using DXA. We have performed bone mineral density measurement by the second metacarpal bone Digital Image Processing (DIP) method. We investigated whether the DIP method is useful for diagnosing osteoporosis in RA. [Methods] YAM values were measured using the DIP method in RA patients. We compared the treatment rate, and the fracture rate over the past 5 years with previous reports. [Results] YAM values were measured in 101 RA patients, and the average YAM value was 72.5%. 17 patients had a history of fragility fractures, and 73 patients (39.2% of the total) received treatment for osteoporosis. The incidence of clinical fractures over the past 5 years was 7.36 per 1000 person-years. [Conclusions] According to the IORRA cohort, osteoporosis treatment was performed in 23.4% of patients, and the incidence of non-vertebral fractures was 35.5 per 1000 person-years. At our clinic, treatment was initiated in 39.2% of all patients and the number of clinical fractures was low. Osteoporosis in patients with RA can be detected with the DIP method at facilities that do not have DXA equipment.

## P1-183

**Study on osteoporosis and sarcopenia in rheumatoid arthritis patients using DXA-Based 3D analysis and body composition**

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Conflict of interest: None

[Objectuve]: The prevalence of osteoporosis and sarcopenia in RA patients is higher than in the general population, and their treatment and management are important. In this study, we retrospectively examined osteoporosis and sarcopenia in RA patients with femoral microstructure. [Methods] 250 RA patients were included in the study. The bone microstructure of the proximal femur was analyzed, and its feature were analyzed in addition to body composition and BMD. [Result] The age was 67.6y, mHAQ 0.29, glucocorticoid administration was 42%, dose was 4.0 mg. The frequency of osteoporosis increased with age in women, while sarcopenia increased with age only in men. L-BMD was correlated with body composition components, skeletal muscle index (SMI), neck BMD and cortical bone. Neck BMD was negatively correlated with age and mHAQ. Body composition component was explained as the first principal component and disease activity as the second principal component and body composition, disease activity, and cortical bone were identified as significant contributing variables to neck BMD in the principal component regression. [Conclusion] Prevention of osteoporotic fractures is important for improving the prognosis of RA patients, and prevention of sarcopenia is essential with osteoporosis treatment.

## P1-184

**Measurement of bone mineral density in the lumbar spine and proximal femur by REMS (Radiofrequency Echographic MultiSpectrometry) -A comparative study with DXA-**

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Conflict of interest: None

[Objective] The purpose of this study was to compare the results of BMD measurement between REMS and DXA for the lumbar spine and proximal femur. [Methods] The study involved 153 subjects (Male/Female: 9/144, 68 +/- 11 years old) who underwent measurements of BMD in the lumbar spine and proximal femur with REMS and DXA. Correlations between REMS and DXA measurements were evaluated by Pearson's correlation coefficient (alpha = 0.05), and the presence or absence of systematic errors due to differences in measurement methods was evaluated by Bland-Altman plots. [Results] Lumbar spine BMD showed no significant correlation (R=0.18), and REMS showed a mean - 17% lower value than DXA. Femur BMD was correlated with proximal (R = 0.50), neck (R = 0.51), and trochanter (R = 0.37), with an average of - 6% lower REMS values than DXA. There were no systematic errors in any of the measurements. A reanalysis of the lumbar spine excluding 75 cases with compression fractures, osteoarthritis (OA) and calcification of the abdominal aorta resulted in R = 0.36 and REMS showed a mean - 11% lower value than DXA. [Conclusions] The results suggest that REMS can reduce the influence of artifacts that are often affected by DXA. And Techniques to identify the umbilical region as L3 should be considered.

## P1-185

**Evaluation Grade-2 using semiquantitative method is not a risk factor of secondary vertebral fracture**

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Conflict of interest: None

[Objective] The existence of prevalent vertebral fracture (pr-VF) is a significant risk factor for secondary VF. The risk is evaluated. [Methods] Eligible patients who measured lateral view of thoracolumbar spine and bone mineral density (BMD) simultaneously (baseline) and followed up for at least 2 years were picked up. The semi-quantitative method (SQ) is used for the evaluation of BMD. The primary endpoint is an incidental VF (inc-VF), used as a dependent factor, and clinical parameters, including SQ classification and BMD, were used as independent factors for statistical analysis. Associations between inc-VF and dependent factors were evaluated. [Results] A total of 1045, 143 males and 902 females were included. The mean age at baseline was 78.3 years old, 49.7 months for follow-up length. inc-VF developed 13 in 419 Grade 0, 9 in 195 Grade 1, 13 in 235 in Grade 2, and 24 in 196 Grade 3. The prevalence of inc-VF in Grade 3 was significantly greater than in the other Grades. However, there was no significant difference among any pairs in the others. There were common risk factors in Grade 0 to 2, whereas other factors were listed in Grade 3. [Conclusions] It is suggested that Grade 3 is the only significant risk for inc-VF; however, the other Grades were not a significant risk factor.

## P1-186

**Characteristics of 25 (OH)D levels in postmenopausal osteoporosis patients**

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Conflict of interest: None

[Purpose] To measure serum 25-hydroxyvitamin D (25 (OH)D) in postmenopausal osteoporotic patients and investigate its characteristics. [Methods] 87 patients diagnosed with postmenopausal osteoporosis. (average age: 78.1 years) The covariates included were DXA, 25 (OH)D, TRACP-5b, P1NP, Alb, and corrected Ca and 25 (OH)D less than 30 ng/ml was group A, and 30 ng/ml or more was group B. These two groups were compared in age, TRACP-5b, P1NP, Alb, corrected Ca, DXA, and presence of a history of fragility fracture. [Results] There were 80 patients in group A and 7 patients in group B. The average value of 25 (OH)D was 15.8 ng/ml in group A and 33.3 ng/ml in group B. Mean value of age (group A 78.2 years, group B 78.0 years), TRACP-5b (group A 466 mU/dL, group B 386 mU/dL), P1NP (group A 63.2 μg/L, group B 42.8 μg/L), lumbar spine YAM (group A 80.6%, group B 79.7%), femoral YAM

(group A 58.0%, group B 60.0%) and history of fragility fracture (group A 28.8%, group B 14.3%, and no significant difference was observed. The average value of Alb (4.1 g/dL in group A, 4.4 g/dL in group B) and corrected Ca value (9.1 mg/dL in group A, 9.3 mg/dL in group B) were significant. [Conclusion] Active therapeutic intervention for osteoporosis using vitamin D preparations was considered.

## P1-187

**Bone mineral density and bone metabolism markers in RA patients with osteoporosis**

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[1]Nagamine Clinic for Rheumatology and Orthopaedic Surgery, [2]Department of Orthopaedic Surgery, School of Medicine, University of Occupational and Environmental Health, Japan, [3]Japan Research Institute of Artificial Joint

Conflict of interest: None

[Objective] This study was performed to investigate the difference of Bone mineral density (BMD) and bone metabolism markers between osteoporosis patients with rheumatoid arthritis (RA) and without RA. [Methods] BMD expressed by %YAM in hip and lumbar, and TRACP-5b and BAP were compared between 73 RA patients and 149 non-RA patients before osteoporosis medicines (PTH medicines, bisphosphonate or Romosozumab) was selected. The mean of age, height and weight in two groups was 73.9 and 75.9 years old, 148.5 and 149.8 cm, 50.0 and 51.5 kg, respectively. [Results] The mean (±standard deviation) of %YAM in hip and lumbar, TRACP-5b and BAP was 65.6±8.6% and 67.3%±9.0%, 77.5±14.0% and 77.7±17.2%, 428.4±204.7 and 431.0±209.8 mU/dL and 12.6±4.7 and 14.0±6.1μg/mL, respectively. There was no significant difference between RA patients and non-RA patients in all parameters. Osteoporosis medicine was decided according to the results of %YAM, TRACP-5b and BAP. There was no significant difference of ratio of three kinds of osteoporosis medicines between two groups. [Conclusions] If RA activity is controlled Properly, BMD is not lower in RA patients compared to non-RA patients. And there was no significant difference in the activity of osteoclast and osteoblast between RA patients and non-RA patients.

## P1-188

**Long-term analysis of bone turnover and matrix markers in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Previous studies have solely focused on the short-term trends of bone turnover markers in patients with rheumatoid arthritis (RA). In this study, we conducted a retrospective longitudinal analysis over 10 years of bone turnover and matrix markers in patients with RA. [Methods] A retrospective analysis was conducted on patients diagnosed with RA over an extensive duration of 11 years. The patients were classified into two groups based on the average of DAS28-CRP: the remission group and the disease-active group. The remission group was further divided into the csDMARD group and the b/tsDMARD group. [Results] Retrospective analysis showed that serum pentosidine level was higher and serum total P1NP level was lower in the disease-active group. Long-term analysis showed that serum pentosidine increased progressively even in the remission group, while serum total P1NP decreased in the disease-active group. The serum levels of pentosidine and total P1NP were significantly lower in the b/tsDMARD group and did not increase over time. [Conclusions] Even in the remission group, there exists a risk of compromised bone fragility and vulnerability fractures. Therefore, the utilization of b/tsDMARDs may exert an osteoprotective effect by suppressing the elevation of serum pentosidine.

## P1-189

**Does cortical hypertrophy around the cemented stem influence the clinical results in primary total hip arthroplasty?**

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Conflict of interest: None

Objective: To evaluate cortical hypertrophy (CH) after primary total hip arthroplasty (THA) using cemented stems, and to examine its association with clinical outcomes. Methods: 135 hips with CMK stem, and 147 hips with Exeter were retrospectively evaluated. They could be followed up for more than 10 years. For imaging evaluation, we used X-rays. We assessed the rate and location of CH. Clinical evaluation was performed using the JOA score. Results: 30 hips (28.0%) with CMK and 22 (24.1%) hips with Exeter had CH and with no significant difference in the frequency of CH between stems, CH was more common in Zones 3, 4 and 5 in CMK, and in Zones 5 and 6 in Exeter. Clinical evaluation showed that the group with CH had significantly better JOA scores in the JOA total score, activities and walking ability. Discussion: The results for the preferred site of CH appearance were similar to previous reports. The patients with CH had better clinical outcomes, suggesting that there may be some association between a high level of activity and the occurrence of CH. Conclusions: In cases 10 years after THA surgery, there was a clear difference in the site of appearance of CH between CMK and Exeter. Clinical outcomes were better in cases where CH appeared.

## P1-190

**Characteristics of spinal alignment in patients with hip osteoarthritis with Developmental Dysplasia of the Hip**

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Department of Orthopaedic Surgery, Chiba University, Chiba, Japan

Conflict of interest: None

[Objective] The purpose of this study was to examine the characteristics of spinal alignment in hip osteoarthritis (OA) associated with DDH compared to healthy cases. [Methods] The subjects were 509 healthy patients with no hip joint abnormalities who participated in a regional cohort study, and 292 patients with Crowe 1, 2 and CE angle of 25° or less among the OA group who underwent THA for OA. Propensity score matching was performed for age, height, and weight, and Pelvic Incident (PI), Lumber Lordosis (LL), Sacral Slope (SS), and Pelvic Tilt (PT) in the whole spine XP were measured for 139 patients in each group. [Results] Age, height, and weight were 68.7±10.3/68.9±9.7 years, 156.4±7.9/156.4±8.3 cm, and 57.4±12.0 kg/57.5±11.6 kg in the healthy/OA groups, respectively. Spinal parameters were 53.4±10.7/47.7±10.2, 37.8±10.8/37.3±14.7, 29.6±7.9/27.2±10.5, and 18.6±7.1/21.9±14.9 for PI, LL, SS and PT in the healthy/OA group. [Conclusions] Recently, THA cup placement using spinal sagittal plane alignment (PI-LL) as an indicator has been proposed. The acetabular implant in THA for OA associated with DDH should be placed in consideration of the characteristics of the spinal alignment.

## P1-191

**Long-Term Clinical and Radiological Outcomes of Primary Total Hip Arthroplasty with S-ROM-A Stem in Patients with Narrow Medullary Cavity**

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Conflict of interest: None

[Objective] In this study, we report the long-term clinical and radiological outcomes of primary THA using the S-ROM-A stem. [Methods] 14

THAs that could be followed up for more than 10 years were included in this study. The study included the changes in JOA scores before and after surgery, radiological findings, and complications. [Results] The mean age at surgery was 54.1 years (48-61 years), and the mean follow-up period was 162.4 months (121-218 months). The JOA score improved from 45.6 preoperatively to 88.4 at the last observation. Radiologically, simple radiographs at the last observation showed that 2 cases (14%) developed more than 3° of varus after surgery, and spot-welds were observed in almost all cases (93%) at the lower end of the sleeve. [Conclusions] Good long-term clinical results have been reported, and good clinical results were obtained in this study. It has been reported that in S-ROM-A, there are cases in which the stem progresses to varus during the follow-up period, and in this study, we also observed cases in which the stem progressed to varus over a long period of time. However, image findings showed that the stem was well anchored to the femur, and clinical results such as the JOA score were not affected even in cases where varus progressed.

## P1-192

**Fracture prevention of periprosthetic femur fracture in VLIAN polished tapered cemented stem**

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Department of Orthopaedic Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Conflict of interest: None

[Objective] In the Japanese arthroplasty registry, the proportion of periprosthetic stem fractures (PPF) among the causes of revision total hip arthroplasty (THA) is on the rise. In addition, it has been reported that the incidence of PPF varies depending on the type of metal used for cemented stems. The purpose of this study was to compare the incidence of PPF between Exeter and VLIAN stems, which are the most frequently used polished taper stems in Japan. [Methods] The subjects were 3148 hips that underwent primary THA with Exeter or VLIAN between 2012 and 2021 at our hospital and affiliated hospitals. The study included the number of first THA cases in the Exeter and VLIAN groups, the number of PPF cases, age at injury, postoperative follow-up period, and injury outcome. [Results] The overall incidence of PPF was 0.32% (10 of 3148), 0.34% in the Exeter group and 0.26% in the VLIAN group; the mean age at PPF was 66.4 years in the Exeter group and 79.5 years in the VLIAN group, with the Exeter group being younger. T [Conclusions] The VLIAN stem has a shoulder shape that allows easy insertion even for small Japanese, which allows the use of a relatively large stem and is expected to prevent the incidence of postoperative PPF.

## P1-193

**A case of systemic lupus erythematosus in which the introduction of Anifrolumab was effective not only in early steroid tapering but also in the remission induction phase**

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Hyogo Medical University Hospital

Conflict of interest: None

[Case] 33-year-old man He was diagnosed as SLE with lupus nephritis type IV + V in X-5, and started treatment with PSL50 mg, HCQ200 mg, MMF1000 mg. The patient was not compliant with the medication and had repeated flare-ups. He was referred to our hospital in February X. He was admitted as a relapse of SLE due to elevated anti-dsDNA antibodies, hypocomplementemia, and worsening proteinuria. The patient relapsed due to self-interruption of medication and was treated with PSL40 mg, IVCY. When the dose was reduced to 20 mg, hemophagocytic syndrome (MAS) was observed. Therefore, he was treated with mPSL 500 mg for 3 days and PSL 30 mg for post-treatment, and Anifrolumab was administered intravenously for early PSL reduction due to existing osteonecrosis of the femoral head. The patient was discharged from the hospital without relapse after tapering down to PSL 20 mg. [Discussion] Anifrolumab has been reported to be effective in reducing PSL, and we confirmed its efficacy in this case and also contributed to induction of remission. Anifrolumab may be effective in preventing relapse and reducing steroid use in patients with poor drug compliance, difficulty in increasing PSL dose due to osteonecrosis of the femoral head, SLE flare-ups and MAS complications during PSL tapering.

## P1-194

**A case of pulmonary arterial hypertension due to SLE successfully treated with Selexipag**

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Conflict of interest: None

A 50-years-old man was referred from the otolaryngologist because of lymphadenopathy and arthralgia during hospitalization for acute pharyngitis. He complained of dyspnea on exertion and underwent echocardiography, which revealed TRPG of 50 mmHg. From the above process, a right heart catheterization (RHC) was performed. It showed mean pulmonary arterial pressure (mPAP) was 33 mmHg, PAWP 5 mmHg and PVR 3.9 Wood Unit. The diagnosis of pulmonary arterial hypertension (PAH) due to SLE was confirmed based on fever, positive anti-dsDNA IgG antibodies, hypocomplementemia and Jaccoud arthropathy. We started immunosuppressive agents and macitentan. RHC was repeated due to persistent symptoms after antibodies became negative. It showed mPAP 24 mmHg, PAWP 5 mmHg, PVR 2.1 Wood Unit. Concerned about male-specific adverse event of PDE5 inhibitors and residual symptoms, we started selexipag, symptoms gradually subsided. After six months, the pressure improved to mPAP 17 mmHg and PVR 1.56 Wood Unit at RHC, and the patient has been doing well up to now. There are several cases in which mPAP does not normalize and symptoms persist, as in this case, even after immunosuppressive therapy. RHC was performed and selexipag was started, which led to normalization of the mPAP and resolution of symptoms.

## P1-195

**A case of neuropsychiatric lupus (NPSLE) successfully treated with moderate-doseprednisolone in combination with anifrolumab**

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Minami Nagano Medical Center, Shinonoi General Hospital

Conflict of interest: None

A 35-year-old woman presented with arthralgia of extremities, edema of eyelids and bilateral lower legs, and skin rash on bilateral lower legs 5 years ago. A renal biopsy revealed the diagnosis of lupus nephritis type V. She was started on high-dose steroids and MMF, with maintenance therapy of PSL 5 mg/day and MMF 3 g/day. She was referred to our hospital 3 years ago, and her initial examination revealed anti-ds-DNA antibody negative, anti-RNP antibody positive, anti-Sm antibody negative, and anti-SSA antibody positive. After gradual reduction of steroids and MMF, she continued to suffer from anxiety for the past five months. She was diagnosed with NPSLE due to high level of IL-6 in CSF (10.7 pg/mL). She was treated with PSL 30 mg/day and anifrolumab 300 mg/4 weeks. After two doses of anifrolumab, CSF IL-6 decreased to 2.1 pg/mL and her anxiety disorder improved. Treatment of NPSLE generally requires strong immunosuppression and prolonged hospitalization. In this case, the use of anifrolumab resulted in improvement of symptoms after a relatively short hospitalization, and the initial dose of steroids could be reduced. Therefore, it was suggested that anifrolumab could be a treatment option for patients with NPSLE.

## P1-196

**A case of systemic lupus erythematosus with fasciitis**

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Conflict of interest: None

25-year-old women diagnosed with rheumatoid arthritis in X-3, started methotrexate (MTX) at family doctor. In mid-February, she presented fever, fatigue, and bilateral thigh muscle pain, and visited family doctor. Prednisone (PSL) 10 mg was added, but no improvement was observed,

and she was referred to our hospital on March. She was pointed out decreased C4, positive antinuclear antibody, positive anti-dsDNA antibody, and positive anti-Sm antibody. She was diagnosed with systemic lupus erythematosus (SLE). A thigh MRI scan revealed a T2 high-signal area along the limbus of the thigh muscle group, suggesting fasciitis. Muscle and fascia biopsies performed on May showed inflammatory cells around the fascia, leading to a diagnosis of SLE with fasciitis. She requested outpatient treatment, so treatment was started with PSL30 mg (0.75 mg/kg). Because of her desire to have a baby, MTX was stopped, and PSL was gradually decreased without relapse under the combination of hydroxychloroquine and tacrolimus. This is a rare case of SLE with fasciitis.

## P1-197

**A case of recurrent necrotizing lymphadenitis associated with SLE and Sjögren's syndrome treated with anifrolumab alone**

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Conflict of interest: None

A 28-year-old woman presented with fever and painful swelling of the lymph nodes in her neck and supraclavicular area. She had 4 years history of Sjögren's syndrome and was diagnosed with systemic lupus erythematosus one year before. Her symptoms improved with the administration of oral NSAIDs. However, her symptoms recurred in two months and the biopsy of the left supraclavicular lymph node revealed necrotizing lymphadenitis, which improved with oral NSAIDs again. Hydroxychloroquine was administrated to prevent recurrence, but it was discontinued due to drug eruption. Two months later, she experienced recurrence of symptoms. She was administrated with intravenous infusion of anifrolumab of 300 mg every 4 weeks from and the condition stabilized, with no obvious recurrence of symptoms until 48 weeks. Anifrolumab may be a treatment option for relapsed and refractory cases.

## P1-198

**A case of multiple fractures and multiple severe abscess formation caused by long-term glucocorticoid treatment**

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Conflict of interest: None

[Case] A 64-year-old woman was diagnosed with SLE in August X-18. Administration of 25 mg/day prednisolone (PSL) was started and continued taking that thenceforth. She developed fractures of L1 vertebra and left third rib on January X. In addition, she also had extensive back pressure ulcers, and right psoas muscle abscess on February X. After admission, not only puncture drainage of the right psoas abscess but also surgical incision and drainage of the back pressure ulcer were immediately performed with treatment of antibiotics because MSSA was detected in both pus cultures and blood cultures. One week after the initiation of treatments, no MSSA was detected. However, after discontinuation of antibiotics, she developed fever and lower limb pain soon. Since MSSA was confirmed by blood culture again and MRI showed an epidural abscess around the L1 and the dural sac, permanent oral administration of antibiotic was started. Then, no MSSA was detected in blood cultures, and CRP elevation was reduced. She was discharged in late May X. [Clinical Significance] Even small doses of glucocorticoid (GC) significantly increase the risk of developing serious side effects such as severe infections, osteoporotic fractures, and atherosclerotic lesions with prolonged administration.

## P1-199

**Successful treatment with belimumab for juvenile-onset autoimmune hemolytic anemia associated with systemic lupus erythematosus: A report of two cases**

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Conflict of interest: None

[Background] The steroid use for pediatric patients should be as low-dose and short-duration as possible. [Case 1] A 14-year-old girl, she had nasal hemorrhage, fatigue. Her hemoglobin was 6.3 g/dl, platelet count was 28,000/μl. She had positive cold agglutination reaction, several irregular antibodies, and positive result of Coombs test. Her PA-IgG was also strongly positive, consistent with Evans syndrome. Later, positive anti-ds-DNA antibodies, hypocomplementemia, and facial butterfly erythema were found as the manifestation of SLE. She used HCQ and MMF to reduce PSL, but her hypocomplementemia had persisted. After starting BEL, her complement levels had increased. [Case 2] An 8-year-old girl with yellowish skin. Her hemoglobin was 3.7 g/dl, platelet count was 100,000/μl. She had positive cold agglutination reaction, positive Coombs test, and a diagnosis of mixed AIHA. She had hypocomplementemia, positive anti-ds-DNA antibody, and hypocomplementemia. The treatment was initiated with PSL and MMF. Unfortunately, the hypocomplementemia flared up again. Finally, we started to introduce intravenous BEL to her, and her serum complement level began to rise. [Conclusion] BEL is effective for normalizing complement levels in pediatric patients with AIHA-associated SLE.

## P1-200

**A Case of Systemic Lupus Erythematosus (SLE) Complicated with Myelitis and Small Intestine Perforation**

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Conflict of interest: None

Case: A 36-year-old female with abdominal pain. History: In February, the patient noted hair loss and joint pain. In March, fatigue and abdominal pain arose. Since initial care for infectious enteritis remained ineffective, she was transferred to our hospital. Findings, such as knee arthritis, serositis, proteinuria, positive antinuclear, anti-ds-DNA antibodies and lymphocytopenia, led to a diagnosis of SLE. Intestinal edema indicated lupus enteritis. Miscarriages and the presence of lupus anticoagulant suggested antiphospholipid syndrome. Treatment was initiated with methylprednisolone pulse therapy, followed by infusion of glucocorticoid (GC) and heparin. Day 3, quadriplegia appeared; day 4, brain MRI showed cerebral infarctions; day 5, cervical MRI confirmed myelitis. Intravenous cyclophosphamide (IVCY) was administered. Day 8, intensified pain and CT findings revealed intestinal perforation, leading to an emergent jejunectomy. Expedited tapering of GC started. We added the treatment of tacrolimus and six courses of IVCY. Both enteritis and myelitis improved, with enhanced mobility, leading to discharge on day 207. Significance: Concurrent myelitis and intestinal perforation are rare in SLE. Early GC reduction with immunosuppressants appeared pivotal for favorable outcomes.

## P1-201

**A case of systemic lupus erythematosus (SLE) that was infected with new coronavirus (COVID-19) immediately after initiation of aniflorumab and required the same treatment as the relapse of the SLE**

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Conflict of interest: None

[case study] 63-year-old woman [chief complaint] fever [History of present illness] Fever, polyarthralgia, butterfly erythema, apraxia appeared, Blood tests show characteristic findings for SLE and SPECT showed decreased parietal blood flow. SLE was diagnosed and improved with prednisolone (PSL) 60 mg/day and cyclophosphamide pulses. Recently, PSL 7 mg/day was used with mycophenolate mofetil. Because of joint pain, aniflorumab 300 mg was administered on X-9 days. On X-4 days, sore throat, fever appeared. This patient was infected with COVID-19. Hypoxemia and ground-glass opacity were noted, Remdesivir 100 mg/day and dexamethasone 6.6 mg/day improved them, But on X±5 day, a fever, hypoxemia, and an expanded ground-glass opacity were ob-

served. PSL 60 mg/day and tocilizumab 500 mg was used to eliminate hypoxemia. Platelets decreased from X+17 to X+32 and improved with baricitinib 4 mg/day. Discussion: Anifrolmab may inhibit interferon and prolong viral infections. Cytokine storms in COVID-19 can also modify the pathogenesis of SLE. This patient was infected with COVID-19 after initiation of aniflorumab and did not improve with standard treatment of COVID-19, requiring the same treatment as SLE flare-ups.

## P1-202

**Efficacy of belimumab for residual activity or relapse associated with lupus nepritis in long-term maintenance therapy: three case series**

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Conflict of interest: None

We report three cases of LN in which BLM adding was effective in treating residual activity or relapse in maintenance therapy, without increasing above the moderate dose of glucocorticoid or adding other immunosuppressive agents. [Case 1] 55-year-old female, onset LN (III/IV) 27 years ago. Her urinary protein creatinine ratio (U-P/Cr) remained around 1g/gCr. Whenever relapse of nephrosis, PSL increased, IVCY, TAC and MMF were combined, but it was difficult to reduce the below 10 mg of PSL. But, 3 months after of BLM was added, her U-P/Cr was decrease. And 5 years after, without renal activity, and PSL tapered down to 4 mg. [Case 2] 58-year-old female, onset LN (IV + tubulointerstitial nephritis) 17 years ago. She flared up of LN (III) 12 years ago, PSL was increased to 35 mg, and maintained with PSL 5 mg and MZR, but relapse of positive ds-DNA antibody and increased U-P/Cr. But, 6 weeks after of BLM was added, her U-P/Cr was decrease, and 3 years after, without renal activity and has been tapered down to 2 mg of PSL. [Case 3] 81-year-old female, onset LN (III+V) 13 years ago. She was maintained with PSL 3 mg and TAC, but increased U-P/Cr 6 months ago. PSL increased to 10 mg, and HCQ and ANF were added, but developed nephrosis. After switching to BLM, U-P/Cr was decreased.

## P1-203

**A case of refractory lupus nephritis with severe nephrotic state treated with belimumab and combination therapy**

Kazunobu Ichikawa[1], Shinya Abe[1], Takaya Suzuki[1], Takaaki Nawano[1], Masahiro Miyata[1], Soichiro Kon[1], Eri Matsuki[1], Yukino Yokokawa[1], Sayumi Watanabe[1], Keita Kamei[1], Natsuko Suzuki[2], Masafumi Watanabe[1]
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Conflict of interest: None

A 35-year-old woman was diagnosed with systemic lupus erythematosus in November 2014 (at age 28) due to fever, leukopenia, proteinuria, oral ulcer, hypocomplementemia, positive antinuclear antibody, and positive anti-dsDNA antibody. A renal biopsy was not performed due to single kidney. In June 2019, she developed nephrotic syndrome. Steroid pulse therapy, MMF, and IVCY were tried, but they were not effective, and she remained nephrotic state. she was referred to our hospital in September 2022, and an open renal biopsy was performed, and she was diagnosed with lupus nephritis type III + V. She was treated with steroid pulse and IVCY (Euro-Lupus method) with belimumab, and MMF after IVCY. Due to persistent nephrosis, tacrolimus was added in February 2023. One year after the induction therapy, the urinary protein has improved to 0.9 g/gCr. In this case, her nephrotic state persisted for a long time without aggressive treatment because a renal biopsy was not performed due to the single kidney, and lupus nephritis was not diagnosed histologically. Even refractory lupus nephritis may improve with biologics and combination therapy of immunosuppressive agents.

## P1-204

**The efficacy of belimumab in systemic lupus erythematosus (SLE) based on a single center analysis**

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Conflict of interest: None

[Objective] To examine whether belimumab (BLM) was effective for SLE based on the single center analysis. [Methods] The SLE patients introduced BLM at our department between January 2018 and August 2023 were consecutively involved. Patients were fulfilled the 2019 ACR/EULAR criteria. Clinical information including and glucocorticoids dosage, disease activity scores (LLDAS, SDI, SLEDAI-2K) and laboratory data were retrospectively collected from records and compared. [Results] Thirty-one cases with median age 40.6 years old, disease duration 11.1 years, and follow-up for 21.8 months were enrolled. All were in the maintenance phase. BLM were introduced in order to taper the GC dose (22 cases), arthralgia (5 cases), skin rash (2 cases), and lupus headache (2 cases). At week 0, 52 and 120, LLDAS was attained by 23%, 52% and 77%, but SDI was comparable, respectively. SLEDAI-2K (7 to 4, $p<0.05$), GC dose (10 to 7 mg/day, $p<0.05$), anti-DNA antibody titer (47 to 30 IU/ml, $p<0.05$), C3 (71 to 78 mg/dl, $p<0.05$) C4 (14 to 17 mg/dl, $p<0.05$) were improved after the treatment. In 19 cases continued BEL for more than 52 weeks, only one case was relapsed. [Conclusions] For the patients with SLE, BEL was effective for improvement for their disease activity and GC dosage even in the maintenance phase.

## P1-205

**Outcome of Anifrolumab Use in Systemic Lupus Erythematosus (SLE)**

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Conflict of interest: None

[Purpose] We report our experience of SLE treated with anifrolumab. [Patients and Methods] We performed a retrospective analysis of the clinical characteristics of SLE patients treated with anifrolumab from 2021 to 2023. Eleven patients were subjected for the study. The patients were all women, age at diagnosis was 39±16 years, age at initiation of anifrolumab was 45±16 years. [Result] Serological evaluation before and after 12 weeks of anifrolumab treatment was as follows; WBC (5745±1887 vs 7948±4128 /μL, P=0.58), IgG (1227±313 vs 1130±209 mg/dL, P=1), CRP (0.38±0.52 vs 0.50±0.51 mg/dL, P=0.02), C3 (96±29 vs 102±31 mg/dL, P=0.61), and C4 (16±10 vs 21±10 mg/dL, P=0.04). PSL was used in ten patients and its reduction was difficult (11±14 vs 7±2 mg, P=0.37), however, SLEDAI showed a significant improvement (12±6 vs 7±7 points, P=0.04). In particular, fever, hair loss, hypocomplementemia, and high DNA antibody levels tended to improve. Unfortunately, two cases showed no improvement in SLEDAI. [Conclusion] Anifrolumab is considered to be useful in some cases of SLE. In our experience, some cases do not respond to the Anifrolumab treatment. It is necessary to clarify the longterm effect of the drug, and to identify the characteristics of patients suitable for Anifrolumab.

## P1-206

**Efficacy and Safety of Anifrolumab for the Treatment of Systemic Lupus Erythematosus: A Single-center, Real-world, Retrospective Study**

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Conflict of interest: None

[Objective] To evaluate the safety and effectiveness of anifrolumab (ANI) in patients with systemic lupus erythematosus (SLE). [Methods] We conducted a retrospective analysis of 28 SLE patients who received ANI for at least 3 months between December 2021 and October 2023. We assessed clinical data, laboratory findings, glucocorticoid (GC) doses, and serious adverse events (SAEs). [Results] The median age of the patients was 50 years. The median disease duration was 197 months. 40.7% had switched from belimumab (BLM). Antibodies profile were as follows: anti-DNA 11.8%, anti-RNP 59.3%, and anti-SS-A 48.1%. GC dosage was significantly decreased at 12, 24, and 52 weeks (7.5 to 4 and 3 mg; $P<0.05$), and SLEDAI-2K at 4, 12, 24, and 52 weeks was also decreased significantly (6.0 to 2.0, 0, 0, and 0; $P<0.05$). DORIS remission rates were 71.4% at 12 weeks and 63.2% at 24 weeks. A significant decrease in the SLEDAI-2K was also observed within the subgroup of patients who switched from BLM. 2 patients were admitted due to mild COVID-19 pneumonia, while 1 patient was admitted with a parainfluenza infection. No other SAE were reported. [Conclusions] Anifrolumab reduced disease activity and GC dosage in SLE and exhibited a favorable safety profile.

## P1-207

**Litifilimab Modulates Type I IFN Biomarkers in Patients with SLE or CLE in the Phase 2 LILAC Study**

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Conflict of interest: None

**[Background/Purpose]** Litifilimab is a humanized IgG1 mAb targeting BDCA2, a receptor expressed on pDCs that negatively regulates the production of Type I IFN and proinflammatory chemokines and cytokines. We evaluated the effects of litifilimab on IFN gene signature (IFNGS) scores, IFNα and other cytokines in LILAC participants. **[Methods]** Expression of 22-gene panel IFNGS scores and concentrations of IFNα and other cytokines were examined. Treatment effects were estimated using a mixed model repeated measures approach. **[Results]** Litifilimab induced reductions in 22-gene IFNGS scores and IFNα. In Part A, TNFα and IL-10 concentrations were reduced (nominal $P<0.05$) with litifilimab 450 mg at W24; no strong evidence of this was seen in Part B. In Part A, a correlation between changes in IFNα concentration and in clinical efficacy parameters (total number of active joints and CLASI-A) was observed at W1 and W24 (Spearman rank correlations; 95% confidence interval). In Part B, the dose-response relationship was similar to that observed with the clinical responses. **[Conclusion]** Litifilimab induced a rapid, substantial, and sustained reduction in 22-gene IFNGS scores and IFNα concentrations, and reductions in some biomarkers correlated with clinical responses.

## P1-208

**Clinical Characteristics of Patients with Systemic Lupus Erythematosus Treated with Belimumab in a Community Hospital in Japan**

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Conflict of interest: None

[Objective] Belimumab (BEL) became available in Japan from 2017, and data on the efficacy of BEL in Japanese SLE patients are increasing. We report the characteristics, concomitant medications, and changes in the organ damage of SLE patients treated with BEL in our department. [Methods] Patients treated with BEL in our department from December 1, 2017 to April 30, 2023 were selected retrospectively, and their age, gender, organ involvement, prednisone (PSL) dose, and those items at the last observation were investigated. [Results] Thirty-seven patients were treated with BEL. The mean age was 49 years, and the median duration of disease was 25 months. There were 17 cases of arthritis (36%), 10 cases of skin rash (27%), and 3 cases of serositis (8%). The mean PSL dose at the start of BEL was 11.4 mg. At the last observation, 26 patients (70%) continued BEL. Of the 11 patients who discontinued BEL, the reasons for discontinuation in 6 patients were the patient decision, injection site pain, or return to home country. Arthritis persisted in 7 patients, skin rash in 4 patients, and serositis in 0 patient. The mean dose of PSL reduced to 6.8 mg. [Conclusions] The efficacy of BEL in our department and the effectiveness of PSL dose reduction were shown to be comparable to existing ones.

## P1-209

**The study of the 4 cases of systemic lupus erythematosus patients treated with aniflolumab**

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Conflict of interest: None

[Objective] To study of the clinical characteristics, efficacy, and achievement of treatment in the systemic lupus erythematosus (SLE) patients treated with aniflolumab. [Methods] The clinical responses of 4 SLE patients treated with aniflolumab were examined using LIT, DORIS, and LLDAS. [Results] All patients were female, the median age at induction was 60.5 years old, disease duration was 32.0 years, and dose of glucocorticoid (GC) was 5.75 mg/day. All patients had arthralgia and fatigue. Psychological disoders were observed in 2 cases. In the serological symptoms, 2 cases were cytopenia, 1 case was hypocomplementemia, 3 cases were anti-ds-DNA antibody (Ab)-positive, 2 cases were anti-phospholipid Ab-positive, and 1 case was positive both anti-U1-RNP Ab and anti-centromere Ab. Tacrolimus was used in 2 cases and hydroxychloroquine was used in 3 cases. Arthralgia, fatigue and cytopenia improved in all cases, LIT was improved in 2 cases and dose of GC decreased in 2 cases. DORIS and LLDAS remission was achieved in 1 case. On the other hand, 2 case was increased anti-ds-DNA Ab. There were no adverse events in any case. [Conclusions] Aniflolumab might be efficacy of minor flares (arthritis, fatigue, cytopenia), and be possible to aim for GC reduction or discontinuation.

## P1-210

**Retrospective study of Belimumab therapy in patients with systemic lupus erythematosus: A single center analysis**

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Conflict of interest: None

[Objectives] Belimumab (BLM) has been proven to improve clinical symptoms of SLE, prevent relapse, and reduce GC dose, but there are some unknowns, such as dose reduction of other immunosuppressants (IS) in patients with remission. The purpose of this study is to analysis the effectiveness of BLM and the effect of dose reduction of other IS. [Methods] We retrospectively investigated 16 SLE patients who have started BLM in our hospital since February 2019 till January 2023. [Results] The average age was 43.5 years old. All patients were treated with GC (average PSL 8.1 mg/day), each of 14 and 11 patients were concomitantly administered HCQ and IS. The median SLEDAI was 12.8, BILAG was 3.8. The purpose of concomitantly administered BLM was each disorders of constitutional: 8, skin and mucocutaneus: 9, neuropsychiatric: 1, musculoskeletal: 6, hematologic and immunological disorder13. The disease activity (DA) at 6

months with BLM was reduced as median SLEDAI 6.7 and median BILAG2.0. An average PSL dose was reduced to 7 mg/day, 3 patients were stopped IS. Although 4 patients had miner flare of SLE, they could continue BLM. [Conclusion] In our hospital, treatment of BLM was associated with a reduction in DA and IS. Further investigation will be important for appropriate case selection of BLM.

## P1-211

**Analysis of the Clinical Practice of SLE with DPC Database**

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Conflict of interest: None

[Background] In Japanese first guidelines for SLE 2019, the use of HCQ and the combination of immunosuppressants (IMs), not GC alone, are recommended. However, in clinical practice, the adherence to the guidelines is not widespread. The DPC (Diagnosis Procedure Combination) data, one of the available real-world data sources in Japan, has the advantage of collecting information on the course of treatment for a wide range of patient populations. [Objective] Analyzing the DPC database, this study aims to clarify the differences in HCQ usage and the combination of IMs between specialized facilities and non-specialized ones, and to examine their relationship with patient outcomes. The goal is to visualize the compliance with guidelines and the role of specialist physicians, contributing to the development of SLE practice. [Methods] Patients with SLE in DPC participating facilities from April 2019 to March 2021 will be extracted. Data analysis will be conducted to compare 1) the rates of HCQ usage and the combination of IMs between specialized and non-specialized facilities, and 2) the length of stay and readmission rates in relation to the presence or absence of HCQ usage and the combination of IMs. [Results] The results of the data analysis will be presented along with discussions.

## P1-212

**Systemic lupus erythematosus-associated hemophagocytic syndrome experienced in our hospital**

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Conflict of interest: None

Representative Case: A 51-year-old woman, treated for systemic lupus erythematosus (SLE) with prednisolone (PSL), belimumab, and cyclophosphamide, had a fever of 39°C two months after diagnosis of SLE. She was suspected of hemophagocytic syndrome (HPS) due to pancytopenia, high CRP level and hyperferritinemia. She repeated relapse, requiring four times methylprednisolone (mPSL) pulse therapy and cyclosporine, and was discharged with PSL tapered to 25 mg. Discussion: Although she had had positive anti-dsDNA antibody and hypocomplementemia at the time of SLE diagnosis, she didn't have them at the time of HPS onset. Among SLE patients who visited our department from 2004 to 2023, 10 cases were suspected HPS, including this case, and anti-dsDNA antibody was negative in 5 of 10 cases. C3 levels ranged from 17 to 91 mg/dL (median: 53.5 mg/dL), and normal C3 level was observed in 3 cases. Even patients with stable disease activity of SLE presented HPS. CRP ranged from 0.1 to 18.9 mg/dL (median: 1.41 mg/dL) and ferritin ranged from 124 to 7102 mg/dL (median: 1681.5 mg/dL) in 10 cases. All cases were treated with steroids, cyclosporine was used in 3 cases, and tacrolimus was used in 4 cases. Conclusion: SLE-related HPS can occur even in the absence of serum immunological abnormalities.

## P1-213

**Comparative of quality of life (QOL) in elderly-onset and young-onset systemic lupus erythematosus (SLE) patients in Yamaguchi: QUOLITY study**

Shun-ichiro Ohta[1], Takashi Nawata[2], Kazuo Kushimoto[1], Tsuyoshi Nakayama[4], Kyohei Nakayama[4], Seiko Oda[7], Fumiko Okazaki[3], Nobuko Ozuno[5], Makoto Kubo[9], Hajime Miyazato[6], Toshiko Watada[8], Hiroyuki Wakiguchi[3], Masaki Shibuya[2]
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Conflict of interest: None

[Objective] To compare the clinical characteristics and QOL of elderly-onset (EO) SLE patients (age > 50 years) with those of younger-onset (YO) SLE patients (age <50 years). [Methods] Patients enrolled in the multicenter QUOLITY study were evaluated for background, QOL score (The Japanese LupusPRO), disease activity, and drug treatment collected from June 2023 to August 2023. [Results] Of the 53 patients, 17 were EO (6 males, 64±9.12 years) and 36 YO (2 males, 29.1±10.7 years), with significantly more males in the EO group (p=0.028). There were no differences in disease activity, PSL dose, HCQ, or immunosuppressive drug use during QOL score assessment, but the rate of use of BLM was significantly lower in EO patients (33.3% vs. 11.8%). The QOL score, HRQOL, which is one of the goals of SLE treatment, and items such as Physical health, Pain/Vitality, and Emotional health, was significantly lower in the EO groups. However, the BLM-using patients showed significantly higher scores than non-users on HRQOL and all related items, as well as on NHRQOL and items such as Desires/Goals and Satisfaction with care. [Conclusions] QOL in EO patients with SLE may not be sufficiently improved by controlling disease activity or reducing drug toxicity, but the use of BLM may contribute to improvement.

## P1-214

**Lupus Impact Tracker in patients with systemic lupus erythematosus (SLE) in our hospital**

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Conflict of interest: None

[Objective] This study aims to assess the impact of SLE patient background, organ complications and drugs used on patient quality of life. [Methods] Among 281 SLE patients who visited our hospital between June and August 2023, for whom LIT could be collected using a self-administered questionnaire, we divided them into two groups: high LIT (LIT≧25 points) and low LIT (LIT<25 points), and conducted a multivariate logistic regression analysis was performed to detect factors influencing LIT. [Results] Patient background was as follows: mean age 50.9 ± 15.2 years, 88.6% female, mean prednisolone (PSL) use 4.53 mg/day, 200 patients using hydroxychloroquine (HCQ), 56 patients using belimumab (BEL), 10 patients using anifrolumab (ANF), mean LIT score 24.2 ± 21.1, with 115 in the high LIT group and 166 in the low LIT group; multivariate analysis between the two groups showed that the odds ratio (95% confidence interval) for high LIT was higher for increased prednisolone dose 1.15 (1.07-1.25) and for increased age 1.03 (1.01-1.05). [Conclusions] In patients with SLE, age and steroid dosage were thought to contribute to patient quality of life.

## P1-215

**Association of SLE disease activity index (SLEDAI-2K/ SLE-DAS), Physician General Assessment (PGA) and steroid use in daily practice**

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Chisato Ashida, Daisuke Tomita, Tetsu Itami, Kazuya Kishimoto, Yuji Nozaki, Koji Kinoshita, Itaru Matsumura
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Conflict of interest: None

[Objective] SLEDAI (-2K) and SLE-DAS are simple measures of SLE disease activity in routine practice, but their individual measures differ in several ways. We will examine the relevance of each activity measure, plus the PGA (0-3 scale), to the adjustment of steroid dosage at each visit. [Methods] Cases in which SLEDAI-2K, SLE-DAS, PGA, and steroid dose (PSL equivalent) were all evaluable on at least two visits dating back to the last observation date between November 2021 and December 2022 at our department were included to examine the correlation between each disease activity index and steroid dose. [Results] 242 SLE patients evaluated were 88.6% female and 50.8 years of age (mean). mean SLEDAI-2K, SLEDAS, PGA and PSL dose (mg/day) were 4.44/3.31, 3.32, 0.57 and 5.01, respectively. PSL dose was not correlated with either SLEDAI-2K or SLE-DAS, but positively correlated with PGA ($r=0.33$, $p<0.0001$). PGA also correlated positively with SLE-DAS ($r=0.32$, $p<0.0001$), but not with SLEDAI-2K. [Conclusions] Steroid dose adjustment at each visit in SLE practice may be more strongly associated with overall assessment by the attending physician than with objective activity measures, and SLEDAS may be a more closely related measure to the attending physician's assessment than SLEDAI-2K.

## P1-216

**Comparison of Childhood-onset Systemic Lupus Erythematosus and Adult-onset Systemic Lupus Erythematosus: A Single Center Cohort Study**

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The University of Tokyo Hospital

Conflict of interest: None

[Objective] Clinical symptoms and organ damage differ between childhood-onset systemic lupus erythematosus (cSLE) and adult-onset SLE (aSLE). We herein examined the clinical characteristics of cSLE at our hospital. [Methods] Patients who visited our department from November 2022 to April 2023 and with insurance registration of SLE were selected. Patients meeting the ACR classification criteria (1997) or the SLICC classification criteria (2012) or the EULAR/ACR classification criteria (2019) were included. Patients with follow-up period less than six months and cases of unknown age at diagnosis were excluded, and patients with onset under 18 years of age (cSLE) and with onset in adulthood (aSLE) were compared. [Results] 42 cSLE patients and 330 aSLE patients were analyzed. The mean age of onset was 14.2±2.6 years for cSLE and 34.1±12.5 years for aSLE. Disease duration was 22.5±11.6 years in cSLE and 18.2±12.6 years in aSLE. The SLICC disability index (SDI) was 0.83±1.07 for cSLE and 2.18±2.68 for aSLE at the time of the study. [Conclusions] The SDI of cSLE was already high at 0.83±1.07 at 22.5±11.6 years after onset, and further studies are needed to improve the prognosis.

## P1-217

**Influence of changing the assay system on the identification of antiphospholipid antibodies in clinical practice**

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Conflict of interest: None

[Objective] To clarify the differences between conventional methods (anti-cardiolipin antibody (CL), human β2GPI-dependent anti-cardiolipin antibody (β2GPI)) and APL panel methods (CL (IgG, IgM), β2GPI (IgG, IgM)) in clinical practice. [Methods] Patients who underwent both conventional and APL panel tests were included. Clinical information including antiphospholipid antibody titers was retrospectively extracted from medical records. We analyzed the characteristics of cases in which the results were dissociated. [Results] The results of the conventional method and the APL panel method were concordant in 98 cases, but discordant in 70 cases. CL and β2GPI, which were positive by the conventional method, became negative in 53 and 1 case, respectively. Similarly, negative to positive results were observed in 7 and 15 cases, respectively. The 53 CL-negative cases were the antibody titer by the conventional method was significantly low. 7 CL-positive cases had high β2GPI titer by the conventional method, and β2GPI was also positive by the APL panel method. Of the 15 cases with positive β2GPI. [Conclusions] The APL panel method may have fewer false-positive CL than the conventional method. However, it should be noted that there are cases of APS even in negative cases.

## P1-218

**Clinical Characteristics of Late Elderly Onset Diffuse Cutaneous Systemic Sclerosis (dcSSc)**

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Conflict of interest: None

[Objective] There is little information on changes of epidemiology in the aging population in SSc patients. We examined the age distribution of onset of dcSSc and clinical features of patients with late elderly onset dcSSc using a single-center prospective registry. [Methods] The age distribution of disease onset was examined in 151 dcSSc patients enrolled in our registry. The clinical features of late elderly onset dcSSc patients were retrospectively analyzed. [Results] The onset age ranged from 12 to 89 years, with a peak between 40-60 years, including 32 patients aged over 65 years and only 6 patients aged over 75 years. All patients with late elderly onset dcSSc were female and were positive for either anti-RNA polymerase III, anti-topoisomerase I, or anti-RuvBL1/2 antibody. The disease duration was within 10 months except one, and the modified Rodnan skin score ranged from 9 to 29. Internal organ involvement including heart involvement and interstitial lung disease were common, and two died of senility. [Conclusion] The onset age distribution of dcSSc is consistent with previous reports. Late elderly onset dcSSc is rare and is characterized by rapid disease progression.

## P1-219

**Raynaud's phenomenon is the most common painful symptom experienced by SSc patients, and fatigue is the least recognized by physicians**

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Conflict of interest: Yes

[Objective] Because symptoms of systemic sclerosis (SSc) are diverse, it is difficult to know how patients (pts) feel and how physicians perceive them. A survey was conducted to provide clarification. [Methods] The survey was conducted via an online questionnaire of pts aged ≧18 years and with an SSc diagnosis, and physicians working in hospitals with ≧20 beds and seeing ≧3 SSc pts monthly. [Results] The respondents were 301 pts and 129 physicians. Most pts were female (63.8%). The ratio of limited to diffuse cutaneous SSc was approximately 1:1. Most of the physicians were rheumatologists (51.2%), followed by dermatologists (20.9%). Raynaud's phenomenon (RP) was the symptom most commonly perceived as painful by pts (30.2%). Fatigue was more commonly perceived as troublesome by pts (21.9%) than by physicians (5.4%). Percentages of respondents who perceived that treatment "relieved" symptoms were lower for pts than for physicians, especially regarding RP (32.0%, 52.7%), pain (43.9%, 66.7%), reflux esophagitis (46.3%, 71.3%), diarrhea (29.2%, 58.9%), constipation (31.1%, 58.1%), and dysphagia (23.3%, 48.1%). [Conclusions] Pts' and physicians' perceptions of SSc symptoms and treatment effectiveness may differ. Understanding this difference is key when setting treatment goals.

## P1-220

**Clinical and serological features of anti-centromere antibody-positive limited cutaneous systemic sclerosis**

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Conflict of interest: None

[Objective] Anti-centromere antibody-positive limited cutaneous systemic sclerosis (ACA-positive lcSSc) has a milder range and severity of skin symptoms than diffuse cutaneous systemic sclerosis. However, it is not well recognized that severe organ damage or other autoimmune diseases may occur. [Methods] We examined the clinical symptoms and laboratory data of 130 ACA-positive lcSSc patients. [Results] There were 115 female cases, with an average age of 67.3 years. Raynaud's symptoms and swelling/hardening of the fingers were observed in 73.8% and 86.9%, and the average period from the onset of Raynaud's symptoms to consultation (duration of illness) was 8.9 years. Organ disorders were interstitial pneumonia, pulmonary hypertension, primary biliary cholangitis, Sjögren's syndrome, and Hashimoto's disease in 27.6%, 23.8%, 43.8%, 48.4%, and 34.6%, respectively. Autoantibody positivity rate was RF 26.6%, SSA antibody 39.0%, TG antibody 21.3%, TPO antibody 42.6%, and mitochondrial M2 antibody 33.0%. [Conclusion] ACA-positive lcSSc occurs more frequently in women and is frequently accompanied by primary biliary cholangitis, Sjögren's syndrome, etc. It was suggested that the longer the disease duration from the onset of symptoms, the higher the prevalence of comorbidities.

## P1-221

**Examination of clinical findings related to QOL after 5 years in systemic sclerosis**

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Conflict of interest: None

[Objective] Regarding the QOL of SSc, we have reported the relationship between clinical findings and functional impairment using EQ-5D and HAQ. The aim was to clarify the clinical findings that affect QOL based on QOL 5 years later. [Methods] Of the 118 cases investigated in the first year, 51 cases were evaluable after 5 years and 23 cases died during the course of the study. EQ-5D and HAQ were measured as QOL evaluation. We examined the changes in QOL at the initial and 5-year follow-up, and their relevance. 5 years later, we investigated the relationship between each of EQ-5D and HAQ and clinical findings in the first year. We also investigated the characteristics of clinical findings in patients who achieved clinical remission on the 5-year HAQ. [Results] After 5 years, QOL showed a significant decline only in HAQ. The initial clinical findings associated with deterioration in QOL after 5 years were age and ILD in the EQ-5D, and age and %DLco in the HAQ. The initial clinical findings related to clinical remission in the 5-year HAQ were age, disease type, and initial QOL. [Conclusions] In SSc, the items related to QOL decline after 5 years are age at initial diagnosis and respiratory organs, and the items related to clinical remission are age, disease type, and initial QOL.

## P1-222

**Survey results on drug costs for Raynaud's phenomenon in patients with systemic sclerosis**

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Conflict of interest: None

[Objective] Since there is no radical treatment for systemic sclerosis (SSc) and it presents with a variety of symptoms, symptomatic treatment is required for each individual symptom. Here, we focused on Raynaud's phenomenon (RP) and investigated the drug costs for RP. [Methods] The subjects were SSc patients who visited the clinical immunology outpatient department (nine physicians) of Osaka University Hospital in January and February 2023. We calculated drug prices based on April 2023 for drugs to treat RP from the prescriptions. The following drugs were selected as anti-RP drugs; nifedipine, diltiazem, nicardipine, beraprost, limaprost, sarpogrelate, cilostazol, isosorbide dinitrate, and bosentan. [Results] Forty-nine patients were included in the study (average age 58.7, 7 males, 42 females, 27 diffuse cutaneous type, 22 localized cutaneous type). Thirty-six (78.3%) were using drugs to treat RP. The overall average cost of drugs to treat RP was ¥1,214 /day, and anti-RP drugs user's average was ¥1,699.65 (approximately ¥60,000 /month). [Conclusions] More than 70% of patients were using drugs to treat RP. Although this amount is not a patient burden because most patients are certified as patients of designated intractable disease, RP is presumed to have a high economic burden.

## P1-223

**Clinical characteristics of anti-RNA polymerase III antibody positive SSc with PPF**

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Conflict of interest: None

[Objective] To report the clinical characteristics of anti-RNA polymerase III (RNAP III) antibody positive SSc with PPF. [Methods] 39 consecutive cases of anti-RNAP III antibody positive SSc. [Results] Of the 39 anti-RNAP III antibody positive SSc patients who visited our department, 10 SSc-ILD patients with PPF (PPF group) and 13 patients in the non-PPF group during the observation period. The 10 patients in the PPF group were 71.5 (62.8-74.3) years old, 6 female, 5 diffuse type, mRSS 7 (0.5-26.3). Six patients had a history of smoking. KL-6 1029 (510-2066.5) U/ml, Cr 0.8 (0.7-1.0) mg/dl, %FVC 77.7 (68.5-90.0)%, %DLco 34.2 (23.4-43.7)%. Among these, there were significantly more males in the PPF group than in the non-PPF group (P=0.016), and KL-6 and Cr were also significantly higher (P=0.016 and 0.028, respectively). There were significantly more patients in the PPF group who used PSL and IVCY during remission induction than in the non-PPF group (P=0.003 and 0.009, respectively). [Conclusions] Among anti-RNAP III antibody-positive SSc-ILD patients, risk factors for PPF complications include male, KL-6, Cr, and smoking history. In addition, acute/subacute ILD was observed in 90% in the PPF group, of which 30% died due to ILD. We need to accumulate more cases in the future.

## P1-224

**Examination of the efficacy and safety of nintedanib for systemic sclerosis**

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Conflict of interest: None

[Purpose] To examine how to initiate the nintedanib therapy for interstitial lung disesase (ILD) in patients with systemic sclerosis (SSc). [Methods] Eighteen patients with SSc who received nintedanib at our hospital were retrospectively evaluated for the clinical characteristics. Patients were divided into 2 group: patients who could continue nintedanib therapy more than 1 year (group A) and patients who could not continue nintedanib therapy due to adverse events or worsening of ILD (group B). Comparisons of clinical features including present status (PS), changes in serum

KL-6, CT findings of lung and respiratory function tests. [Results] Of 18 patients (male/female: 2/16 female), eleven patients were group A (an average age: 60.5 years) and 7 patients were group B (an average age 67 years). Two patients in group B were died due to deterioration of SSc or acute exacerbation of ILD. The average serum KL-6 level was decreased at 1 year after starting nintetanib compared to before nintetanib therapy (1307.8 U/ml to 1085.6 U/ml). There were significant differences in age, disease duration, and PS between the two groups. [Conclusion] These results suggest that the early initiation of nintedanib therapy might be usuful in terms of PS and risk reduction of side effects.

## P1-225

**Current status and safety of rituximab treatment for systemic scleroderma at our institution**

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Conflict of interest: None

[Objective] To evaluate the current status and short-term safety of patients treated with rituximab (RTX) for systemic scleroderma at our institution. [Methods] Patients who received RTX for systemic scleroderma at our institution from June 2021 to October 2023 were included. Efficacy after 24 weeks of treatment was analyzed using modified Rodnan's total skin thickness score (mRSS) for skin stiffness and %FVC, KL-6, and HRCT for ILD, respectively. Safety was evaluated for adverse events up to 24 weeks after administration. [Results] Twenty-eight patients were included in the study, with a mean age of 61.7±11.5 years and disease duration of 10.2±8.8 years at the time of RTX induction. All patients had skin hardening, 21 had interstitial lung disease (ILD), 3 had pulmonary hypertension, and 11 had reflux esophagitis. The mRSS at the beginning of treatment was 11.1±11.4 points, %FVC was 73.3±17.5%, DLCO was 58.7±20.3%, and KL-6 was 703.6±460.8 U/mL in ILD cases. 75% of HRCT patterns were NSIP patterns. Adverse events included bacterial pneumonia, two cases of COVID-19 infection, and severe Grade 4 thrombocytopenia in one patient. [Conclusions] Infections should be kept in mind in AEs associated with RTX administration. We report a case of severe thrombocytopenia, including details.

## P1-226

**Evaluation of the risk of relapse after tocilizumab discontinuation in patients with giant cell arteritis: a single-center cohort study**

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Conflict of interest: None

[Objective] The efficacy of tocilizumab (TCZ) for the treatment of giant cell arteritis (GCA) has been demonstrated in recent years. However, it remains unclear whether discontinuation of TCZ is possible after remission is achieved. The aim of this study is to assess the risk of relapse after TCZ discontinuation in the Japanese population. [Methods] This study is a retrospective analysis of GCA patients treated with TCZ, who later stopped receiving TCZ treatment at our institution between January 2011 and September 2023, [Results] 11 GCA patients satisfied the above criteria. 3 patients received small doses (<5 mg/day) of prednisolone (PSL), and 8 patients had already withdrawn PSL at the time of TCZ discontinuation. TCZ was discontinued due to satisfactory remission achievement in 5 (45.5%) patients, and adverse events in 6 (54.5%) patients. Disease relapse was observed in 7 (63.6%) patients, and the average time to relapse was 246±141 days [range: 56 to 441 days]. Of these patients, 6 (85.7%) experienced polymyalgia rheumatica-resembling symptoms, and elevations in inflammatory markers were observed in all 7 patients. [Conclusions] A high incidence of disease relapse was observed in GCA patients after TCZ discontinuation in the Japanese population.

## P1-227

**Real-World Data on Tocilizumab Use for Giant Cell Arteritis in Japan**

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Conflict of interest: Yes

[Objective] Japan didn't join the global GiACTA Phase III trial on Tocilizumab (TCZ) for Giant Cell Arteritis (GCA). Furthermore, real-world data is scarce. This study aims to describe the epidemiology of GCA patients receiving TCZ in Japan. [Methods] We retrospectively analyzed GCA patients who received TCZ in 7 Japanese hospitals. [Results] We identified 62 patients with a median age of 74 years (69-79), 65% of whom were female. The symptoms at diagnosis were headache (73%), fever (32%), jaw claudication (26%), scalp tenderness (23%), visual symptoms (11%). Diagnostic tests included CT (87%), cranial MRI (16%), temporal artery ultrasound (58%), PET-CT (27%), and temporal artery biopsy (71%). Positive rates of each modalities were 41%, 70%, 47%, 94%, and 80% respectively. TCZ was initiated in 45 cases (73%) for new-onset GCA and 17 (27%) for relapse. The median time from diagnosis to TCZ initiation was 53 days (15-225), with a median prednisolone dose of 25 mg (12.5-45). Among patients who experienced relapse and initiated TCZ, the median prednisolone dose at the time of relapse was 10 mg (3-15) [Conclusions] This study provides insights into the characteristics of GCA patients treated with TCZ. TCZ was introduced relatively early to minimize glucocorticoid-related adverse events.

## P1-228

**Association of pathological findings with temporal artery biopsy and clinical and imaging findings in patients with giant cell arteritis**

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Conflict of interest: None

[Objective] To investigate the association of pathological findings with temporal artery biopsy (TAB) and clinical and imaging findings in patients with giant cell arteritis (GCA). [Methods] We reviewed consecutive patients who had visited our hospital between August 2011 and November 2022 and met the 2022 ACR/EULAR GCA classification criteria. Pathological findings with TAB, clinical findings, and imaging were collected retrospectively, and their associations were analyzed. [Results] Forty-two patients were included in the analysis. The median age was 74 years, and 24 (57.1%) were female. TAB was performed in 30 (71.4%) and led to pathological diagnosis in 25 (83.3%). Comparison of TAB pathological findings with clinical symptoms identified association of multinucleated giant cell infiltration (p=0.009), vascular obstruction, and luminal narrowing (p=0.018) with jaw curettage and of positive intimal thickening with fewer ocular symptoms (p=0.035). Disruption of the internal elastic plate was not associated with clinical and imaging findings. Thrombi in the TAB pathological findings was associated with a positive Halo sign in the imagings (p=0.005). [Conclusions] Association between TAB pathological findings, clinical symptoms, and imaging findings was clarified in GCA.

## P1-229

**A case of giant cell arteritis complicated by gastric aneurysm**

Hiromitsu Akamatsu, Anri Mori, Megumi Ikeda, Kaho Hayashi, Hiroaki Saito, Akira Sakata, Hiroyoshi Yanagisawa, Fumitaka Yamamori, Akihiko Koshino, Hajime Sanada, Daiki Hayashi, Keisuke Sako, Yoshinori Takahashi, Shunsuke Tsuge, Tadashi Toyama, Megumi Oshima, Keisuke Horikoshi, Ryo Nishioka, Takahiho Yuasa, Takeshi Zoshima, Satoshi Hara, Kiyoaki Ito, Shinji Kitajima, Ichiro Mizushima, Norihiko Sakai, Akinori Hara, Mitsuhiro Kawano, Yasunori Iwata, Takashi Wada
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Conflict of interest: None

(Case) 68-year-old woman (Case presentation) One year before hospitalization, she was diagnosed with episcleritis. She was treated with Prednisolone (PSL) 20 mg/day. Six months before admission, A Computed tomography (CT) image which was taken for lightheadedness showed extensive aortic wall thickening and markedly narrowed bilateral subclavian arteries. She was diagnosed with giant cell arteritis and was referred to our hospital for admission. An upper gastrointestinal endoscopy revealed a pulsatile submucosal mass. Contrast-enhanced CT imaging revealed an aneurysm formation in the same area, and a gastric aneurysm was diagnosed and treated with coil embolization. After treatment of gastric aneurysm, PSL 40 mg/day and subcutaneous injection of tocilizumab 162 mg/week were successfully used to induce remission. (Clinical Significance) Gastric aneurysms are fatal when ruptured but are difficult to diagnose before the rupture. On the other hand, steroids used to treat aortitis may promote aneurysm rupture and should be used with caution in patients with coexisting aneurysms. Visceral aneurysm can be associated with giant cell arteritis. Treatment with steroid agents may cause its rupture. To check for visceral aneurysms in detail with enhanced CT imaging before treatment is crucial.

## P1-230

**A case of giant cell arteritis with bilateral sensorineural hearing loss**

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Conflict of interest: None

[Case] 74-year-old woman. She was referred to our otolaryngology department due to otalgia, temporomandibular joint pain, headache, nasal pain, dizziness, and bilateral sensorineural hearing loss. She was admitted to the hospital due to high inflammatory response. A contrast-enhanced CT scan showed circumferential thickening of the aortic wall and inflammation around the cervical branch, and she was referred to our department. She had significant tenderness in the bilateral temporal arteries, near the left carotid artery, and in the right supraclavicular fossa. Neurological examination revealed ataxia. Based on the results of ultrasonography and MRI, a diagnosis of giant cell arteritis and hypertrophic pachymeningitis was made. After steroid pulse therapy, post-treatment with prednisolone 50 mg/day was started. Tocilizumab was then added. She was discharged from the hospital, but her hearing impairment remained. [Clinical Significance] Although there are limited reports of sensorineural hearing loss in giant cell arteritis, early treatment with steroids has been suggested to be important for improving hearing. In this case, treatment was initiated 3 days after the onset of hearing loss, but the patient did not achieve satisfactory improvement.

## P1-231

**A case of giant cell arteritis with abdominal angina due to stenosis of a branch of abdominal artery, which was difficult to diagnose because of preceding arthralgia**

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Conflict of interest: None

63 years old woman. Predonisolone were started 6 months ago for undiffrentiated arthritis, and she was referred to our clinic. She was diagnosed with peripheral spondyloarthritis and anti-rheumatic drugs were started. One month before, she was admitted to the hospital due to abdominal pain. Abdominal plain CT and colon endoscopy revealed no abnormalities, and her symptoms became mild, but C-reactive protein was elevated. 2 weeks later, she visited again due to abdominal pain and abdominal vascular murmur was heard. Contrast-enhanced CT showed inflammatory findings in aorta and stenosis of the origin of both celiac and superior mesenteric artery, indicating to diagnosis of giant cell arteritis with branching lesions. Abdominal ultrasonography showed significant accelerated blood flow of celiac artery flow and the cause of the postprandial abdominal pain was diagnosed as abdominal angina. Predonisolone 40 mg/day and tocilizumab s. c 162 mg/week were started, and symptoms gradually improved. Clinical Significance: In a case of seronegative arthritis with abdominal pain, it is important to distinguish giant cell arteritis with abdominal angina.

## P1-232

**A case of giant cell arteritis presenting with peripapillary optic nerve contrast enhancement on contrast-enhanced MRI of the head**

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Conflict of interest: None

[Case] 61-year-old man [Chief complaint] Fever, temporal headache [History] Hypertension [Clinical Course] The patient began to feel fatigued around the middle of July 202X. Towards the end of July, a fever exceeding 38°C and bilateral temporal pain appeared. Contrast-enhanced CT and blood culture tests showed no abnormalities, however, the symptoms worsened over time, so he was referred to our hospital. CRP was 26.46 mg/dL, and PR3-ANCA, MPO-ANCA, and antinuclear antibodies were all negative. Contrast-enhanced MRI scan of the head revealed thickening and enhancing effects on the left temporal artery and arterial walls within the bilateral temporalis muscles, as well as contrast effects around the optic nerve. IgG4 or angiotensin I-converting enzyme were within normal range, and anti-aquaporin 4 antibody and anti-Tp antibody were negative. We diagnosed him as giant cell arteritis with peripapillary optic neuritis and started prednisolone 80 mg/day. 14 days after treatment, CRP level had decreased to 0.13 mg/dL, and the peripapillary contrast effect had disappeared on MRI. [Discussion] Peripapillary optic neuritis associated with giant cell arteritis has been reported infrequently, so we report this case with a review of literatures.

## P1-233

**Usefulness of FDG-PET in the Diagnosis of Giant Cell Arteritis: two case reports**

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Conflict of interest: None

Case 1: An 80-year-old female was diagnosed with PMR in October 20XX-2 and was treated with PSL 2.5 mg/day. In October 20XX, she was referred to our hospital for further examination due to persistently high level of CRP after gingivitis. She was diagnosed with GCA by FDG-PET. After increased dose to PSL 40 mg/day, and her symptoms releaved. Case 2: An 83-year-old woman with persistent elevated level of CRP to 3-7 mg/dL since December 20XX-1 was referred to our hospital in July 20XX to investigate the source of inflammation. She was diagnosed with GCA and PMR by FDG-PET. Treatment with PSL 40 mg/day was started and her symptoms improved. GCA is classified into two types: cranial type (C-GCA) and large vessel type (LV-GCA). C-GCA can be diagnosed by ultrasonography, while LV-GCA can be diagnosed by contrast-enhanced CT, which reveals circumferential thickening of the arterial wall, stenosis, occlusion, or aortic aneurysm, Diagnosis using conventional imaging tests is often difficult in some cases. The sensitivity and specificity of FDG-PET in GCA were reported to be 90% and 98%, respectively, and it was considered to be a useful tool for cases in which diagnosis is difficult with conventional imaging. maging tests.

## P1-234

**A Case of Malignancy-Associated Giant Cell Arteritis with Delayed Therapeutic Intervention Due to Advanced Colorectal Cancer Treatment Resulting in Ocular Manifestations**

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Conflict of interest: None

<Case Presentation> An 86-year-old woman visited another medical facility's oral surgery department with the chief complaints of limited mouth opening in February X. She was diagnosed with peri-implantitis and osteomyelitis. Despite surgery and antibiotic therapy, she held headaches and fatigue. In June X, she was referred to the department of general medicine in our hospital. The temporal artery ultrasonography revealed halo signs in both, and PET-CT showed FDG uptake on the arterial branches of the bilateral carotid to brachial arteries, thoracoabdominal aorta, and superior mesenteric artery. We diagnosed giant cell arteritis (GCA). However, the colonoscopy revealed an Isp-type advanced colorectal cancer in the ascending colon, and the laparoscopic right hemicolectomy was performed in August X. In September X, she was readmitted for the treatment of GCA. New fundus findings related to GCA were detected in her right eye. Following steroid pulse therapy, high-dose steroid therapy was initiated, resulting in a favorable response and remission. <Consideration> We encountered a case of GCA associated with advanced colorectal cancer. In this case, the delay in treatment of GCA due to cancer treatment led to new ocular symptoms. We report based on our own experience.

## P1-235

**A case of GCA with visual impairment complicated by pyogenic arthritis and iliopsoas muscle abscess that required differentiation from infection**

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Conflict of interest: None

We report a case of GCA with visual impairment complicated by pyogenic arthritis and iliopsoas abscess, which required differentiation from infection. 94-year-old woman. On September 7th, X she was hospitalized due to fever, visual disturbance in the right eye, multiple joint pains and high inflammatory response. A swollen joint in her left knee after joint fluid culture test revealed α-streptococcus and a diagnosis of pyogenic arthritis. Blood culture revealed the same bacteria, and there was an abscess of the left iliolumbar muscle. The patient has received antimicrobial treatment, but continues to have a high inflammatory response, polyarthralgia, myalgia, and general malaise. No new fever sources were identified, and infection control was effective. GCA was suspected based on the clinical course of the patient, who had visual impairment. Temporal artery biopsy revealed GCA. The patient was high risk of infection. Treatment with 10 mg steroid was started to improve ADL. After the intervention, the reduction in subjective symptoms and improved inflammatory response were observed. If there is persistent inflammation that is unresponsive to antimicrobial agents, appropriate imaging studies, and a temporal artery biopsy necessary to consider GCA.

## P1-236

**Treatment outcome of avacopan for ANCA-associated vasculitis focusing on three cases with abnormal liver function tests**

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Conflict of interest: None

[Background] Avacopan, a selective C5a receptor antagonist for ANCA-associated vasculitis (AAV), became available in Japan in 2022. We report the treatment outcome of avacopan in our institute and three cases with abnormal liver function tests. [Method] We reviewed AAV patients treated with avacopan in our institute between June 7, 2022, and September 30, 2023. We retrospectively collected medical records on blood tests, glucocorticoid and avacopan doses at AAV onset, avacopan initiation, avacopan treatment duration, relapses and adverse events. [Results] Six patients (three males, four cases with microscopic polyangiitis) were enrolled in the study. Although there were no AAV relapses during avacopan treatment, three patients experienced abnormal liver function tests. The time from starting avacopan to abnormal liver function tests was 64 [48-91] days. In two cases, avacopan had to be discontinued. In one patient, avacopan can be continued at a reduced dose of 30 mg/day without abnormal liver function tests. [Conclusion] No relapses of AAV were observed in patients treated with avacopan, but abnormal liver function tests were observed in 50% of cases. Rheumatologists should remember that liver function abnormalities with avacopan may occur several months after the first treatment.

## P1-237

**Efficacy and Safety of Avacopan in ANCA-Associated Vasculitis**

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Conflict of interest: None

[Purpose] A phase III study on avacopan for ANCA-associated vasculitis reported earlier glucocorticoid (GC) tapering during remission induction. We assessed the efficacy and adverse events in patients treated with avacopan for AAV at our hospital. [Methods] We retrospectively evaluated five patients who received avacopan treatment for 26 weeks from October 2021 to March 2023. [Results] The mean age at avacopan administration was 79.6 years. One (20%) patient was male. All patients had MPO-ANCA-positive MPA, and four (80%) were relapsed cases. Four patients (80%) received IVCY for remission induction, while one (20%) received RTX. Severe liver dysfunction led to avacopan discontinuation in two patients (40%) within 26 weeks. In the three patients who took avacopan regularly for 26 weeks, the mean BVAS at the beginning was 9.3. However, all patients achieved BVAS 0 at 26 weeks. Additionally, GC doses were tapered to PSL 5 mg, 10 mg, and 7.5 mg, respectively, at 4 weeks after avacopan administration. At 20 weeks, one patient discontinued GC, while the other two continued with PSL 2 mg and 5 mg. [Conclusion] Avacopan may enable earlier GC reduction compared to conventional therapy. However, it should be used with caution due to the potential risk of severe liver dysfunction.

## P1-238

**Efficacy of Rituximab in Microscopic Polyangiitis and Granulomatosis with Polyangiitis in our Department**

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Conflict of interest: None

[Objective] To assess the efficacy of RTX for MPA and GPA. [Methods] We examined 1) patient backgrounds, 2) treatment course, and 3) adverse events in patients with MPA or GPA treated with RTX at our hospital. [Results] 1) 13 MPA and 6 GPA patients; mean age at RTX initiation was 67.4 years, 10 women/9 men, were selected. Mean observation period was 27.6 months. The following organ involvement was observed: 18 lung, 7 renal, 4 otitis media, 4 nasal, 3 scleritis, 2 mononeuritis multiplex, and 1 hypertrophic pachymenigitis. RTX was used for induction therapy at initial onset in 10, relapse in 8, or PSL tapering in 1 patient. 2) 18/19 received 4 weekly doses of RTX at initiation, 7 of which were readministered at 6 months later. 1/10 for initial induction therapy and 3/8 for relapse had post-RTX relapse. No relapse occurred during RTX maintenance. The mean PSL dose was reduced from 31.4 mg/day at initiation to 9.7 mg/day 6 months later. 3) No deaths during the observation period. RTX was discontinued in 1 case due to pneumonia and diverticulitis at initiation of RTX, and in 1 case due to Herpes Zoster after transition to maintenance administration. [Conclusions] RTX is an effective for MPA and GPA with a variety of pathological conditions with no significant adverse events.

## P1-239

**A case of hypocomplementemic urticarial vasculitis successfully treated by rituximab**

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Conflict of interest: None

A 77-year-old man was admitted to our hospital because of fever, skin rash, and fatigue. He developed widespread geographic erythema all over the body, and laboratory tests revealed elevated levels of C reactive protein and serum creatinine, low serum complement, levels proteinuria and urinary occult blood. The skin biopsy showed urticarial vasculitis, and the renal biopsy showed crescentic glomerulonephritis. These results led to the diagnosis of hypocomplementemic urticarial vasculitis. The patient received the remission induction therapy with 30 mg/day of prednisolone and rituximab followed by clinical improvement and disappearance of proteinuria. After prednisolone was tapered off, the patient was still in remission. Hypocomplementemic urticarial vasculitis is a rare small vessel vasculitis characterised by consistent urticarial lesions with histologic findings of leukocyte clastic vasculitis, low serum complement levels and typically ocular, renal, and pulmonary involvements. Given the limited number of cases and the heterogeneity of the symptoms, no standard treatment is established. However, several reports highlighted the higher response rate of rituximab compared to corticosteroids with conventional immunosuppressive agents. Our case will be discussed with literature review.

## P1-240

**Two cases of eosinophilic polyangiitis granulomatosa with severe cardiac involvement (EGPA) treated with early combination of IVCY, high-dose immunoglobulin therapy, and mepolizumab**

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Conflict of interest: None

[Background] IVCY is recommended for EGPA patients with severe cardiac involvement, but its cardiac burden and toxicity have raised safety concerns. [Case 1] 55-year-old female. She developed bronchial asthma in X-1. In X-1, neurological symptoms, increased eosinophils, and elevated CRP were observed, and a diagnosis of EGPA was made. Diffuse hypokinesia (EF: 43.8%) was observed, and mPSL pulse and IVCY were started, followed by MEP and IVIG. Cardiac function improved to EF: 58.1% within one month. [Case 2] A 56-year-old male. He had chronic sinusitis since X-4, bronchial asthma, increased eosinophils and neurological symptoms in X-1. He was diagnosed as eosinophilic sinusitis by a local doctor, and was urgently brought to our hospital because of marked progression of weakness and diffuse wall hypokinesia (EF: 20.4%). There was no significant coronary artery stenosis, and mPSL pulse and IVCY were started as myocarditis associated with EGPA, and IVIG and MEP were added. One month after the start of treatment, EF improved to 43.2%. Clinical Significance] IVCY can be safely used in patients with severely impaired cardiac function, and the combination of IVIG and MEP at an early stage can improve cardiac function.

## P1-241

**A case of microscopic polyangiitis started with refractory diarrhea, with MPO-/PR3-ANCA co-positivity and complicated with cardiac tumor**

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Conflict of interest: None

[Case] An 82-year-old woman presented with anorexia and weight loss 2 years ago and diarrhea 1 year ago. Abdominal CT scan showed small bowel inflammation and colonoscopy (CS) showed an ulcer at the end of the ileum, but biopsy results did not lead to a definitive diagnosis. She was initiated mesalazine as Crohn's disease, but the diarrhea continued. She had difficulty eating as her diarrhea worsened, and was admitted to the department and introduced to intravenous hyperalimentation (IVH) 2 months ago. CS showed nonspecific colitis, and small intestine angiography showed small bowel inflammation. She was referred to rheumatology when her antinuclear antibody was positive (x160). Her blood test showed MPO-ANCA 50.7U/mL and PR3-ANCA >350U/mL. After further diagnosis exclusion, she was diagnosed with microscopic polyangiitis (MPA). Echocardiography showed a tumor likely myxoma in the left ventricle, but she did not wish to undergo surgery. She was initiated prednisolone (PSL) 40 mg/day. Her diarrhea improved markedly and she was weaned from IVH. Azathioprine 50 mg/day was added and PSL was tapered off. [Conclusion] MPA should be considered in cases of refractory diarrhea that cannot be diagnosed after endoscopy and biopsy.

## P1-242

**Efficacy and safety of avacopan for ANCA associated vasculitis**

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Conflict of interest: None

[Objective] We investigated the efficacy and safety of avacopan in patients with ANCA-associated vasculitis (AAV). [Methods] We investigated the disease activity and safety of AAV after 48 weeks of avacopan administration in AAV patients who started administration of abacopan. [Results] Twelve AAV patients were treated. Remission induction in 3 cases, relapse in 3 cases, and steroid reduction in 6 cases. 2 male and 10 females, age 79.0±5.6 years, disease duration 2.4±2.4 years, MPO-ANCA positive in 11 cases and PR3-ANCA positive in 1 case at the time of first onset. During administration of abacopan, prednisolone dose of 11.5 ± 12.8 mg/day, immunosuppressants in 5 cases, interstitial lung disease in 11 cases, and renal dysfunction in 10 cases. After administering abacopan, the dose of prednisolone could be reduced in patients who induced remission, but in patients who relapsed, relapse occurred 24 and 40 weeks after administration, so additional treatment was performed. One patient each contracted COVID-19 and pyelonephritis during the course of the treatment. The dose of abacopan was reduced in 2 patients with diarrhea and elevated liver enzymes. [Conclusion] Abacopan was introduced to AAV without major side effects, but it is necessary to follow the progress carefully.

## P1-243

**Avacopan for the treatment of hypertrophic pachymeningitis in ANCA associated vasculitis; case reports**

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Conflict of interest: None

[Objective] There are no reports on the use of avacopan for hypertrophic pachymeningitis associated AAV. We report two patients with hypertrophic pachymeningitis associated ANCA associated vasculitis (AAV) who was successful treated with avacopan. [Case 1] A 76-year-old man was diagnosed with AAV with scleritis and OMMAV 4 years ago. He improved after treatment with PSL and MTX. He developed headache and diagnosed hypertrophic pachymeningitis associated AAV. Avacopan were added, and after 5 years the symptoms improved. [Case 2] A 65-year-old woman was diagnosed AAV with alveolar hemorrhage and abnormal urinary sediment 7 months ago. She improved after treatment with high dose PSL and IVCY. She diagnosed with hypertrophic pachymeningitis associated with AAV when PSL was tapered to 20 mg. She was treated with high dose PSL and immunosuppressants (MTC, TAC, RTX), however she did not improve. She developed limb paralysis after 2 months. Contrast-enhanced MRI showed thickening and enhancement of the dura mater of cervical spinal cord. She was treated with higher dose dexamethasone.

After 4 months treatment, her neurological symptoms improved. She received avacopan as remission-maintenance treatment, therefore PSL was tapered to 7.5 mg.

## P1-244

**A case of microscopic polyangiitis that relapsed during remission maintenance therapy with rituximab**

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Conflict of interest: None

A 67-year-old man was diagnosed with MPA due to alveolar hemorrhage, rapidly progressive glomerulonephritis, and elevated MPO-ANCA levels. As remission induction therapy, IVCY was administered 6 times in combination with high-dose GC, resulting in remission. AZA was used as remission maintenance therapy, while GC was tapering off, MPO-ANCA rose again and alveolar hemorrhage occurred again, causing a relapse. The second remission induction therapy was RTX at 375 mg/m$^2$, administered weekly for 4 times in combination with high-dose GC, and the patient went into remission again. For remission maintenance therapy, RTX was used every 6 months for remission maintenance therapy, but MPO-ANCA rose again and urinalysis findings worsened, so it was determined that the patient had relapsed. The third remission induction therapy used RTX in conjunction with high-dose GC, and the patient achieved remission again. AZA was previously used as remission maintenance therapy for microscopic polyangiitis, but recently rituximab has been used as the first-line drug. Here, we experienced a case of MPA that relapsed during remission maintenance therapy with RTX. Currently, the dosage and administration interval for RTX as a remission maintenance therapy have not been established.

## P1-245

**A case of multiple vasculitis granulomatosa with recurrent transient lower extremity weakness**

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Conflict of interest: None

Case: 79 years old male He was diagnosed with renal dysfunction, sinusitis, and mixed hearing loss. He had dyspnea on exertion and was admitted to the hospital after chest CT showed pulmonary infiltrates and pleural effusion. PR3-ANCA was positive, and he was considered to have acute progressive glomerulonephritis due to ANCA-associated nephritis. Dialysis induction was inevitable, and we decided not to use steroids because of comorbidities. He was admitted to the hospital with worsening weakness and numbness in the lower extremities. On the fifth day of admission, the patient had impaired consciousness, dysarthria, and right hemiplegia, and a head MRI scan showed signal changes and a CSF scan showed protein-cell discrepancy. Encephalopathy was suspected. We administered a steroid pulse, and his paralysis and impaired consciousness improved. He was started on 25 mg/day (0.5 mg/kg) of prednisolone and rituximab as post-therapy. A repeat MRI showed cerebral venous sinus thrombosis, and he was started on warfarin. He was transferred to the hospital on the 75th day for rehabilitation. The presence of transient neurological symptoms should be considered in the differential of encephalopathy associated with vasculitis and is considered an educational case and is reported here.

## P1-246

**Sjogren's syndrome complicated with positive antineutrophil cytoplasmic antibodies and coronary artery aneurysms: A Case Report**

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Conflict of interest: None

[Case] A 15-year-old female visited our clinic with complaints of polyarticular pain and fatigue. There was no medical history, including Kawasaki disease. Although there were no sicca symptoms, there was a history of parotid gland swelling, and salivary gland scintigraphy revealed decreased uptake in the parotid and submandibular glands. Although anti-SS-A and anti-SS-B antibodies were both negative, ANA 80x (homo, spe), hypergammagloburinemia, and positive rheumatoid factor were observed and Sjögren's syndrome was suspected. Positive anti-MPO-ANCA and anti-PR3-ANCA were also revealed. At the age of 19, the patient visited our clinic with the complaint of chest pain. Although the electrocardiogram and cardiac sonography were normal, myocardial markers (CK-MB, troponin T) were increased. Cardiac MRI also revealed a myocardial delayed contrast area on the left ventricular wall and coronary angiography revealed dilatation along the entire length of the left and right coronary arteries. [Discussion] A patient with probable Sjögren's syndrome and positive for ANCA presented with coronary aneurysms. Although the origin of aneurysms is strictly unkown, we speculate that the vasculitis is caused by autoimmunity. [Clinical Significance] We report a patient with vasculitis unclassified.

## P1-247

**Hypereosinophilic syndrome associated with multiple coronary aneurysms**

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Conflict of interest: None

A 43-year-old man with eosinophilia developed acute myocardial infarction. Percutaneous coronary intervention at Hospital A revealed diffuse dilatation and aneurysmal changes in the coronary arteries. Eosinophilia (WBC 10300/μL, Eos 53%) was also seen, so EGPA was suspected and he was referred to Hospital B, finally diagnosed with HES. Coronary artery lesions were also considered unrelated, and antiplatelet therapy was continued. At the age of 45, he was referred to our department for investigation of the underlying cause of eosinophilia. Because hemato-oncological diseases were ruled out and any organ damages requiring treatment were not detected, he was kept under observation as an outpatient. At the age of 46, spinal MRI revealed multiple vertebral compression fractures. At the age of 50, a cardiac catheterization performed to investigate chest discomfort during exercise revealed an increase in coronary artery aneurysms and severe stenosis in multiple locations, so glucocorticoid administration was started at our department. Although myocardial lesions are known as cardiovascular organ damage caused by HES, there are only a few reports of coronary artery aneurysms, so we report this case with literature reviews.

## P1-248

**A case of granulomatosis with polyangiitis (GPA) diagnosed with hoarseness as the chief complaint**

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Conflict of interest: None

We report a case of granulomatosis with polyangiitis (GPA) diagnosed with hoarseness as the chief complaint. The patient was a 59-year-old woman who was referred to our hospital due to bilateral hearing loss after treatment of otitis media. The laboratory data showed elevation of MPO-ANCA and CT-scan revealed mass shadow in the right upper lung field. Bronchoscopy was performed and right vocal cord paralysis was noted, but the pathological examination of the mass in the right upper lung showed no evidence of malignancy or granulomatous lesion. However, PET-CT showed abnormal accumulation in the right upper lung, nasal septum, and multiple lymph nodes. In addition head MRI revealed hypertrophic pachymeningitis. From the above reasons, the patient was diagnosed with GPA and treatment was initiated with glucocorticoid and rituximab as remission induction therapy. Subsequently, MPO-ANCA became negative, symptoms including hoarseness disappeared, and hypertrophic pachymeningitis and mass shadow in the right upper lung improved. Al-

though there have been reports of hoarseness due to subglottic stenosis in GPA, this case did not show any abnormal lesion of the larynx. We report a case of GPA diagnosed with hoarseness due to hypertrophic pachymeningitis or recurrent nerve paralysis.

## P1-249

**Analysis for clinical aspects on adult IgA vasculitis**

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Conflict of interest: None

[Objective] IgA vasculitis (IgAV) is common and self-limiting systemic vasculitis in children. However, IgAV has clinically different characteristics between children and adult. The objective of this study is to clarify clinical aspects of adult IgAV. [Methods] We reviewed medical records of 21 adult IgAV patients diagnosed at our hospital from July 2014 to October 2023. EULAR/PRINTO/PRES classification criteria (2010) were used for the diagnosis of IgAV. [Results] The median age on IgAV onset was 42 years and females accounted for 62%. All patients exhibited purpura/petechiae. The rash extended to trunk and upper limbs over lower limbs in many cases. Approximately a half of the patients had the history of infection 14 days before the onset of IgAV. Joint, gastrointestinal and renal involvement was present in 76.2%, 42.9% and 55% of the patients, respectively. Fever concomitant with the rash was shown in 9.5% of them. Prednisolone was initiated at the median dose of 30 mg/day for the treatment in 71.4% of the patients. Notably, serum cryoglobulines were detected in five of 13 patients who were tested. Only one patient had organ involvement caused by the cryoglobulinemiad. [Conclusions] A biopsy to affected lesions should be considered for the diagnosis of IgAV.

## P1-250

**Analysis of MRI findings of the lower extremity in patients with ANCA-associated vasculitis**

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Conflict of interest: None

[Objective] It is reported that muscle MRI of patients with ANCA-associated vasculitis (AAV) show intramuscular signal abnormalities. However, there are few reports focusing on and analyzing perivascular signal abnormalities. In this study, we quantified perivascular signal abnormalities on muscle MRI and analyzed the relationship between these indices and clinical symptoms. [Methods] We retrospectively analyzed 20 patients with AAV who underwent lower extremity MRI. We defined perivascular abnormal signals on STIR as abnormal vessels (AV) and measured the number and diameter of AV. These indices were compared with and without organ lesions. We also examined the correlation between these indices and BVAS, CRP, MPO-ANCA, and PR3-ANCA. [Results] There were 9 cases of GPA, 2 cases of EGPA, and 9 cases of MPA. The mean number and diameter of AV were $8.99 \pm 2.24/4$ cm$^2$ and $2.64 \pm 0.60$ mm (mean ± SD). The number of AV was significantly higher in patients with peripheral neuropathy. No correlation was found between the number or diameter of AV and BVAS, CRP, or PR3-ANCA. No significant correlation was found between the number of AV and MPO-ANCA, but it tended to be correlated. [Conclusions] The number of AV was associated with the presence of peripheral neuropathy in patients with AAV.

## P1-251

**A case of eosinophilic granulomatosis with polyangiitis (EGPA) complicated by inappropriate ADH secretion syndrome (SIADH) without intracranial or pulmonary lesions**

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Department of Allergy and Rheumatology, Asahi General Hospital

Conflict of interest: None

[Case] 59-year-old woman [Present illness] Three years before admission, she developed bronchial asthma, and pain, swelling, and numbness in the right plantar region appeared two years later. She was admitted to the hospital because of increased eosinophils and myositis-like findings. [Progress] Physical examination revealed decreased peripheral palpation and muscle weakness in the lower extremities. ANCA tests were negative, and nerve conduction study showed peripheral neuropathy. There were no intracranial or pulmonary lesions. There was asymptomatic severe fluid volume normal hypotonic hyponatremia with ADH: 0.7 pg/ml. She was diagnosed with EGPA complicated by SIADH and was started on high dose prednisolone and IVIG therapy. Hyponatremia, neurological and muscular symptoms were improved. [Clinical Significance] There have been only 6 reported cases of EGPA complicated by SIADH at this time. No studies have evaluated autonomic dysfunction in patients with EGPA, but since vasculitis syndrome has been shown to impair autonomic function, it is assumed that autonomic dysfunction may also occur in EGPA. It is possible that SIADH may be present when the peripheral ascending afferent autonomic nerves, which carry stimulation from the baroreceptors to the hypothalamus, are injured.

## P1-252

**Two cases of IgA vasculitis caused by endocrine therapy for elderly breast cancer patients**

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Itami City Hospital, Hyogo, Japan

Conflict of interest: None

objective: In recent years, endocrine therapy with aromatase inhibitors (AI) and tamoxifen (TAM) for breast cancer treatment has been widely used. We report two cases of IgA vasculitis caused by endocrine therapy for elderly breast cancer patients. Case 1: An 82-year-old female. After breast cancer surgery, she was treated with oral anastrozole (AI). Nine months after starting endocrine therapy, she developed lower leg edema, purpura, and abdominal pain. Skin biopsy from purpura showed deposition of IgA and C3 in the vessel walls, leading to the diagnosis of IgA vasculitis. After discontinuing anastrozole, the purpura quickly disappeared, and other symptoms gradually improved. Case 2: An 80-year-old female. TAM therapy was chosen after breast cancer surgery. Two years after starting endocrine therapy, she developed fever and purpura on the lower leg. Skin biopsy from the lower leg purpura revealed deposition of IgA and C3 in the vessel walls, resulting in a diagnosis of IgA vasculitis. After discontinuing TAM, the purpura improved, but fever persisted. Treatment with steroid (30 mg/day) led to the improvement of all symptoms. Discussion: The number of breast cancer patients is increasing, and an increase in IgA vasculitis associated with endocrine therapy is also expected.

## P1-253

**Microscopic Polyangiitis Complicated by Stroke**

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Department of Rheumatology, Hiroshima Red Cross Hospital and Atomic-bomb Survivors Hospital

Conflict of interest: None

Objective: Microscopic polyangiitis (MPA) is a rare complication of cerebrovascular disease, and its relation to stroke in patients with MPA is discussed. Case: A 77-year-old man was diagnosed with subarachnoid hemorrhage. Abnormal urinalysis, rennal dysfunction and elevated MPO-ANCA levels, leading to a diagnosis of microscopic polyangiitis. The patient was treated with glucocorticoid and RTX to induce remission. Three months after diagnosis, he developed COVID-19 infection and was hospitalized. He had acute exacerbation of interstitial pneumonia and was difficult to treat. On the 15th day of his illness, his level of consciousness decreased, and multiple cerebral infarctions were noted. He also had bacterial pneumonia and died on the 17th day of his illness. Discussion: In the past 10 years, we have had only two cases of concomitant stroke in the year before and after the diagnosis of MPA, including this case. The mean

age at diagnosis was 66.8 years, and more than half of the patients had renal involvement. Peripheral neuropathy and interstitial pneumonia were complications in about 40% of the patients. Although stroke is a rare complication, it is included in the Brmingham vasculitis activity score and is an important complication of small vessel vasculitis.

## P1-254

**A case of MPO-ANCA positivity with pulmonary nodules and renal interlobular arteritis**

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Conflict of interest: None

[Case] A 73-year-old man, diagnosed with diabetes 20 years ago, had been suffering from fatigue for a month. His serum CRP level was elevated at 12 mg/dL, and chest CT depicted multiple nodules, which did not disappear even after treatment with antibiotics. His serum Cr level was 1.66 mg/dL, accompanied by MPO-ANCA of 37 U/mL. ANCA-associated vasculitis (AAV) with rapidly progressive glomerulonephritis was suspected and he was transferred to our hospital. He showed further deterioration of serum Cr levels on admission and was clinically diagnosed as having granulomatosis with polyangiitis (GPA). He was treated with high-dose glucocorticoid (GC) and rituximab, including GC pulse therapy. Pulmonary nodules resolved, and serum Cr and MPO-ANCA titers decreased. A renal biopsy performed on the 7th hospital day showed only mild mesangial lesions consistent with diabetic nephropathy and necrotizing vasculitis of interlobular arteries and arterioles, without crescentic glomerulonephritis. [Clinical Significance] This patient was clinically diagnosed as and treated for GPA based on ANCA positivity and clinical pictures, but renal pathology findings did not support the diagnosis. This case suggests the importance of biopsy even in the presence of clinical findings consistent with AAV.

## P1-255

**A case of granulomatosis with polyangiitis (GPA) complicated by multiple cerebral neuropathy**

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Conflict of interest: None

Cerebral neuropathy in GPA is associated with either vasculitis-induced, or strangulated cranial neuropathy mediated by pachymeningitis. Here, we present a 75-year-old woman with GPA and multiple cranial neuropathy. She developed hearing loss about 4 years ago. She was diagnosed as otitis media with ANCA-associated vasculitis, and was treated with 30 mg/day prednisolone (PSL) for 6 months. Half a year ago, she presented with bilateral scleritis and elevated MPO-ANCA, and was treated with PSL 10 mg/day. However, she developed hoarseness, difficulty in swallowing, and was hospitalized. On admission, she had mouth drooping, positive curtain's sign, restricted movement of vocal cords, swallowing dysfunction, and elevated CRP and MPO-ANCA levels. Brain MRI showed the presence of soft tissue extending from the nasopharynx to the skull base, suggesting that strangulated cranial nerve damage was due to skull base lesions. Nasal mucosal biopsy was suggestive of GPA. PSL was increased to 60 mg/day, and IVCY was initiated. Although multiple cranial neuropathy resolved in 2 months, the improvement of the skull base lesions was limited. Neurological disorders in GPA are diverse, and skull-base lesions should be included in the differential diagnosis, as suggested by the present case report.

## P1-256

**The utility of monocyte fraction in the differentiation between adult-onset Still's disease and intravascular large B-cell lymphoma**

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Conflict of interest: None

[Objective] This study aimed to investigate factors that are useful in the differentiation between adult-onset Still's disease (AOSD) and intravascular large B-cell lymphoma (IVLBCL) in the diagnosis of the fever of unknown origins. [Methods] We conducted a retrospective observational study of patients diagnosed with AOSD or IVLBCL at our hospital from April 1, 2010, to July 19, 2022. AOSD was diagnosed based on the Yamaguchi criteria, and IVLBCL was confirmed through pathological findings. Statistical analysis was performed using R. Exploratory analysis was conducted to identify factors useful in discriminating between the two groups. For identified factors, discrimination ability was assessed using ROC curves and AUC. Sensitivity and specificity were calculated at the threshold determined by the Youden method. The statistical significance level was set at 0.05. [Results] This study included 30 patients of AOSD and 14 patients of IVLBCL. Focusing on monocyte fraction (%), an AUC of 0.8143 (95% CI 0.6465-0.9821) demonstrated high discrimination ability. When the threshold was set at 9.650%, sensitivity was 64.3%, and specificity was 96.7%. [Conclusions] The findings showed that a monocyte fraction (%) greater than 9.650 suggests IVLBCL in differentiation between AOSD and IVLBCL.

## P1-257

**Three cases of HTLV-I positive hemophagocytic syndrome with recurrence in a short period of time and requiring differentiation from adult-onset Still's disease**

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Conflict of interest: None

We have experienced three cases of suspected adult-onset Still's disease (AOSD) with recurrent hemophagocytic syndrome (HPS) and positive HTLV-I. [Case 1] A 76-year-old woman. She had been visiting the hospital for polymyalgia rheumatica. In April X, she developed fever and elevation of hepatobiliary enzymes. She showed hyperferritinemia and bone marrow biopsy showed hemophagocytosis. Cytomegalovirus antigenemia was found, and the diagnosis of virus-related HPS was made, and the patient was treated with antiviral drugs. [Case 2] A 73-year-old man. He was hospitalized for fever. Antimicrobial therapy was started, but fever, thrombocytopenia, and hyperferritinemia were observed. Bone marrow biopsy showed hemophagocytosis, which was diagnosed as HPS, and the patient was started on prednisolone (PSL). [Case 3] A 69-year-old woman was admitted to the hospital with fever, erythema, and elevated liver enzymes. Bone marrow biopsy showed hemophagocytosis, which was diagnosed as HPS, and the patient was treated with PSL and cyclosporine, but relapsed 6 months after discharge. The three patients were positive for HTLV-I antibodies, and the fact that they relapsed within a short period of time may have contributed to the pathogenesis of the disease.

## P1-258

**A rare case of Adult Still's Disease complicated by Sjögren's syndrome in which serum Leucine-Rich Alpha-2 Glycoprotein (LRG) levels were useful in evaluating in evaluating treatment response**

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Conflict of interest: None

Adult Onset Still's Disease (AOSD) is a systemic inflammatory disease of unknown cause, and its coexistence with other collagen diseases is rare. AOSD lacks specific markers. Leucine-rich alpha 2 glycoprotein (LRG) is expected to be useful as an inflammatory biomarker. We experienced a rare case of AOSD complicated by Sjögren's syndrome, in which LRG levels were useful for disease evaluation. The patient lasting high fever was referred to our department and was admitted. After admission, the patient had a spike fever, sore throat, arthralgia, high white blood cell count, high ferritin level, and elevated LDH. CT scan also revealed bilateral lung ground glass opacities and hepatosplenomegaly. Anti-SS-A/Ro antibody were positive and a lip biopsy showed findings consistent with Sjögren's syndrome. However, during the course, cervical lymph node swelling, systemic rash appeared and ferritin level elevated to 57321 ng/ml. Based on the Yamaguchi classification criteria, she was diagnosed as AOSD and treated with high-dose glucocorticoid. Serum IL-6, IL-18, and LRG values were all elevated before the start of treatment, and they tended to decrease according to therapeutic intervention.

## P1-259

**Analysis of cytokine profiles and their dynamics in AOSD patients in our hospital**

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Conflict of interest: None

[Objective] The cytokine storm has been implicated in the pathogenesis of Adult Still's Disease (AOSD), and IL-18 in particular is useful for the diagnosis of AOSD. However, there are few reports on the relationship between cytokine dynamics and prognosis in AOSD. The aim of this study is to investigate the cytokine profiles in AOSD and how they change with treatment. [Methods] We collected clinical data of patients whose IL-18 was measured and investigated the relationship between their cytokine profile and their clinical characteristics. The clinical data examined included the medications used during the clinical course or whether they flared during our follow-up. [Results] Most of the patients with elevated IL-18 were diagnosed with AOSD or SLE (systemic lupus erythematosus). In our study, patients diagnosed with AOSD tended to have higher IL-18 levels than those diagnosed with SLE, suggesting that IL-18 may be useful for diagnosing AOSD. In addition, elevated IL-18 levels were sometimes found before patients became aware of symptoms or before clinicians found other blood test abnormalities, suggesting that IL-18 may be a predictor of disease relapse. [Conclusions] IL-18 may be useful not only in the diagnosis of AOSD but also in the prediction of disease flares.

## P1-260

**A case of remission with simple plasma exchange and baricitinib for refractory adult-onset Still's disease**

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Conflict of interest: None

A 71-year-old woman. She was transferred to our hospital in late May X with a fever in the 38°C range, knee arthritis, salmon pink rash, leukocytosis, elevated liver enzymes, and high ferritin (Fer) level. Fer rose to the 30,000 ng/mL range and pancytopenia developed. Bone marrow biopsy was negative for hematologic malignancy, and a diagnosis of adult-onset Still's disease was made, with hypercytokinemia centered on IL-18 30,2086 pg/mL, consistent with macrophage activation syndrome (MAS) complications. she was started on PSL 1 mg/kg/day after pulse therapy but after poor improvement, TCZ was introduced, and MAS worsened and she responded poorly to IVIg, high-dose PSL and CyA, requiring plasma exchange (PE). After 7 PE sessions, Baricitinib (Bari) was introduced and allowing PSL reduction. The efficacy of PE in AOSD/MAS has been reported in a few cases. In this case, we performed a longitudinal cytokine analysis, which showed that PE is useful for improving hypercytokinemia, with a decrease in IL-18 to about 3000 pg/mL after PE. There are reports that JAK inhibitors are useful in refractory AOSD. In this case, PSL was reduced with the combination of Bari and she passed without a re-elevation of IL-18. Further case series, including cytokine analysis, are desirable.

## P1-261

**A refractory case of adult-onset Still's disease with cytomegalovirus-triggered macrophage activation syndrome successfully treated with plasma exchange**

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Conflict of interest: None

A 74-year-old female was administered in our hospital with fever, sore throat, joint pain, skin rash, liver dysfunction, and elevated CRP, WBC, and ferritin (6,445 ng/mL). PSL 70 mg (1 mg/kg) was started under the diagnosis of adult-onset Still's disease (AOSD), but fever persisted and the elevation of CRP and ferritin continued, even after the combination use of CyA and MTX. Introduction of TCZ resolved fever, while ferritin increased to 18,249 ng/mL, concurrent with thrombocytopenia. As bone marrow assessment revealed hemophagocytosis, which was diagnosed as macrophage activation syndrome (MAS), steroid pulse therapy was performed. At the same time, GCV was started to CMV antigenemia. Despite various therapeutic attempts including a repeated steroid pulse, liposomal steroid, TCZ, and tacrolimus, ferritin surged to 89,420 ng/mL and CMV antigenemia escalated simultaneously. Three sessions of plasma exchange for the refractory MAS, and high dose of GCV more than 10 mg/kg/day for treatment-resistant CMV antigenemia were conducted, resulting in a reduction in ferritin and CMV antigen. Continuous therapy with PSL, TCZ and tacrolimus allowed a steroid taper afterward. We report a case of AOSD in which plasma exchange was effective for MAS considered to be induced by CMV infection.

## P1-262

**A case of unknown origin developed the second trimester of pregnancy, where adult-onset Still's disease was suspected and treated**

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Conflict of interest: None

[Objective] Adult-onset Still's disease (AOSD) is treated with high-dose steroids, immunosuppressive drugs, and biologics, but there are limited drugs available for use in pregnant patients. We experienced a case of AOSD occurring during the second trimester of pregnancy. We report this case with some literature review. [Methods] A case report [Results] The patient is 35 years old woman 26 weeks pregnant. We considered AOSD based on physical findings, erythema on both upper and lower limbs and myalgia in the lower limbs, and blood test results. We used methylprednisolone, cyclosporine and tocilizumab. We got improvement and no worsening of AOSD was observed. During prednisolone tapering, cytomegalovirus (CMV) has appeared in the blood, and then disappeared and no obvious malformation were observed in the fetus. [Conclusions] While also inducing remission of primary disease, we considered it important to reduce the dose of steroids early from the perspective of pregnancy complications.

## P1-263

**Adult Still's disease complicated with severe hepatic and renal failure after COVID-19: A case report**

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Conflict of interest: None

[Case] A 56-year, previously healthy man presented at his local doctor with a two-day history of fever and sore throat. He was diagnosed with COVID-19 but the fever persisted, and admitted to another hospital with generalized myalgia and difficulty in movement 3 days later. The condition persisted despite the antibiotic administration, and he was transferred to our department on suspicion of collagen vascular disease. We diagnosed him with adult Still's disease (ASD). He was in stable condition with steroid pulse and prednisolone (PSL) 60 mg thereafter, but he had a fever after the second administration of tocilizumab (TCZ). His blood test showed deterioration on the 22nd day of hospitalization: AST 7,289 IU/L, ALT 7,423 IU/L, Cre 2.8 mg/dL, T-Bil 4.2 mg/dL, and Ferritin (FER) 275,118 ng/mL. We diagnosed him with macrophage activation syndrome (MAS), treated with steroid pulse, dexamethasone palmitate (DP-SAL), and cyclosporine (CYA), also with plasma exchange and continuous hemodiafiltration as in fulminant hepatitis, and he recovered. [Conclusions] We suggest: FER may play an essential role in inflammation in ASD, and COVID-19 might have contributed to the increased risk of developing ASD. In addition, the early administration of TCZ during treatment for ASD may have caused MAS.

## P1-264

**A case of adult-onset Still's disease complicated by severe anemia**

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Conflict of interest: None

[Case] Male in his 20s [Chief complaint] Dyspnea [Present medical history] He had been aware of multiple arthralgias since X-1, and had fever since Y-3, X. When he visited his doctor in Y-1, he was found to be anemic with Hb 6.3 g/dL. He was referred him to our department in Y to investigate collagen disease because of high inflammatory response with WBC 13700/μL, CRP 15.97 mg/dL, and ferritin 15570 ng/mL. He was admitted to our hospital because his anemia had progressed to Hb 2.0 g/dL on blood test. A bone marrow biopsy was performed on the first day, and the smear showed no evidence of hemophagocytosis by macrophages and erythroblastocytes were decreased. On the fourth day, acute pericarditis developed and colchicine 0.5 mg/day was started. He was treated with prednisolone 60 mg/day on the 22nd day as adult-onset Still's disease because of elevated ferritin levels. He responded to steroid treatment, and his anemia reached Hb 9.4 g/dL on the 33rd day. Prednisolone was tapered off and tocilizumab 380 mg (8 mg/kg) was started on the 35th day, and on the 41st day the patient was discharged from hospital. This is a case of adult-onset Still's disease complicated with severe anemia, and we had a difficult time investigating the cause of the anemia.

## P1-265

**A case of adult Still's disease that did well with oral treatment alone in combination with methotrexate and glucocorticoid**

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Conflict of interest: None

[Case] 34 years, Female [Chief complaint] fever [Current medical history] She was admitted to previous hospital with pancytopenia, elevated hepatobiliary enzymes and CRP, hepatosplenomegaly, and enlarged para-aortic lymph nodes. The blood sample findings were improved with antipyretic and analgesic medication, so she was discharged. After discharge, joint pain and frequent erythema on the trunk and legs were appeared, and hepatomegaly persisted on CT scan when she returned to the hospital. Adult Still's disease (ASD) was suspected, and she referred to us. She was admitted to our department. After Prednisolone (PSL) 1 mg/kg/day therapy started, joint pain remains but she refused continuous intravenous infusion therapy. She was discharged from our hospital and was reducing PSL basis on methotrexate (MTX) therapy while raising her children. [Clinical Significance] The current Japanese guidelines of ASD says while MTX combination therapy is useful for ASD, it must be used with caution because it's not covered by insurance for ASD. Alternatively, Tocilizumab therapy is also limited to slow intravenous infusion for ASD. In this case, rheumatoid arthritis was thought be presented, and the patient wished oral therapy became a good outcome.

## P1-266

**A case of severe adult-onset Still's disease that was successfully treated with dexamethasone palmitate**

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Conflict of interest: None

[Case] A 31-year-old woman was admitted to a hospital with fever and sore throat. Skin rash and lymphadenopathy accompanied with elevation of serum LDH and soluble interleukin-2 receptor were emerged. Pancytopenia and elevated serum ferritin were observed, and bone marrow examination revealed hemophagocytosis with abnormal cells suspicious of malignant lymphoma (ML). We started chemotherapy under the tentative diagnosis of ML. Subsequently pathological diagnosis of bone marrow and skin biopsies revealed no findings of hematopoietic tumors. We finally diagnosed her with adult onset Still's disease (AOSD) and macrophage activation syndrome (MAS) in accordance with Yamaguchi's criteria. Prednisolone (PSL) up to 90 mg/day, steroid pulse, tocilizumab and cyclosporine were challenged, but her fever was not dissolved. We considered MAS is the primary for her symptoms, we finally selected dexamethasone palmitate (DP). Her fever was resolved and she had no flare, and PSL taper was successfully done. [Clinical Significance] We experienced a patient with treatment resistant AOSD. DP is a lipid emulsion combined with dexamethasone suggested its unique feature of delivery to macrophages and high efficacy against MAS. DP may be a treatment option for AOSD patients with PSL resistance.

## P1-267

**Patients with Systemic Juvenile Idiopathic Arthritis Complicated with Sacroiliitis and Ulcerative Colitis During the Course of the Disease**

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Conflict of interest: None

[Case] A 20-year-old female. She was diagnosed with sJIA at the age of 8. She had difficulty in inducing remission, and TCZ was introduced. At the age of 16, she complained of back pain, and MRI showed high-signal areas in bilateral sacroiliac joints, which improved with the addition of methotrexate. At the age of 19, she relapsed with MAS-like findings and sacroiliitis. She was switched from TCZ to canakinumab CAN, and her systemic inflammation improved. Three months after the CAN change, abdominal pain, diarrhea, and bloody stools were observed. She had no anemia, mildly elevated erythrocyte sedimentation rate, and high level of fecal calprotectin. Colonoscopy revealed coarse erythema of the mucosa from the rectum to the descending colon. Based on the histopathological findings, the patient was considered to have complicated UC. Mesalazine was started, and gastrointestinal symptoms became mild, but the mucosa did not heal. Arthritis flared up at the same time, and CAN was changed to a JAK inhibitor. [Clinical Significance] The patient had difficulty in selecting a treatment for sacroiliitis, UC, arthritis, and a history of MAS. It is controversial whether UC is an incidental complication or not, or whether IL-1 inhibitors have an effect.

## P1-268

**A case of juvenile psoriatic arthritis in which arthritis preceded skin manifestations and it took 4 years until the diagnosis**

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Conflict of interest: None

In 80% of psoriatic arthritis (PsA), rash precedes arthritis. In childhood, arthritis precedes rash more frequently than in adults. Nail abnormalities and dactylitis occur in 70% and 50% of PsA, respectively. We report a case of a female with juvenile PsA (j-PsA), having been preceded by sacroiliitis and enthesitis, diagnosed 4 years later only when psoriatic eruptions appeared, without nail abnormalities and dactylitis. [Case] 18-year-old female with no family history of psoriasis. She developed pains of predominantly lower extremities at night at age 14 and visited our hospital because of worsening pains and difficulty in sleeping at age 16. She was diagnosed with juvenile spondyloarthritis from left sacroiliitis revealed by MRI scan. The treatment with MTX and ADA relieved her pains, but vaccination and other triggers worsened the pains in the neck. At age 18, she was hospitalized for dysphagia and respiratory distress due to pains and was diagnosed with j-PsA from psoriatic rash on the occipital area. Switching to SEC made her back pains improve, but 10 months later she was hospitalized again for poor oral intake due to pains and was switched to GUS. [Clinical Significance] We report a case of j-PsA which was preceded by arthritis, and in which management of pains was difficult.

## P1-269

**A case of a 13-year-old girl with peripheral polyarticular arthritis and psoriasis-like rash**

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Conflict of interest: None

The case is a 13-year-old girl. The patient developed pain in the PIP joints of both hands, both shoulders, both elbows, and both ankle joints, which gradually worsened, and was referred to our department. Swelling and pain in movement were observed in PIP joints of the fingers on both sides, wrist joints on both sides, and ankle joints on both sides, pain in movement in the 3rd MP joint of the left hand, both knee joints, right elbow joint, and both shoulder joints. Blood tests showed that CRP was 4.56 mg/dl, MMP-3 was 289.1 ng/ml, and RF, anti-CCP antibody, and antinuclear antibody were negative. Wrist joint MRI and ancle joint MRI showed joint synovitis and tenosynovitis. When the skin rash was confirmed, an erythematous plaque with scales and punctate eschars extending to the hair covering was found on the back of the neck hidden by the hair. Pathological findings at the same site showed dermatitis similar to psoriasis. Although psoriatic arthritis is not common in children, it is considered essential to check the skin findings when treating children with arthritis, and in the case of girls, careful examination was considered necessary as hair areas are often hidden.

## P1-270

**Clinical features of uveitis in children and adolescents**

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Conflict of interest: None

[Introduction] Clinical features of idiopathic and rheumatic disease associated with uveitis in children remain unknown. [Methods] We retrospectively analyzed clinical features of the patients with uveitis under 18 years old who had visited our hospital from April 2020 to March 2023. [Result] Sixty-eight patients were included in this study. 48 were females and 20 were males. Median age at the diagnosis of uveitis was 10 years (min 2 - max 16). Background diseases were tubulointerstitial nephritis and uveitis syndrome (13), juvenile idiopathic arthritis (12), Bechet disease (5), Sarcoidosis (4), and 30 were idiopathic uveitis. Duration from onset of background diseases to the onset of uveitis were 0 year (min 0 - max 11). All patients were treated with topical glucocorticoid (GC) and 28 withsystemic GC. 41 patients were treated with MTX, 4 with tacrolimus, 1 with CyA, 5 with MMF, 3 with MZR, 29 with biologics. Complete remission was achieved in 42 patients. However, ophthalmological complications including cataract and iris adhesion were observed in 32 patients. 21 patients underwent ophthalmic surgery. [Conclusion] Immunosuppressive drugs and biologics were effective, however some patients underwent surgery. Careful observation with ophthalmologist is important.

## P1-271

**A pediatric case of anti-AQP4 antibody/anti-NMDR antibody-positive CNS inflammatory demyelinating disease complicated by recurrent pulmonary lesions**

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Conflict of interest: None

We report the case of a 9-year-old girl with anti-aquaporin 4 antibody (AQP4-Ab)/anti-N-methyl-D-aspartate receptor antibody (NMDAR-Ab)-positive demyelinating disease and recurrent pulmonary lesions. She presented with somnolence and seizures, and head MRI revealed extensive cerebellar and midbrain lesions. Brain biopsy sshowed demyelinating disease. AQP4-Ab and NMDAR-Ab were detected in the blood and spinal fluid, respectively. Chest CT revealed a small left lung lesion. After methylprednisolone pulse therapy, her neurological symptoms rapidly improved, and AQP4-Ab level decreased. However, her AQP4-Ab level rebounded after post-therapy corticosteroid dose reduction. Despite no new clinical symptoms or head MRI changes, a new left lung lesion appeared on chest CT. Satralizumab therapy led to decreased AQP4-Ab levels and stabilization of the neurological lesions, but the lung lesions repeatedly recurred. Paraneoplastic neurological syndrome or autoimmune complications should be considered in patients with AQP4-Ab- or NMDAR-Ab-positive disease and lung lesions, but they were absent in this case. Although a case of AQP4-Ab-positive neuromyelitis optica with transient interstitial pulmonary lesions has been reported, additional analysis is necessary.

## P1-272

**Experience with two cases of pediatric systemic lupus erythematosus with suppressed disease activity after COVID-19 infection**

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Conflict of interest: None

Introduction: We report two cases in which COVID-19 reduced the disease activity of systemic lupus erythematosus (SLE). Case 1: A 14-year-old boy with 10-year-old-onset SLE. Hypocomplementemia (CH50 23.0 IU/ml, C4 11 mg/dl), elevated anti-dsDNA antibody (343 IU/ml), proteinuria and hematuria were observed under treatment with prednisolone, mycophenolate mofetil, hydroxychloroquine and tacrolimus. He had COVID-19 at the same time as the relapse. After healing of COVID-19, the maintenance therapy was not changed, but no relapse was observed (anti-dsDNA antibody 23 IU/ml). Case 2: A 16-year-old girl with 12-year-old-onset SLE. She had hypocomplementemia (CH50 20.2 IU/ml, C416 mg/dl) and elevated anti-dsDNA antibodies (148 IU/ml) due to medication non-adherence. After COVID-19 infection, the medication non-adherence situation did not change, but complement elevation (CH50 33.9 IU/ml, C4 28 mg/dl) and decreased anti-dsDNA antibodies (22 IU/ml). Clinical Significance: COVID-19 has been a worldwide problem for autoimmune overreaction such as cytokine storm, but it is also said to suppress the production of interferon. From the two cases we experienced, the immunosuppressive mechanism of SARS-CoV-2 may shed light on some of the pathogenesis of SLE.

## P1-273

**A case of lupus nephritis with negative antinuclear antibody but positive IgM-type anti-ds-DNA antibody**

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Conflict of interest: None

[Objective] In Japan, IgM-type anti-ds-DNA antibody is rarely measured in clinical practice. We report a case of lupus nephritis with positive only for IgM-type anti-ds-DNA antibody, and discuss the significance of this antibody. [Methods] A 6-year-old girl. She presented with complaint of fever, proteinuria, renal dysfunction, low complement, leukopenia, and thrombocytopenia. She was transferred to our hospital, because her urinary protein and Cr level were increased. She was negative for antinuclear antibodies and SLE-specific antibodies, but positive for IgM-type anti-ds-DNA antibody. [Results] After performing a renal biopsy, she underwent two courses of steroid pulse therapy as induction therapy, which resulted in normalization of renal function and negative urinary protein. We diagnosed lupus nephritis Class IV-G (A). The initial therapy was followed by PSL, MMF, and HCQ, and the dose of PSL was reduced after one month. [Conclusion] It has been reported that IgM-type anti-ds-DNA antibody is protective against lupus nephritis and inversely correlate with the disease activity of nephritis. In this case, the serum antibody level was decreased as the disease stabilized, suggesting that the significance of this antibody may be different from previous reports.

## P1-274

**Clinical characteristics of patients with rheumatoid arthritis developed iatrogenic immunodeficiency-associated lymphoproliferative disease related with methotrexate**

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Conflict of interest: None

[Objective] To examine clinical characteristics of patients with rheumatoid arthritis (RA) developed iatrogenic immunodeficiency-associated lymphoproliferative disease (IIA-LPD) related with methotrexate (MTX) in our hospital. [Methods] We identified clinical characteristics of patients treated with MTX for RA and developed IIA-LPD from Oct. 2013 to Aug. 2022. [Results] 14 patients (10 females, 4 males) were identified. Ages at onset of RA and LPD were 62.2±14.3, 72.5±5.6. Disease duration of RA until onset of LPD was 10.2±10.8 years. Duration of treatment with MTX was 7.2±4.1 years, and dosage of MTX was 7.3±2.8 mg/week. We diagnosed 1 case clinically and 13 cases pathologically (9 DLBCL, 4 Hodgkin's lymphoma) as LPD. Lymphocyte count was 825.5±563.9/μl and increased to 1351.1±831.1/μl after MTX discontinuation. 3 cases went into spontaneous remission, and 11 cases required chemotherapy. The values of sIL-2R were 1102±668U/ml in the spontaneous remission group and 6665±8845U/ml in the chemotherapy group, and there is a statistically significant difference between the two groups. [Conclusions] Lymphocyte counts were decreased at onset of LPD and increased after MTX discontinuation. It was also suggested patients with low levels of sIL-2R were likely to go into spontaneous remission.

## P1-276

**A case of rheumatoid arthritis with diffuse lung disease immediately after treatment for pancytopenia**

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Conflict of interest: Yes

A 78-year-old man developed multiple joint pains since November X-1, and was referred to our hospital in February X. Although anti-CCP antibodies and rheumatoid factor were negative, the patient was diagnosed as rheumatoid arthritis due to high titer of CRP and multiple swollen and painful joints, and treatment with Prednisolone (PSL) and methotrexate (MTX) 6 mg/week was started. In June of X, he visited our emergency center because of fever and oral pain. In addition to a fever and severe erosion of the oral mucosa, he had WBC 800/μL, 14% neutrophils, so he was admitted to the hospital as febrile neutropenia due to MTX. After admission, she presented with pancytopenia, which improved with folic acid rescue, G-CSF, antibiotics, and blood transfusion. However, on the 9th day of hospitalization, the patient developed hypoxemia and required high-flow oxygen. Imaging studies were suspicious for interstitial pneumonia, and he was started on methyl prednisolone pulse therapy and made a recovery. Conclusion: The pancytopenia in the present case may have been caused by MTX, but the subsequent pulmonary injury may have been caused by various factors including other drugs, viruses, and so on, in addition to MTX.

## P1-277

**A case of malignant nephrosclerosis with thrombotic microangiopathy (TMA) in the course of tacrolimus (TAC) treatment for dermatomyositis**

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Conflict of interest: None

[Case] A 59-year-old woman was diagnosed with dermatomyositis 10 years ago, and treated with PSL. She had TAC added 8 years ago. Her serum Cr began to rise 4 months ago, so TAC was reduced 2 months ago. One week ago, serum Cr worsened to 3.22 mg/dL, so TAC was discontinued, and PSL was increased from 8 mg to 20 mg. But serum Cr worsened to 5.84 mg/dL and her blood pressure rose to 226/130 mmHg, and TMA was suspected, so she was admitted. ADAMTS13 activity didn't decrease, and blood pressure stabilized with hypotension, but her renal failure progressed and she was started on hemodialysis 4 days later. After 35 days, she underwent renal biopsy, which revealed glomerular collapse and sclerosis, interstitial fibrosis and tubular atrophy in 40% of the area, with marked narrowing of the vascular lumen in some areas, consistent with malignant nephrosclerosis and secondary TMA. The findings were consistent with malignant nephrosclerosis and secondary TMA. Immunofluorescent staining was negative, and she was uncomplicated with systemic scleroderma, suggesting a TAC-induced condition. [Clinical Significance] Although TAC is often used in routine practice for dermatomyositis, reports of sudden renal failure due to malignant nephrosclerosis during the course of TAC administration are rare.

## P1-278

**Transient malignant lymphomatous state induced by strengthened toxic effect of MTX by PCP**

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Conflict of interest: None

A 71 y.o. female RA patient came to our hospital because of fever and dyspnea. She had been treated by MTX and TAK for 15 years without AE. At march of certain year, she was diagnosed to have pneumonia at nearest clinic but detail was unknown. Next visit to our hospital she had still pneumonia on Xp and Labo Data showed positive CRP, pancytopenia and positive β-D-glucan. And positive test for PCP by BALF, she suffered from PCP. On admission, her CBC test showed 9% of atypical lymphocyte, which showed lymphomatous nuclear abnormality. Elevated IL2R and positive monoclonal band of Immunoglobulin gene rearrangement reconfirmed she had malignant lymphoma but atypical lymphocyte and hematological abnormality disappeared in the course of PCP recovery. We considered that the case was transient malignant lymphomatous state which was caused by strengthened toxic effect of MTX by PCP.

## P1-279

**A case of progressive multifocal leukoencephalopathy (PML) during treatment for rheumatoid arthritis (RA)**

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Conflict of interest: None

This is a case of the man, no special notes regarding medical history or family history. At the age of 30, he was diagnosed with RA and was treated with bucillamine, salazosulfapyridine, and 5 mg of PSL, but control of his RA activity was difficult. At the age of 36, methotrexate 6 mg/week was added. Since then, he has been put under RA control and retired from the PSL at the age of 41. From around December X (at the age of 51), he gradually developed aphasia. PML could not be ruled out for him, and the methotrexate was discontinued from February, X+1. JCV-DNA was detected by PCR from the brain biopsy sample tissue, and the diagnosis of PML was confirmed. Symptoms peaked in late April, and clinical symptoms slowly improved thereafter. On August, he had high RA disease activity with DAS28 and SDAI. Drug-induced PML has been reported to occur with immunosuppressants, biological agents, csDMARDs, and steroids, so drug therapy was judged to be difficult. RA treatments for him were a brace for the left knee joint which was seen to be progressing on images, rehabilitation therapy, and oral NSAIDs. In the future, we will evaluate his ADL and consider surgical treatments as an option. In the treatment of RA in patient with PML, RA treatment strategies other than drug therapy are required.

## P1-280

**Investigation of factors involved in nintedanib-induced gastrointestinal disorders**

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Conflict of interest: None

[Objective] Nintedanib (NTB) is a tyrosine kinase inhibitor that frequently causes diarrhea. Although the mechanism of diarrhea is due to inhibition of VEGF receptors on intestinal epithelial cells, this remains unclear. To investigate the factors that influence the gastrointestinal disorders caused by NTB. [Methods] A retrospective single center study was performed in 14 patients with connective tissue disease treated with NTB. Background and concomitant drugs, adverse events, KL-6, and effects after NTB dose reduction were surveyed. [Results] Patients were consisted of 7 SSc, 3 PM/DM, 2 MCTD, 2 RA patients. Mean age was 59.6 years. Mean disease duration was 7.7 years. Concomitant drugs were steroids (10), tacrolimus (7), MMF (4), vasodilators (7), endothelin receptor antagonists (2), and phosphodiesterase 5 inhibitors (2). Mean %VC was 66.4%, KL-6 1314.4 U/ml before NTB treatment. 12 patients required dose reduction or withdrawal. Adverse events were diarrhea (9), hepatotoxicity (2), epigastric pain (1), and pneumatosis cystoides intestinalis (2). KL-6 was reduced to 91.5% at 6 months after NTB dose reduction. [Conclusions] Factors related to NTB-induced gastrointestinal disorders could not be clarified. NTB should be continued if diarrhea symptoms are tolerable.

## P1-281

**A case of RA with suspected septic arthritis after total knee arthroplasty**

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Conflict of interest: None

(Purpose) When arthritis occurs in the patients with rheumatoid arthritis (RA) after total joint arthroplasty, it is difficult to diagnose infection and RA flare. We report a case of RA with suspected septic arthritis after total knee arthroplasty. (Case) 83-year-old female had been diagnosed with RA more than 5 years ago. She underwent total knee arthroplasty (TKA) with a diagnosis of right knee osteoarthritis. Four years postoperatively, swelling and pain around the knee had been worsened and she visited our institution. Arthropuncture was performed and 15 ml of cloudy joint fluid was aspirated. Bacterial culture was negative, but the blood test data showed elevated CRP 6.50. Periprosthetic joint infection (PJI) after TKA was suspected, we performed arthroscopic synovectomy. A biopsy of the synovial membrane suggesting RA. After surgery, the patient was treated with Iguratimod and disease activity was controlled. (Clinical Significance) Postoperative infection, flare of rheumatoid arthritis, gout, pseudogout, prosthesis wear, metal allergy, and nonspecific arthritis are differential causes of arthritis flare-ups after arthroplasty, but it is difficult to rule out PJI. RA flare should be considered as a differential disease in post-TKA knee arthritis.

## P1-282

**Pyoderma gangrenosum developing during the course of rheumatoid arthritis: two cases**

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Conflict of interest: None

[Case 1] A 71-year-old man, who had treatment for rheumatoid arthritis (RA) with prednisolone (PSL) and methotrexate (MTX) for 9 months, developed cutaneous ulcers on the right lower leg. He was admitted to our hospital because of no improvement despite being treated with PSL at 30 mg daily. Skin biopsy revealed mononuclear cell infiltration and hypervascularization in the dermis and subcutaneous tissues, leading to pyoderma gangrenosum (PG) diagnosis. Topical therapy, along with orally administration of PSL and MTX, resulted in remission. [Case 2] A 73-year-old woman with a 16-year history of RA had treated with bucillamine, PSL, and MTX. She developed a painful nodule on the left lower leg 3 months ago. The biopsy of the nodule demonstrated a rheumatoid nodule. However, ulcers developed on the biopsy site during one month. The histology of the ulcer involvement revealed extensive necrosis along with infiltration of inflammatory cells and histiocytes in subcutaneous tissue, resulting in the diagnosis of PG. Cutaneous lesion was improved after administering PSL at 30 mg daily and tacrolimus. [Conclusion] RA can be the representative underlying disease causing PG known as an ulcerative and neutrophilic dermatosis.

## P1-283

**A case of Juvenile Idiopathic Arthritis (JIA) who had reconstructive surgeries and rehabilitation for functional disturbances of boutonniere deformity and swan-neck deformity**

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Conflict of interest: None

[Objectives & Clinical Significance] We aim to report on the importance of surgery and rehabilitation which contributed to improving grasping function and continuing work for the JIA patient. [Case] A female in her forties who was diagnosed as having JIA at the age of 15. An office worker. Although the disease activity was maintained at low levels due to ETN, dexterity impairment became evident due to boutonniere deformity of the thumb, swan-neck deformity of the index finger, and boutonniere deformity with PIP joint contracture in the middle, ring, and little fingers of the left hand. Eight months after the introduction of ETN, grip strength of left hand was 58 mmHg, and Disabilities of the Arm, Shoulder and Hand (DASH) score was 54.2. The Simple Test for Evaluating Hand Function (STEF) score was 80. Functional reconstruction surgeries were conducted on her left hand. Dynamic splints were used to expand joint range of motion and programs for various object manipulations were performed. Three months after surgery, grip strength was 56 mmHg. DASH score was 43.3, STEF score improved to 96. She returned to work at 6 months after surgery. [Conclusion] It was suggested that complex finger deformities can be improved through drug therapy and specialized surgery, rehabilitation programs.

## P1-284

**Trial of a foot and ankle exercise program for patients with forefoot deformities due to rheumatoid arthritis: a case report**

Itsuki Urayama[1], Yuya Takakubo[1,2], Suran Yang[2], Yoshihiro Wanezaki[2], Masashi Aso[2], Jun Nagai[2], Miyuki Murakawa[1], Masaki Ishikawa[1], Michiaki Takagi[1,2]
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Conflict of interest: None

[Background] The strengthening and stretching for rheumatoid arthritis of the foot and ankle (Foot-ex) was designed as an exercise program for the foot and ankle to strengthen the foot's intrinsic muscles. [Case Report] 70 years old, female. The patient had RA 15 years ago and is on medication. Two months ago, the patient developed pain in the left 2nd MTP joint while gait. At initial evaluation, DAS28-CRP was 1.1, HVA (left, right) was 14.8°,7.5°, M1M2 was 10.6°, 10.5°, M1M5 was 30.6°, 31.1°. Arch ratio (AR) was 16.7%, 14.6%. The bilateral forefoot forces (BFF) were 8.3 kg. Self-Administered Foot Evaluation Questionnaire (SAFE-Q) scored pain and pain-related 77 points, physical function and daily living 86, social functioning 96, shoe-related 75, and general health and well-being 75. Physical therapy provided Foot-ex and self-exercise coaching. One month later, AR improved 14.6%, 12.5%. BFF enhanced to 11.1 kg. SAFE-Q increased to 85, 98, 100, 100, and 95, respectively. [Discussion] Foot-ex may have increased the strength of the foot's intrinsic muscles and corrected the medial longitudinal arch. Moreover, it appears to have reduced pain and improved quality of life in patients with RA. [Clinical Implications] Foot-ex for forefoot deformities caused by RA may decrease pain during gait.

## P1-285

**A case of an elderly patient with rheumatoid arthritis refractory to disuse prophylaxis during hospitalization**

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Conflict of interest: None

[Introduction] We report a case of an elderly patient with rheumatoid arthritis (RA) who was hospitalized for revision surgery of total elbow arthroplasty (TEA). Physical therapy was started before the surgery. However, delirium and refusal of rehabilitation were observed during her hospitalization. [Case] The patient was a woman at age 80s. Her duration of RA was 49 years. She received the primary TEA for her left elbow 27 years ago. On X day, left revision surgery of TEA was performed, and physical therapy was resumed the next day after the surgery. her delirium was observed around X+2 weeks and refused to participate in prolonged physical therapy. Therefore, the focus of physiotherapy was switched from improving her gait ability and balance exercises. The patient was discharged to her home after X+3 weeks due to her disturbing behavior and difficulty continuing hospitalization, however, her gait ability with a cane was maintained at the discharge from the hospital. [Conclusion] When physical therapy is difficult to continue due to delirium or other reasons, it seems to be important to change the focus and aim of physical therapy. [Clinical Significance] Accumulation of reports on difficult-to-treat RA with delirium or other reasons will be helpful and important for the future.

## P1-286

**Introduction of Hand Exercises for Hospitalized Patients with Rheumatoid Arthritis ~ A case report using the SARAH Exercise ~**

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Conflict of interest: None

[Introduction] We have introduced the SARAH (Strengthening and Stretching for Rheumatoid Arthritis of the Hand) modified exercise program (SARAH-modified ExP) for hospitalized patients with rheumatoid arthritis (RA). [Case Report] The patient was a 70's female. Her duration of RA was 39 years. She was induced SARAH-modified ExP in her hospitalization for arthroplasty with resection of her forefoot deformity. [Rehabilitation treatment course] The loading amount and the overall goal were determined on the seventh after the foot surgery. The hand therapist proceeded with the program by intervening five times a week. The therapist checked the exercise diary daily and shared her status and information with the patient. When the patient was discharged from the hospital 35 days after the forefoot surgery, her grip strength improved from 176/170 mmHg (right/left) to 250/262 mmHg (right/left), and she was able to squeeze as a goal in her SARAH-modified ExP. [Discussion] The introduction of SARAH-modified ExP enabled the patient and therapist to share a common goal and rehabilitation treatment plan, and to continue the program which improved disuse and movement ability. [Clinical Significance] Usefulness of SARAH exercise.

## P2-001

**The Status of Rheumatoid Arthritis Patients from the Onset of Disease to Diagnosis and Treatment**

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Conflict of interest: None

[Objective] The purpose of this study was to investigate the status of consultations, from the manifestation of RA symptoms to consultation, diagnosis, and treatment. [Methods] The subjects were 1599 patients (average age 67.9±13.1 years) who were undergoing RA treatment at our department or other hospitals. Age at onset of RA, painful joints, time from onset of symptoms to hospital visit, first hospital/clinical department, whether the patient was an RA specialist, name of diagnosis at first visit, period until diagnosis of RA, and RA A questionnaire survey was conducted regarding the department in which the patient was diagnosed, whether the patient was a specialist in RA, the length of time until the first RA drug was prescribed, and the prescribing doctor. [Results] The age at onset of RA was 54.4 ± 15.2 years old. Painful joints were mostly fingers and wrists. rice field. Time from first visit to diagnosis of RA was 7 days (median) for RA specialists, 28 days (median) for non-specialists., time from diagnosis to medication was 1 day (median) for RA specialists, 3 days (median) for non-specialists. [Conclusions] The majority of patients saw an orthopedic surgeon, and the time from diagnosis to initiation of treatment was shorter for patients who saw an RA specialist.

## P2-002

**Risk Factors for Chronic Kidney Disease in Rheumatoid Arthritis: a single-center, retrospective study**

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Conflict of interest: None

[Objective] We aimed to investigate the risk factors for CKD in RA at our institution. [Methods] We retrospectively evaluated RA patients treated at Fukui Prefectural Hospital for more than five years between April 2002 and October 2023. We compared CKD progression group (eGFR <60) with non-CKD progression group (eGFR ≧ 60). [Results] Of 88 patients, 33 patients were males, 55 patients were females. 45 patients had CKD progression. The mean±SD age was 58.4±13.6 years and the mean±SD observation period was 3393±1731 days. In univariate analysis, CKD progression group had older, hypertension, dyslipidemia, higher CRP, higher RF, and proteinuria. Kaplan-Meier method with the stratified log-rank test showed that CKD progression group had CRP > 0.5 mg/dL, proteinuria, use of prednisolone (PSL) at first visit, and diabetes. Cox regression analyses showed older, use of PSL at first visit, proteinuria at first visit, and diabetes were significant effects on CKD progression. [Conclu-

sion] Even after excluding the effects of common CKD risk factors, proteinuria was an independent risk factor. It suggested that regular urinalysis could help predict CKD progression. Furthermore, Avoiding administering PSL for pain management may be a strategy to prevent CKD.

## P2-003

**5-year survival rate and its risk factors in RA patients with onset of RA at age 75 years or older**

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Conflict of interest: None

[Object] In recent years, elderly-onset RA patient has been increasing, and the number of RA patients with onset at age 75 or older has also been increasing. We investigated the 5-year survival rate and its associated factors in RA patients with onset at age 75 or older. [Methods] We retrospectively examined patients who were diagnosed with RA and started treatment at our hospital. Cox proportional hazards regression analysis were used for assessing the impact of comorbidities and data at baseline on increase in mortality. [Results] 67 patients were included, 23 males and 44 females, with a median age at onset of 81.5 years. Of these, 16 (23.9%) patients died during the observation period: 7 from senility, 5 from malignancy, 3 from infection, and 1 from cerebrovascular disease. The median age at death was 88.0 years, and the median time from the start of RA treatment to death was 37.5 months. Cox regression analysis suggested that pretreatment HAQDI (HR [95% CI] 2.021 [1.177-3.469]) ACPA (4.428 [1.581-12.399]) was significantly associated with 5-year survival [Conclusions] The 5-year survival rate for RA patients with onset at age 75 or older was 76.1%. The most common cause of death was senility. In our study, HAQDI and ACPA were found to affect survival for elderly-onset RA patient.

## P2-004

**Clinical characteristics of polymyalgia rheumatica in our hospital**

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Conflict of interest: None

[Objective] To characterize the clinical features of polymyalgia rheumatica (PMR) in our hospital. [Methods] We retrospectively identified patients who were diagnosed with or suspected of PMR in our hospital and analyzed the clinical features. [Results] 117 patients were identified (female: 75), with mean age of 74.0 year-old. 87 were finally diagnosed with PMR (definite PMR), whereas 25 were finally diagnosed with rheumatoid arthritis (14 initially suspected of PMR). Diagnosis was uncertain in 5 patients. Concomitant diagnoses of definite PMR patients were malignancy (n=10), osteoarthritis (n=5), giant cell arteritis (n=2), and crystal-induced arthritis (n=1). 43 patients with definite PMR received glucocorticoid monotherapy (median prednisolone dose 10 mg/day). Of these patients, only 2 patients withdrew from glucocorticoids within 1 year but 32 achieved prednisolone dose =< 5 mg/day. Drugs used other than glucocorticoids were IL-6 inhibitors (n=7), methotrexate (n=5), salazosulfapyridine (n=4), TNF inhibitors (n=3), and tacrolimus (n=2). [Conclusions] Glucocorticoid monotherapy rarely led to discontinuation of glucocorticoid within 1 year in our practice.

## P2-005

**Investigation of polymyalgia rheumatica outcome in our hospital**

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is an inflammatory disease of unknown cause. We report on the results of examining the outcomes in October 2023 of 70 PMR patients who have visited our hospital. [Method] All cases of PMR were checked by medical record contents and confirmed PMR cases, select cases with onset date up to October 2019. [Results] 28 male cases and 42 female cases. The average age of onset is 74.7 years. 25 patients are currently attending the hospital. 10 cases of death, 10 cases of patients changing to a doctor due to improvement, 9 cases of changing due to difficulty in visiting the hospital, 3 cases of changing for malignant tumor treatment, 13 cases of changing for other reasons. The age at the time of death was 78.8 years for men, 90.0 years for women and the cause of death was 1 death due to malignant tumor, 3 cases of aspiration pneumonia, 1 case of renal failure. There were 2 cases of septic shock, 1 case of acute epidural hematoma, 1 case of cerebral thrombosis, and 1 case of gastrointestinal bleeding. [Conclusion] Regarding patients who died during PMR treatment, compared to the average life expectancy of Japanese people in in2023, men had a slightly shorter life expectancy and women had a slightly longer life expectancy.

## P2-006

**A Retrospective Multicenter Study of the Efficacy and Safety of Early Triple-Drug Combination Therapy for Anti-MDA5 Antibody-Positive Dermatomyositis with ILD**

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Conflict of interest: None

[Objective] Evaluating the efficacy and safety of early dispersal combination therapy for Anti-MDA5 Antibody-Positive Dermatomyositis with ILD. [Methods] We conducted a retrospective study of patients diagnosed between April 2014 and October 2023 for up to 3 years. [Results] (1) The total number of patients was 58, mean age 55.0 years, and 32 patients had severe disease at the start of treatment. (2) 54 patients were treated with triple therapy, and 43 patients were treated with triple therapy at an early stage. Within 2 years of treatment, 31 patients achieved therapeutic remission, but 8 patients relapsed. Death occurred in 13 patients, and 84.6% of them died of respiratory failure. The safety and efficacy of early triple therapy were investigated. The time to remission tended to be shorter in the early triple therapy group. There was no difference in relapse rate, number of adverse events per case, and mortality rate. The same study was conducted in patients with mild disease. There was no difference in time to remission, number of adverse events per case, and mortality rate between patients treated with early triple therapy and those not treated with triple therapy. [Conclusions] These results suggest the merit of early triple therapy even in mild cases.

## P2-007

**Four cases of anti-MDA5 antibody-positive dermatomyositis with interstitial pneumonia treated with Tofacitinib or plasma exchange therapy**

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Conflict of interest: None

[Background] The prognosis of Anti-MDA5 antibody-positive dermatomyositis with interstitial pneumonia is poor. Combination treatment of glucocorticoids, tacrolimus (TAC), and cyclophosphamide (IVCY) is recommended. Recently, JAK inhibitor and plasma exchange have been reported to be effective. We report four cases of tofacitinib (TOF) and plas-

ma exchange (PE) therapy for this disease between July 2020 and August 2023 at our institution. All patients were treated with triple therapy. [Case 1] 81-year-old woman. Skin ulcers developed and CT finding was exacerbated. After switching from TAC and IVCY to TOF, improved lung changes. [Case 2] 62-year-old woman. Interstitial pneumonia did not progress but developed leukopenia. Then changed IVCY to TOF. The leukopenia improved and there was no exacerbation of interstitial pneumonia. [Case 3] 66-year-old woman. Due to respiratory failure, PE and TOF was started. But she died. [Case 4] 59-year-old male. Due to exacerbation of interstitial pneumonia, PE was added and switched from IVCY to TOF. Then chest finding was improved. [Conclusion] Extensive lung involvement and hypoxemia at the start of treatment may be a poor prognostic factor. It is also suggested that TOF may avoid adverse effects of IVCY.

## P2-008

**A case of advanced interstitial pneumonia associated with anti-MDA5 antibody-positive dermatomyositis treated with a triple combination of steroid, tacrolimus, and cyclophosphamide plus baricitinib**

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Higashi-Hiroshima Memorial Hospital

Conflict of interest: None

[Background] Anti-MDA5 antibody-positive dermatomyositis is associated with a high rate of rapidly progressive interstitial pneumonia. We report a case in which the progression of interstitial pneumonia was controlled by the introduction of baricitinib in addition to the three-drug combination therapy. [Case] 44 year old male. He was admitted to the hospital for suspected dermatomyositis due to heliotrope rash, Gottron's sign, high creatine kinase level, and some frosted shadows at the base of the lungs. He was given high-dose intravenous methylprednisolone. The patient was found to be positive for anti-MDA5 antibodies and was started on oral tacrolimus and intermittent intravenous cyclophosphamide. A chest CT scan to determine treatment intensification showed increased interstitial pneumonia, and started on concomitant baricitinib. At approximately 6 weeks after initiation of therapy showed no significant progression of interstitial pneumonia. [Discussion] Although not all dermatomyositis-associated pulmonary disorders with positive anti-MDA5 antibodies are fatal, there are cases in which the disease progresses rapidly from mild to diffuse lung injury. In this case, the addition of baricitinib to the three-drug combination therapy was suggested to increase the survival rate.

## P2-009

**Opportunistic infections caused by triple combination therapy + Janus kinase inhibitor for anti-MDA5 antibody-positive dermatomyositis**

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Conflict of interest: None

[Background] Anti-MDA5 antibody-positive dermatomyositis (anti-MDA5 DM) has poor prognosis and is sometimes resistant to treatment. Janus kinase (JAK) inhibitors may be added to combination therapy (high-dose corticosteroid therapy, calcineurin inhibition, intermittent intravenous cyclophosphamide therapy), but the side effects of infection are more of a concern. [Case] 69-year-old male. Anti-MDA5 DM was treated with triple combination therapy and tofacitinib. Some improvement was achieved, but he repeatedly developed cytomegalovirus (CMV) infection, bacterial pneumonia, and fungal infections, and finally died. [Discussion] Including our case, 12 cases of combination of four drugs for anti-MDA5 DM have been reported. Concomitant infections included 5 bacterial infection, 11 CMV infection, 4 varicella zoster, and 4 fungal infection. For patients who require a combination of four drugs, robust measures against opportunistic infections are required, and regular monitoring for CMV and fungal infections should be performed, as well as preemptive treatment should be considered. Vaccinations such as varicella-zoster may also be helpful. [Conclusion] Strict measures against opportunistic infections are necessary when using triple-drug combination therapy and JAK inhibitors for anti-MDA5 DM.

## P2-010

**A case of anti-MDA5 antibody-positive dermatomyositis complicated with trichosporonemia and cytomegalovirusemia**

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Conflict of interest: None

[Case] A 81-year-old female with a history of anti-MDA5 antibody-positive dermatomyositis, who had been in a stable condition with prednisolone, tacrolimus, baricitinib, and intravenous cyclophosphamide therapy, presented with general malaise at a follow-up. Laboratory tests revealed elevated ferritin levels and thrombocytopenia. Chest CT showed slight worsening of nodular shadows in the right upper lobe, but other ground-glass opacities remained stable. Cytomegalovirus (CMV) infection was primarily suspected due to the recent decrease in anti-MDA5 antibody levels. On admission, she received oral valganciclovir (CMV antigenemia was positive). 3 days later, yeast-like fungi were detected in blood culture and empirical treatment with micafungin was started. *Trichosporon asahii* was identified over the next 2 days, and antifungal therapy was changed to voriconazole. However, exacerbation of pneumonitis was subsequently observed. She was treated, as a progression of anti-MDA5 antibody-positive dermatomyositis, with IV methylprednisolone and immunoglobulin therapy, concurrently with treatment of the infections. [Discussion] Trichosporonemia is a rare disease which has been reported in only two cases in rheumatic diseases. We report a case with a review of the literature.

## P2-011

**Anti-MDA5 antibody-positive rapidly progressive interstitial pneumonia with effective plasmapheresis therapy despite JAK inhibitor combination therapy ineffectiveness: A case study**

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Conflict of interest: None

A patient presenting with heliotrope rush, Gottron's sign, and dyspnea presented ground-glass opacities and positive anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5). Consequently, the patients was diagnosed with rapid progressive interstitial-lung disease (RP-ILD), relevant to clinically amyopathic dermatomyositis (CADM). She was treated with combination of prednisolone, cyclophosphamide, and tacrolimus, but the ILD progressed. Accordingly, tofacitinib was administered to combat ILD. However, her respiratory symptoms continuously worsened, despite the oral tofacitinib administration. The anti-MDA5 titer also remained continuously high in spite of the administration of multiple immunosuppressant drugs. Thus, we initiated plasmapheresis therapy for anti-MDA5 depletion and inflammatory cytokine reduction. Dyspnea improved and oxygenation decreased. Anti-MDA5 disappeared immediately plasmapheresis administration; however, it returned. Thus, we administered rituximab for the anti-MDA5 production reduction.

## P2-012

**Two cases of anti-MDA5 antibody-positive amyotic dermatomyositis accompanied by rapidly progressive interstitial lung disease treated with extracorporeal membrane oxygenation**

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Conflict of interest: None

[Case 1] 58-year-old male. One month ago, fever and finger joint pain appeared. Gottron's sign, palmar erythema, and multiple GGO were observed. The patient was diagnosed with CADM/RP-ILD based on lung lesions without muscle weakness and positive anti-MDA5 antibody. De-

spite early administration of high-dose steroids, IVCY, TAC, and PE, hypoxemia worsened. He was placed on ventilator support on the 33rd day and VV-ECMO was started on the 41st day, but died on the 88th day of illness. [Case 2] A 55-year-old man was diagnosed with CADM/ILD in X-3 years without muscle weakness based on heliotrope rash, mechanic's hands, and positive anti-MDA5 antibody. In year X, acute respiratory distress developed, and CT showed worsening of ILD. High-dose steroids were started on the first day of illness, and the patient was managed with a ventilator, but hypoxemia rapidly progressed. VV-ECMO was started on the same day, but the patient died of respiratory failure on the 14th day. [consideration] Anti-MDA5 antibody-positive CADM/RP-ILD has a poor prognosis. If it is difficult to manage with a ventilator, introduction of ECMO is considered, but there is little experience. We report on two cases in which ECMO was introduced although life could not be saved, with a review of the literature.

## P2-013

**A life-saving case of anti-MDA5 antibody-positive dermatomyositis due to advanced age and many poor prognosis factors**

Yuki Mizutani, Kyoko Takano, Shuntaro Kojima, Kahori Oshima, Takakazu Hasegawa, Masao Katayama
National Hospital Organization Nagoya Medical Center

Conflict of interest: None

[Case] 72 F [Chief complaint] Skin rash, breathing difficulty on exertion [Current medical history] She has had joint pain since September 20XX. She has had a skin rash on her elbows and buttocks. She had been experiencing shortness. In October, she experienced malaise and dyspnea, and there was erythema on the neck, fingers of both hands, and both knees. Chest CT revealed active interstitial pneumonia (IP), and asymptomatic dermatomyositis (CADM) was suspected. She was diagnosed with rapidly progressive IP, and it was started with steroid pulses, tacrolimus, and cyclophosphamide (IVCY). It was positive for anti-MDA5 antibodies. Treatment was started, but a new symptoms developed, so steroid pulses were administered again, and plasma exchange was performed. IVCY couldn't be performed due to bacteremia and pulmonary aspergillosis. After combined use of plasmapheresis, her symptoms is good. IVCY was resumed. She required oxygen (4L rest, 5L activity). Oxygen administration was required due to exertion, so home oxygen was introduced. IVCY continued and home oxygen was no longer required during outpatient visits. [Clinical Significance] Treatment may be difficult for patients who are elderly and have many factors that contribute to poor prognosis. We report an important case.

## P2-014

**Three cases of anti MDA-5 antibody-positive amyopathic dermatomyositis with long-term follow-up**

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Conflict of interest: None

Anti-MDA5 antibody-positive dermatomyositis is known as a disease with poor prognosis. In this report, we describe three cases of anti-MDA-5 antibody-positive dermatomyositis that were amenable to long-term observation. The patients had cutaneous symptoms. Although these drugs improved the skin symptoms, long-term use of corticosteroids and immunosuppressive drugs was difficult because of aplastic anemia, frequent recurrent subcutaneous abscesses, and self-interruption due to mental instability. They experienced a temporary exacerbation of their symptoms during the reduction of corticosteroid dosage and self-interruption, but they were able to improve with repeated intensification of treatment and therapeutic intervention. Anti-MDA-5 antibodies decreased in all patients and became negative in one patient. Interstitial pneumonia has been non-progressive in all three patients for more than two years, and prednisolone has been successfully maintained at 15 mg or less. It is known that anti MDA-5 antibody-positive amyopathic dermatomyositis is associated with rapidly progressive interstitial pneumonia with a fatal clinical course. If antibody titers can be lowered by immunosuppressive therapy, a good prognosis may be expected.

## P2-015

**A Case Report of Anti-MDA-5 Antibody-Positive Dermatomyositis Achieving Spontaneous Remission Upon Pregnancy-Triggered Treatment Discontinuation**

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Conflict of interest: None

A woman in her 30s with joint pain and hand rash for three months was referred to our hospital. She exhibited periungual erythema, Gottron's papules, and the reverse Gottron's sign on her fingers. Blood tests showed liver issues, but muscle enzyme levels were normal. Notably, her anti-MDA-5 antibodies (Abs) were significantly elevated (>150 IU/mL). Pulmonary findings included bilateral lower lung base ground-glass opacities, and pulmonary function tests revealed a restrictive pattern (%VC 73.7%). A skin biopsy showed the finding comparable with dermatomyositis, leading to a diagnosis of amyopathic dermatomyositis. Treatment with prednisolone (30 mg/day) and tacrolimus (3 mg/day) began in February of year X, effectively treating her rash and joint pain. In August of year X+1, while on PSL 8 mg/day and TAC 6 mg/day, she developed muscle pain and tremors attributed to TAC. She transitioned to mycophenolate mofetil (MMF). PSL was gradually tapered and discontinued, and she continued on MMF monotherapy. She ceased MMF in July of year X+3, confirmed her pregnancy in September, gave birth to her first child in year X+4, and her second child in year X+5. Presently, her anti-MDA-5 Abs remain weakly positive, with no progression of interstitial lung disease without treatment.

## P2-016

**A case of interstitial pneumonia complicated by anti-MDA5 antibody-positive dermatomyositis that relapsed after a re-elevation of anti-MDA5 antibody titer**

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Conflict of interest: None

[Case] X-7 months, 67-year-old man developed interstitial pneumonia complicated by dermatomyositis with positive anti-MDA5 antibody, and was started on prednisolone (PSL) 60 mg, tacrolimus (TAC) 5 mg, cyclophosphamide pulse therapy (IVCY) 500 mg, plasma exchange therapy (PE). After improvement of skin rash and interstitial shadows and decrease of anti-MDA5 antibody titer (from 5465 to 1500 index), the patient was discharged at X-5 months. At X-1 week, when PSL dose was reduced to 12.5 mg, anti-MDA5 antibody titer increased to 2000 index. The patient was re-hospitalized at X due to flare-up of skin rash and worsening of interstitial shadows on CT scan. After admission, he was treated with mPSL pulse therapy (1000 mg for 3 days), and PSL was increased to 60 mg, and PE was performed. One month after admission, anti-MDA5 antibody titer decreased to 500 index, improvement in interstitial shadows was observed. [Clinical Significance] Anti-MDA5 antibody titer reflects disease status and is a predictor of relapse, but actual cases of relapse are rare. In the present case, the patient experienced a relapse due to a re-elevation of the titer during PSL reduction. The possibility of relapse should be kept in mind when anti-MDA5 antibody titer rises again.

## P2-017

**A Case of Anti-MDA5 Antibody-Positive Interstitial Pneumonia with Dermatomyositis Showing Elevated Serum Calprotectin Levels During Acute Exacerbation of Interstitial Lung Disease**

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Conflict of interest: None

Case: A 78 y.o. female was admitted to our hospital with fever, fatigue. She was diagnosed as dermatomyositis-interstitial lung disease (DM-ILD) and Anti-MDA-5 antibody positive rapid progressive-ILD (RP-ILD) based on clinical signs including reverse Gottron's signs, elevated serum CK and KL-6 levels, a positive anti-MDA-5 antibody test, and the presence of ILD on chest HRCT. Triple combination therapy, including prednisolone, cyclosporine, intravenous cyclophosphamide (IVCY), and tofacitinib (TOF) were initiated as remission induction therapy. Despite this, her condition deteriorated on X+7 day, indicated by increases in ferritin and KL-6 levels and extension of ground-glass opacities on HRCT. Therefore, plasma exchange (PE) was initiated, and RP-ILD temporarily improved on X+30 day. However, ILD progressively worsened, unesposive to immunosuppressive therapy, and she died due to acute exacerbation on X+71 day. Calprotectin levels decreased after remission induction therapy, but were elevated with the acute exacerbation of ILD. Clinical Implications: We present a case of anti-MDA-5 antibody-positive DM-ILD that was unresponsive to triple combination therapy with a JAK-i and PE. This shows the potential utility of serum calprotectin level as a marker of disease activity.

## P2-018

**Japan's first two cases of localized eosinophilic myositis presenting in the upper extremities**

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Conflict of interest: None

[Case 1] 33-year-old female. She presented with swelling and warmth in her left forearm that began 7 months prior to her visit. Eosinophilia was observed, and an MRI showed high signal intensity on STIR imaging in the left flexor digitorum muscle and its fascia. Localized eosinophilic myositis was diagnosed. After prednisolone 50 mg/day was initiated, the myositis responded well to the therapy. [Case 2] 32-year-old female. She presented with swelling and pain in her right forearm that started 6 days before her visit. Elevated creatine kinase levels (7500 U/L) and eosinophilia were observed. T2-weighted MRI revealed hyperintensity in the right forearm muscles and fascia. Localized eosinophilic myositis was diagnosed. Prednisolone 40 mg/day led to favorable clinical course thereafter. [Clinical Significance] This is the first report of localized eosinophilic myositis of the upper extremities in Japan. In these two cases, their lesions in the upper extremities were adjacent to neurovascular bundles, which made muscle biopsy highly risky. Therefore, the diagnoses were made based only on physical examination findings, blood tests results, and MRI imaging. The treatment with high dose glucocorticoid has been successful in both cases.

## P2-019

**A case of idiopathic hypereosinophilic syndrome who presented with multiple cerebral infarctions and myositis**

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Conflict of interest: None

The case is 31-year-old male who was admitted for progressive dysphagia and weakness in limbs. Blood tests revealed a significant increase in eosinophils, muscle enzymes, and inflammatory markers. Head MRI showed multiple watershed infarctions. Transesophageal echocardiography and contrast-enhanced CT did not indicate any obvious embolic source. Because of the rapid progression of symptoms, steroid pulse followed with prednisolone at 1 mg/kg was initiated upon admission. In addition, continuous intravenous heparin was administered for the cerebral infarctions. After starting treatment, eosinophil counts, inflammatory markers, and muscle enzymes quickly normalized, and there was a significant improvement in swallowing function and limb muscle strength within a few days. Although various autoantibodies, including myositis-specific antibodies, were negative, the electromyogram showed myogenic changes, and muscle pathology findings were consistent with the course of myositis. Regarding eosinophilia, no hematologic malignancy, or other underlying causes, including vasculitis, were identified. Thus, the patient was diagnosed as idiopathic HES. Here, we report a case of HES with characteristic symptoms of myositis, which emphasizes the importance of prompt treatment initiation.

## P2-020

**A case of focal gastrocnemius myositis responding to nerve root block**

Taro Kamemura[1], Hirotaka Tsuno[1], Ayaka Ito[1], Mayuka Tanimura[1], Rikuo Hase[1], Yusuke Yano[1], Shinichi Nogi[1], Toshihiro Matsui[2]
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Conflict of interest: None

[Case] 54-year-old male. He had been experiencing discomfort in his left lower leg for about 30 years, and pain in the left lower leg had increased for the past 8 years. He visited several hospitals, mainly orthopedic surgeons, but the cause was unknown. He came to our hospital for further close examination. At the time of consultation, there were no abnormalities including autoantibodies, except for a serum creatinine kinase level of 329 IU/l. A needle electromyography scan showed neurogenic changes. MRI showed spinal canal stenosis and bilateral S1 nerve root compression, and T2-weighted images showed high signal in bilateral gastrocnemius muscles. Since the symptoms were atypical for lumbar spinal canal stenosis, we suspected left gastrocnemius focal myositis due to S1 radiculopathy, and performed a left S1 nerve root block in the orthopedic surgery department. The patient's Visual Analog Scale (VAS) improved from 10 to 3 during 2 days, and his serum creatine kinase level improved to within the reference range. Future treatment may include repeat left S1 nerve root block or surgical treatment. [Clinical Significance] Surgical treatment may be an effective option for focal myositis caused by S1 radiculopathy.

## P2-021

**A case of dermatomyositis after induction of immune checkpoint inhibitors for advanced small cell lung cancer**

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Conflict of interest: None

<Case>A 70-year-old male. He was referred to the Department of Respiratory Medicine of our hospital with a chief complaint of abnormal chest shadows. After examinations, he was diagnosed as advanced small cell lung cancer (cT4N2M1a, stage IVA). He was started on primary chemotherapy with carboplatin, etoposide, and atezolizumab. On day 33 of treatment, he presented to our hospital with complaints of limb weakness, dysphagia, and erythema. He was admitted to the hospital for suspected immune-related adverse events (irAEs). An examination revealed positive anti-TIF1-γ antibody, and electromyography, skin biopsy and muscle biopsy were consistent with dermatomyositis. He was treated with steroid pulse therapy followed by prednisolone 50 mg and high-dose intravenous immunoglobulin started. Although there was temporary improvement, the tumor grew slowly, and on day 138 of chemotherapy, he died of respiratory failure. <Conclusion>With the recent expansion of the indication for immune checkpoint inhibitors (ICIs), irAE should always be kept in mind in patients treated with ICIs. Differentiating between irAE or anti-TIF1-γ antibody-positive dermatomyositis was difficult, but it is important to understand the characteristics of each, and we report this case.

## P2-022

**A case of polymyositis complicated by severe myasthenia gravis crisis during treatment**

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Conflict of interest: None

(Case) A 73-year-old woman with 20-year history of Graves' disease was admitted to our hospital for detailed evaluation of bilateral thigh swelling and persistently hyperCKemia (3544 IU/mL) for 6 months, with normal thyroid function and negative myositis-related autoantibody. T2-weighted MRI showed high-signal areas in bilateral thigh, and quadriceps biopsy showed lymphocytic infiltration around muscle fibers and positive anti-OJ antibody (Ab). Polymyositis (PM) was diagnosed. During admission, she developed ptosis, repetitive stimulation testing revealed median and facial nerve warning, and positive anti-AchR Ab led to the diagnosis of complication of myasthenia gravis (MG). Initiation of prednisolone (PSL) 20 mg did not resolve the hyperCKemia, and treatment was intensified to PSL 40 mg with tacrolimus 3 mg. However, 2 days later she developed dysarthria and dysphagia, leading to the diagnosis of MG crisis, and plasma exchange and IVIg therapy were initiated. CK was normalized and she was discharged 16 days after the MG crisis. (Clinical significance) This case was a PM complicated with MG, which is not always easy to distinguish since inflammatory myositis has also been reported in MG. In cases of PM complicated with MG, glycocorticoid dosage should be prioritized according to MG.

## P2-023

**A case of autoimmune encephalitis during the course of polymyositis responding to rituximab**

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Conflict of interest: None

79-year-old woman. During treatment for Hashimoto's disease and primary biliary cholangitis, subacute progressive muscle weakness, positive anti-ARS antibody, elevated myogenic enzymes and inflammatory response and muscle biopsy results led to the diagnosis of polymyositis. After starting treatment, poor communication and hypoactivity developed. Head MRI showed a high-signal area around the lateral ventricles, slowing of the EEG and elevated protein in the spinal fluid. Suspecting metabolic encephalopathy, drug-induced encephalopathy and infection, no improvement was observed with treatment of these diseases. The diagnosis of autoimmune encephalitis was made. The patient showed no obvious improvement after steroid pulse therapy or high-dose immunoglobulin therapy, but after rituximab administration, improvement in MMSE score and improvement in arousal state were observed. Autoimmune encephalitis is a CNS disease that develops via immunological mechanisms. In this case, the diagnosis was difficult due to the wide range of differentiation, but clear improvement was observed after rituximab administration. The possibility of autoimmune encephalitis should be considered when acute or subacute CNS involvement is observed during the course of an autoimmune disease.

## P2-024

**A survey of patients at our newly opened "Outpatient clinic for Fever of Unknown Origin**

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Conflict of interest: None

[Objective] The COVID-19 pandemic also increased the need to treat patients with fever, especially fever of unknown origin (FUO). In 2021, we opened an outpatient clinic for patients with FUO. We report the clinical characteristics, diagnosis, and course of patients who visited our outpatient clinic for FUO. [Methods] We retrospectively analyzed patients with FUO who visited our hospital from November 2021 to September 2023. [Results] Thirty-nine patients were included. The mean age was 60.5±24.0 years, 56.4% were female, and 13 patients (33.3%) met the classic definition of FUO. Nineteen patients (48.7%) were hospitalized. Six patients (15.4%) were finally diagnosed with rheumatic diseases (2 with rheumatoid arthritis, 2 with polymyalgia rheumatica, 1 with rheumatoid pleurisy, and one with SAPHO syndrome). Infectious diseases accounted for 17 (43.6%), malignant tumors for 3 (7.7%), and other diseases for 4 (10.3%). We could not make a final diagnosis in 10 cases; however, all eight cases resolved spontaneously except for two cases lost to follow-up. [Conclusions] During the COVID-19 pandemic, many patients with FUO were diagnosed with common febrile illnesses such as infectious diseases. we need to take them into account in our examination of FUO.

## P2-025

**Analysis of pain sensation in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The purpose of this study was to compare the patient backgrounds of a group of patients who feel pain strongly when injecting subcutaneous injections and a group of patients who do not feel pain very much. [Methods] A questionnaire on injection pain was administered to 119 patients receiving etanercept 50 mg pen formulation subcutaneously. Based on Injection Pain Score, patients were divided into two groups for analysis: 1: Painless group (20 patients from the lowest pain score) and 2: Painful group (20 patients from the highest pain score) [Results] In 119 patients (28 males, 91 females), age 66.0 (56.0-72.5) years, there was a negative correlation between age and Injection Pain Score ($r= -0.332$, $p<0.001$). The Painful group was older. No statistically significant differences were detected in mean duration of disease, HAQ-DI, PainVAS for rheumatoid arthritis, number of swollen and tender joints, or general evaluation by patients and physicians. Only in the Painful group was there a positive correlation between Pain VAS and age ($r=0.64$, $p<0.005$). [Conclusions] Injection Pain Score was negatively correlated with age, while Pain VAS for rheumatoid arthritis was positively correlated with age in the Painful group. The results suggest that age may play a role in pain perception.

## P2-026

**Clinical investigation of 4 cases of polymyalgia rheumatica during the course of rheumatoid arthritis**

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Conflict of interest: None

[Objective] To clarify the characteristic features of cases with polymyalgia rheumatica (PMR) during the course of rheumatoid arthritis (RA). [Methods] Clinical features (symptoms and serological factors, treatment and disease activity, CRP levels at the onset of PMR and clinical course) were examined in four RA patients who developed PMR. [Results] At the onset of RA, swelling and tenderness of finger and knee joints were observed. Rheumatoid factors and anti-CCP antibodies were strongly positive. Iguratimod was used in all cases. Only one patient received metho-

trexate (MTX). Of the three cases not receiving MTX, two cases received 4 mg prednisolone (PSL) and one case received tocilizumab. At the onset of PMR, the mean SDAI was 5.0 and bilateral myalgia and high CRP levels were observed. There was no worsening of joint symptoms. The mean CRP levels increased from 0.24 mg/dL to 3.12 mg/dL. All cases received 10 mg PSL. Myalgia improved 2 days later in all cases and the mean CRP levels decreased to 0.11 mg/dL after starting PSL in a couple of weeks. [Conclusions] In PMR complicated with RA, bilateral myalgia and increased CRP without worsening of joint symptoms are thought to be characteristic features. Immediate treatment with PSL could be useful in those cases.

## P2-027

**A case of rheumatoid arthritis with autoimmune neutropenia**

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Conflict of interest: None

[Case Presentation] The case was a female who was diagnosed with rheumatoid arthritis and treated with methotrexate and prednisolone. The blood test showed neutropenia (229/μL) so methotrexate was discontinued. The situation continued, high transaminase and splenomegaly were discovered, so she consulted to our hospital. Several tests were performed but no diseases discovered without mild liver cirrhosis. She was hospitalized due to cellulitis at left lower limb and toes ulcer. The blood test also showed neutropenia (206/μL) so she was treated with repeated administration of G-CSF. Despite antibiotic treatment, left toes were partially necrotic so there were amputated and the wound improved. Since the anti-neutrophil antibody test was positive, the final diagnosis was autoimmune neutropenia. The neutrophil score was 1000/μL by treating with hydroxychloroquine and salazosulfapyridine [Discussion] The autoimmune neutropenia is rare disease and there isn't typical treatment. In this case, using G-CSF was not effective under infection. Cytopenia is common symptom during the treatment of rheumatoid arthritis. On the other hand, autoimmune neutropenia is rare, so it is important to diagnose them carefully.

## P2-028

**A case of adult-onset Still's disease (AOSD) during maintenance therapy for Eosinophilic Granulomatosis with Polyangiitis (EGPA)**

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Conflict of interest: None

[Case] A 76-year-old man was diagnosed with EGPA in X-11 due to bronchial asthma, eosinophilia, mononeuritis multiplex and positive MPO-ANCA, and started treatment with prednisolone (PSL) 30 mg. Benralizumab was also used for maintenance. In May X-2, he presented purpura in both lower legs, muscle weakness with distal muscle predominance, decreased pain/vibration sensation and eosinophilia, and received steroid pulse treatment with a diagnosis of EGPA relapse. He was transferred to our hospital and after 2 course of IVIG, started mepolizumab which got him into remission. PSL was decreased to 1 mg. In April X, he had a sore throat and elevated CRP which was refractory to antibiotics, had synovitis in the right wrist, intermittent fever in the 39°C range, mediastinal lymphadenopathy and a marked increase in ferritin to 12762 mg/dl. He was judged to have concurrent AOSD, as lymph node biopsy showed no evidence of malignancy and other diseases could be ruled out. With increased PSL, his symptoms relieved rapidly, and with small dose PSL and cyclosporine, he remains in remission. EGPA is susceptible to relapse and the use of mepolizumab is expected to reduce PSL and prevent relapse. This case was considered report-worthy as it showed concurrent AOSD, not the relapse of EGPA.

## P2-029

**Clinical results of arthroscopic rotator cuff repair in the patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The purpose of this study was to evaluate the clinical results of arthroscopic rotator cuff repair (ARCR) in the patients with rheumatoid arthritis (RA). [Methods] The RA group included 10 patients (3 males, 7 females), and the non-RA group included 151 patients (104 males, 47 females). We have evaluated JOA score after 6 and 12 months postoperatively and MRI findings. [Results] Their average age was 67.5 years old with RA group, and 65.2 years old with non-RA group. Six patients with RA group were treated with mettrexate, and one patient was treated with infliximab. There were no difference with age, disease duration of cuff tear, and cuff tear size between two groups, but female patients in RA patients was statistically more than non-RA group. JOA total score was statistically improved before and after surgery both of two groups. JOA functional score 6 months after surgery was 18.8 points in the non-RA group and 17.3 points in the RA group, which was significantly lower. There were no retear patients in RA group, and 14 patients in non-RA group. [Conclusions] The clinical results of ARCR for rotator cuff tears were as good in the RA group as in the non-RA group. However, muscle strength recovery was expected to be insufficient as early as 6 months after surgery.

## P2-030

**Two cases of distal humerus fracture in rheumatoid arthritis**

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Marunouchi Hospital

Conflict of interest: None

We performed operations in two cases of distal humerus fracture in rheumatoid arthritis. One case was 69 year-old female. Before operation elbow joint was destructive. Total elbow replacement (Nexel, Zimmer) was performed. After operation, patient complained of no pain. Range of motion was improved. Second case was 70 year-old female. Before operation elbow joint was destructive. Open reduction and internal fixation (ORIF) was performed using LCP plate and screw. Bone union of fracture site was achieved. Patient had no pain but ROM was not improved. [Conclusions] In distal humerus fracture with destructive elbow joint, total elbow replacement should be performed better than ORIF, if infection was not occurred after operation.

## P2-031

**Clinical results of linked total elbow arthroplasty for rheumatoid elbow**

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Conflict of interest: None

[Objective] Total Elbow Arthroplasty (TEA) is a useful surgical procedure to obtain a stable and pain-free joint for elbow joint destruction. We reviewed the cases in which consolidated TEA was performed at our department. [Methods] Thirty-two cases of linked-TEA performed at our department were included in the study. The range of motion, Mayo Elbow Performance Score (MEPS), and Quick Disabilities of Arm, Shoulder and Hand (DASH) score were evaluated before and after surgery. [Results] The mean MEPS score was 88, excellent in 20 cases, good in 11 cases, and fair in 1 case. Quick DASH scores ranged from 25 to a mean of 35.2. Seven patients had intraoperative fractures. No postoperative infection was observed. Postoperative ulnar nerve irritation was present in about half of the patients, but permanent ulnar neuropathy was present in two patients. Loosening of the artificial joint was observed in two patients, but no revision was required. [Conclusions] Our results show that linked TEA for RA

elbow can achieve good elbow function and pain relief in cases with severe bone loss and/or painful unstable joints.

## P2-032

**Clinical and radiographic outcomes of the Discovery total elbow arthroplasty for rheumatoid arthritis**

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Department of Orthopaedic Surgery, Osaka Rosai Hospital, Sakai, Osaka, Japan

Conflict of interest: None

[Objective] The purpose of this study was to examine the clinical and radiographical outcomes of Discovery total elbow arthroplasty (TEA) for patients with rheumatoid arthritis (RA). [Methods] 26 Discovery TEA (primary TEA: 22, revision TEA: 4) in 25 patients were examined clinically and radiographically. There were 22 women and 3 men with a mean age at operation of 68 years. The mean follow-up period was 66 months. [Results] The mean Mayo Elbow Performance Score was 94 points. The mean postoperative range of motion was 139°of flexion and -32°of extension. No patient underwent revision surgery due to infection or aseptic loosening. Four patients had intraoperative fractures and 10 had postoperative fractures. 3 non-unions were seen on the final radiographs. These non-union patients had no complaints and did not require additional surgery. [Conclusions] The mid-term clinical and radiographical outcomes of Discovery TEA for RA were good.

## P2-033

**Indications and limitations of total elbow arthroplasty by lateral para-olecranon approach**

Naoki Okubo[1,3], Ryo Oda[1,3], Daisaku Tokunaga[1], Kazuki Fujioka[2,3], Masataka Kohno[2], Yutaka Kawahito[2,3], Kenji Takahashi[1]
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Conflict of interest: None

[Objective] The purpose of this study was to investigate the applicability of the lateral para-olecranon approach for total elbow arthroplasty and to investigate postoperative triceps dysfunction. [Methods] Six patients who underwent TEA for RA were included in this study. The mean age was 67.3 ± 11.3 years, and the preoperative Larsen classification was Grade 4 in 4 cases and Grade 5 in 2. We investigated whether the lateral para-olecranon approach was feasible. Pre- and postoperative range of motion was measured, and postoperative subjective elbow extension muscle weakness was investigated. [Results] Four patients were operable with the lateral para-olecranon approach, all with preoperative Larsen grade 4, and two patients were converted to the Campbell approach, both with preoperative Larsen grade 5. Preoperative range of motion was 114.2 ± 15.0 degrees of flexion and -39.2 ± 22.0 degrees of extension; postoperative range of motion was 123.3 ± 10.3 degrees of flexion and -27.5 ± 14.4 degrees of extension. Postoperative triceps dysfunction was not observed in all patients. [Conclusions] Lateral para-olecranon approach is useful for TEA in patients with Larsen grade 4.

## P2-034

**Two cases of severe distal radial joint dysfunction treated with ulnar shortening osteotomy and joint reconstruction with the ZipTight system**

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Conflict of interest: None

[Objective] For severe distal radioulnar joint (DRUJ) deformity, the Sauve`-Kapandji procedure or the Darrach procedure are often chosen. In this study, we report the excellent results of ulnar shortening and Zimmer ZipTight reconstruction of the DRUJ for a severely DRUJ deformity. [Case 1] 80-year-old male. The patient developed extensor tendon rupture of the little finger and ring finger due to severe deformity of the DRUJ caused by osteoarthritis of the wrist. Xp showed that the ulnar head was dorsally dislocated and the ulnar variance (UV) was +10 mm. The ulnar shortening osteotomy of 8 mm was performed, and the DRUJ was reconstructed using a ZipTight. The ruptured tendon was sutured interlacing to the adjacent finger. Postoperatively, the pain disappeared completely, and the patient returned to work. [Case 2] 74-year-old woman. She had been treated with tocilizumab for rheumatoid arthritis, but developed joint destruction of the left wrist and extensor tendon rupture of the little finger. The ulnar shortening osteotomy of 5 mm was performed, and the DRUJ was reconstructed using a ZipTight. Postoperatively, the patient had no pain and movement of the fingers, wrist was excellent. [Conclusion] The above procedure may be an effective treatment option for a severely DRUJ deformity.

## P2-035

**The treatment and outcome of periprosthetic elbow fractures after unlinked total elbow arthroplasty for rheumatoid arthritis**

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Conflict of interest: None

[Objective] Periprosthetic fractures are becoming frequent due to aging population and growing number of total joint replacements. Total elbow arthroplasty (TEA) is broadly classified into unlinked and linked prosthesis. The purpose of the present study is to describe the management of periprosthetic fractures after unlinked prosthesis for rheumatoid arthritis (RA) at our institution. [Methods] 13 periprosthetic were occurred. 11 elbows underwent surgical treatment and 2 elbows underwent conservative treatment. We reviewed preoperative, immediate postoperative, and latest follow-up radiographs for all elbows to confirm the fracture type. We evaluated the range of motion and the Mayo Elbow Performance Score (MEPS) at the final follow-up. [Results] The mean age at the time of periprosthetic fracture was 72.3 years. 11 elbows had unions. Eight elbows had no history of trauma, and loosening was observed in all of them. [Conclusions] We suggested that fractures around the periprosthetic elbow fractures are caused by slight force in the loosening. It was considered important to perform revision before fracture even if loosening occurs. Revision and osteosynthesis after unlinked type are possible without bone grafting, and is considered useful for rheumatoid arthritis patients with low bone stock.

## P2-036

**Early aseptic loosening of the ulnar component in primary total elbow arthroplasty for bilateral humeral fractures with rheumatoid arthritis: a case report**

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Conflict of interest: None

We reported the case of a 71-year-old women with rheumatoid arthritis (RA) who injured bilateral humeral transcondylar fractures. We performed total elbow arthroplasty (TEA) using linked-type prosthesis. However, the ulner stem became loosed 1 year after surgery at left side. Because infection could not be ruled out, two stage revision surgery TEA using an appropriate cementing technique was performed. A brace was used to limit range of motion after revision TEA, so we instructed not to use their upper limbs too much. Radiographs taken 4 months after the revision sur-

gery at left side and 19 months after the primary surgery at right side showed no evidence of implant loosening. The causes of early loosening of TEA were thought to be poor bone quality and fragility, cement technique, and repeated heavy housework. TEA for distal humerus fractures in patients with RA is an excellent method for early pain relief and acquisition of range of motion. But due to the trauma, insufficient time for patient education and osteoporosis treatment, it was thought that adaptation should be judged carefully.

## P2-037

**Assessing Angles Between Metacarpal Head Rotational Axes and Dorsal Tangents of Neck in 2nd-5th Metacarpals**

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Conflict of interest: None

[Objectives] MCPA is often employed for rheumatoid ulnar drift cases. The Integra implant requires diagonal osteotomy to the metacarpal axis, leading to potential alignment issues with the metacarpal head's rotational axis. This can result in radial or ulnar flexion installation of the implant. Our study quantified and compared the 2-5DTA to understand these alignment dynamics. [Methods] We examined 29 hands (16 female, 13 male) using 3D-CT scans. The 2-5 metacarpal coordinate system was established from the metacarpal's longitudinal and rotational axes. The rotational axis connected the metacarpal head's distal and palmar ends. We evaluated the DCS 8 mm proximal from the distal end and analyzed the palmar radial angle differences in 2-5DTA using the Friedman test. [Results] The DCS displayed a predominant bimodal nature. The 2-5DTA measurements of 77.6°, 81.6°, 87.1°, and 91.2° showed significant reductions in the 2 and 3DTA compared to the 5DTA ($p<0.001$, $p<0.05$), and the 2 DTA compared to the 4DTA ($p<0.05$). [Conclusions] The 2/3DTA was notably smaller than the 5DTA, indicating the criticality of alignment precision during osteotomy with the Integra implant.

## P2-038

**Comparison of Diagnostic Evaluation by Internists and Orthopedic Surgeons for Extensor Tendon Rupture Predictors in Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] Predictors for tendon rupture, such as a dorsal subluxation of the ulnar head, the scallop sign, and carpal collapse in X-ray images, have been reported. The objective of this study is to assess whether these predictors hold equivalent diagnostic value when evaluated by rheumatologists and orthopedic surgeon. [Methods] The study included 92 cases that underwent hand joint reconstruction with tendon transfer or synovectomy between February 2008 and July 2021. Rheumatologists and orthopedic surgeons, each specializing in rheumatology, evaluated the presence of dorsal subluxation of the ulnar head, the scallop sign, and Carpal Collapse in preoperative X-ray images. The study investigated significant differences and inter-rater agreement between the tendon transfer group and the synovectomy group. [Results] Both of them observed significant differences in dorsal subluxation of the ulnar head and the scallop sign, but rheumatologists did not find a significant difference in Carpal Collapse. [Conclusions] If any of the three indicators, dorsal subluxation of the ulnar head, the scallop sign, or Carpal Collapse, is observed in hand joint X-rays, it is advisable to have a suspicion of tendon rupture and consider an early referral to orthopedic surgery.

## P2-039

**Reconstruction of side pinch by tendon graft for flexor of index finger and arthrodesis of the IP joint of the thumb for subcutaneous rupture of the flexor tendon of the index finger: a case report**

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Conflict of interest: None

[Purpose] Side pinch is the important function in the grasping. We report a case of reconstruction of side pinch by tendon graft for the flexor digitorum profundus (FDP) of the index finger and arthrodesis for the interphalangeal (IP) joint of the thumb for deformity caused by rheumatoid arthritis (RA). [Case] A 76-year-old woman, Stage 4 RA, was referred to us with a difficulty in the pinching. Flexion of the metacarpophalangeal (MP) joint of the index finger was 50° and thumb was 60°, while the IP joint of the thumb was hyperextended. CT image showed osteophyte on the palmar side of the STT joint, and the FDP of the index finger and flexor pollicis longus (FPL) had unclear continuity. Intraoperatively, the palmar capsule of the STT joint was ruptured, exposing the scaphoid, and the FDP of the index finger was ruptured. The scaphoid tubercle was excised, and a tendon graft was performed on the FDP. The IP joint of the thumb underwent arthrodesis. Postoperatively side pinch became possible, and satisfied. [Discussion] Tendon graft for FDP of the index finger improved activities of daily living by improving side pinch. Although subcutaneous rupture of the flexor tendon is rare, aggressive consideration of surgery in conjunction with a procedure on the thumb was necessary.

## P2-040

**A case report of single extensor tendon rupture of ring finger in rheumatoid arthritis**

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Conflict of interest: None

[Case] A 59-year-old female. She complained that she couldn't extend left ring finger a month ago without any traumatic episodes. She had no findings of arthritis and couldn't extend only her left ring finger. X-ray and computed tomography of her left hand showed bony destruction and partial fusion of carpal bones, and dorsal subluxation of ulnar head. Anti-cyclic citrullinated peptide antibodies were positive. She was diagnosed with extensor tendon rupture of the ring finger due to wrist disorders in rheumatoid arthritis, followed by reconstruction of extensor tendon. It was found that a tendon rupture of EDC IV and partial rupture of EDC III. Extensor digitorum communis of little finger was anomaly deficient and EDM was deviated to the palmar ulnar side. EDC IV was transferred to EDM, and EDC III was sutured to prevent for rupture. [Discussion] The rupture of extensor tendons in rheumatoid arthritis is caused by tendon weakening due to impaired blood circulation and friction between the dorsally subluxed ulnar head and tendon, and typically begin with the ulnar side fingers. In this case, EDM had no conexus intertendineus to the radial tendon because of anomaly deficient of EDC V and was deviated to the palmar ulnar side resulting to avoid the rupture.

## P2-041

**Examination of type I interferon-stimulated gene signature in the evaluation of systemic lupus erythematosus**

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Conflict of interest: None

[Objective] Type I interferon-stimulated gene (ISG) expression is an important pathological feature of systemic lupus erythematosus (SLE). This study aims to identify a type I ISG signature suitable for the evaluation of SLE. [Methods] Peripheral blood RNA sequencing was performed on 122 samples from 45 SLE patients and 20 samples from 20 healthy subjects. For the type I ISG signature, scores were calculated for previously reported ones and a comprehensive combination of 21 type I ISG genes (27,374 signatures), and the correlation with SLEDAI and changes before and after treatment were evaluated. [Results] The correlation between the previously reported type I ISG signature and SLEDAI ranged from significant (r=0.2647207, *P* =0.0041) to no correlation. Among the type I ISG signatures that were comprehensively created, there was a tendency for the smaller the number of selected genes, the higher the correlation with SLEDAI, and it was important that IFI27 and PLSCR1 were included. [Conclusions] When evaluating SLE using type I ISG signatures, the correlation with SLEDAI and post-treatment changes varied greatly depending on the genes and number of genes selected. In the future, it is necessary to verify the results with different datasets.

## P2-042

**Efficacy of Belimumab for Systemic Lupus Erythematosus in Our Hospital by Purpose of Use**

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Conflict of interest: None

[Purpose] In recent years, belimumab (BLM) has been used for a variety of purposes in the treatment of systemic lupus erythematosus (SLE). We summarize the use of BLM in our hospital and examine its efficacy and safety. [Methods] From December 2017 to June 2022, we analyzed the clinical course of 91 of 121 SLE patients who were initiated on BLM at our hospital and treated for at least 6 months. [Results] BLM was introduced in 60 cases for the purpose of symptom improvement, of which 48 cases were introduced for the purpose of GC weight loss, the largest number. The introduction of BLM in the process of GC reduction was effective, but anti-DNA antibody titers did not improve in the three cases in which the drug was inactivated. Induction in the early stage of remission induction resulted in activity control and no relapse, and SACQ cases showed slow improvement in blood tests and GC reduction effect. [Conclusion] The evidence for BLM in moderately active cases is abundant, but the induction effect was demonstrated especially in SACQ cases.

## P2-043

**New Strategic Development of RP105-Negative B Cell Targeted Therapy for Refractory Autoimmune Diseases by t-SNE**

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Conflict of interest: None

[Objective] B-cell-targeted therapies have been proposed for refractory autoimmune diseases. However, their efficacy is not complete. We perform B cell cluster analysis using t-SNE to identify real autoantibody-producing B cells and develop new therapeutic strategies against these cells. We will summarize the findings of RP105 so far. [Methods] We analyzed clusters of RP105-negative B cells derived from SLE. Based on these results, we will identify the abnormal B cell population involved in the pathogenesis and develop new therapeutic strategies. We also summarized the literature on RP105 as a basis for new drug development. [Results] In SLE, ratio of the plasmablasts was increased among the RP105-negative B cell fraction, with increased expression of BCMA and decreased BAFF-R and earlier loss of CXCR5. A preliminary cluster analysis of B cells using t-SNE showed that RP105-negative B cells consisted of more than 20 subsets beyond the 5 previously reported subsets. In the literature, RP105 plays important roles in various pathological conditions, including autoimmune diseases and malignancy. [Conclusions] Using t-SNE, we will perform a detailed cluster analysis of RP105-negative B cells to identify true pathological B cells and to develop novel therapeutic strategies.

## P2-044

**ADAM10 expressed on SLE CD8+ T cells is involved in shedding of FasL**

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Conflict of interest: None

[Objective] To clarify the role of ADAM10, a protease expressed on the cell membrane surface of immune cells, and its relevance to the pathogenesis of SLE. [Methods] (1) We analyzed the expression level of ADAM10 in PBMCs using FACS, and compared it between healthy controls (HC) and SLE patients. (2) PBMCs obtained from HC and SLE patients were treated with Ionomycin with or without ADAM10 inhibitor (GI254023X; GI) for 24 hours, and culture supernatants were collected and analyzed for the concentration of soluble TNFSF molecules using LEGENDplex™. (3) $CD8^+$ T cells and NK cells were sorted from PBMCs by FACS, and each cell was treated with Ionomycin, anti-CD3/CD28 antibody, and/or GI for 24 hours. In addition, the concentration of soluble FasL in the culture supernatant was analyzed by ELISA. [Results] (1) ADAM10 expression in the $CD3^+$ T-cell fraction of SLE patients was significantly higher than that in HCs. (2) The soluble FasL concentration was increased by stimulation with Ionomycin, and its production was suppressed by GI treatment. (3) Similar results to (2) were obtained when $CD8^+$ T cells were treated with anti-CD3/CD28 antibodies and GI. [Conclusions] Our results suggest that ADAM10 expressed on the membrane surface of $CD8^+$ T cells may be associated with shedding of FasL.

## P2-045

**Elucidation of the mechanism of a novel miRNA involved in deterioration of lupus nephritis**

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Conflict of interest: None

[Objective] miRNA is involved in the regulation of biological processes by inhibiting mRNA translation and degradation. Recently, it has been revealed that miRNAs are involved in the pathogenesis and have a potential as disease biomarkers and therapeutic targets. We aimed to find the disease specific miRNAs in lupus nephritis (LN) and verify their roles. [Methods] Total RNA was extracted from PBMC before and after treatment of patients with LN and miRNA array analysis was performed. Significantly changed miRNAs were confirmed by qRT-PCR. The mimic of miRNAs identified by these methods were transfected into Normal Human Mesangial Cells (NHMC) and other various cells. Biological functions of these transfected cells were investigated. [Results] miR-6516-3p was found to promote MMP-9 in NHMC. We also found that miR-6516-3p downregulated the expression of RECK, an endogenous inhibitor of MMP-9. However, endogenous miR-6516-3p in renal component cells such as NHMC was not present in functional amounts under an inflammatory environment. miR-6516-3p in vascular endothelial cells and macrophages was upregulated. [Conclusions] miR-6516-3p may be associated with LN exacerbation by increasing MMP-9 expression via suppression of RECK expression.

## P2-046

**Growth inhibitiory effect on SLE-associated enterobacteria by Lactobacillus sp. culture supernatant mixture**

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Conflict of interest: None

Dysbiosis in SLE has been linked to reports of increased *Streptococcus anginosus (Sa)* and *S. intermedius (Si)* as well as bacterial transloca-

tion of *Enterococcus gallinarum (Eg)* to the liver. We examined whether co-culturing with medium containing *Lactobacillus* spp. metabolites inhibits the growth of these enterobacteria. Five different *Lactobacillus* species were independently cultivated both aerobically and anaerobically. The supernatants were then combined based on each conditions. Following the inoculation of the *Sa*, *Si*, and *Eg*, *Lactobacillus* supernatant mixture (LSM) to the nutrient broth, the colony counts were determined 0-7 hours after co-culturing at 37°C in an aerobically. The bacterial growth curve was compared to the untreated LSM under the specified culture conditions after the LSM was adjusted to pH 6.5 using NaOH. The growth of *Sa*, *Si*, and *Eg* was inhibited by the LSM. Two *Streptococcus* strains were more effectively inhibited from growing by the anaerobic LSM. The inhibitory effects on *Eg* was reduced by half in the LSM when pH 6.5 was adjusted. The LSM has a growth inhibitory effect on the three enterobacteria species linked SLE. Additionally, it was proposed that a pH change carried on by metabolites in the LSM is a component of the growth inhibition mechanism.

## P2-047

**A case of Sjögren's syndrome patient that presented with giant pyelolith**

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Conflict of interest: None

[Case] A 36-year-old woman presented with serum K level 2.6 mmol/L and venous blood pH 7.26. The patient was admitteded to our hospital for close examination including renal biopsy. She tested positive for anti-SS-A antibody, anti-SS-B antibody, and Saxon-Shirmer test, and based on the results of salivary gland scintigraphy, a diagnosis of Sjögren's syndrome was made. As the organ manifestations included interstitial nephritis and distal tubular acidosis, sodium bicarbonate and potassium supplementation was initiated. Eight years later, a chest radiograph taken during a routine health check examination revealed abnormal calcification of the abdomen which turned out to be a giant pyelolith. [Clinical Significance] In this case, early diagnosis and therapeutic intervention failed to prevent worsening of the pyelolithiasis. We here report a case of refractory Sjögren's syndrome with renal tubular manifestation and present a review of the literature.

## P2-048

**A case of Sjögren's syndrome with suspected concurrent infection with cytomegalovirus and EB virus**

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Conflict of interest: None

29-year-old female. She was diagnosed as having decreased blood cell counts during a physical checkup in March X. She was suspected to suffer from rheumatic disease and visited our hosipital. Physical examination revealed no abnormality, although blood tests revealed pancytopenia. We diagnosed as Sjögren's syndrome based on elevated anti-SS-A antibody and the results of a lip biopsy. Anti-dsDNA antibody was negative, and SLE was not diagnosed. Because no other disease causing cytopenia could be detected, the cytopenia was diagnosed as due to Sjögren's syndrome, and prednisolone (PSL) 20 mg was started. After starting steroids, cytopenia improved and PSL was tapered. In December X, taking PSL 4 mg, she was admitted to the hospital because of the elevated fever that persisted for 7 days. She was found to have cytomegalovirus (CMV) antigen and was treated with ganciclovir. The fever resolved after starting ganciclovir, and CMV antigen became negative. But EBVCA-IgM was also found to be positive. The fever gradually resolved with symptomatic treatment, and the EBV nucleic acid became negative. CMV infections in patients receiving immunosuppressive drugs were experienced frequently. Such patients who have persist fever should be considered having multiple infectious disease.

## P2-049

**Sjögren's syndrome complicated by interstitial pneumonia and pulmonary hypertension, improved by steroid therapy: a case report**

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Conflict of interest: None

28 years old, female. In X-7 year, she was diagnosed with Sjögren's syndrome (SS) due to thirst, dry eyes, positive anti-SS-A antibody, and positive anti-SS-B antibody, but she self-interrupted her visits to the hospital. In May of X year, right parotid swelling and fever in the 38°C range appeared, and she resumed her visits to our hospital in July of X year. When she came to our hospital, dyspnea on exertion was observed. Upon close examination, she was diagnosed with interstitial pneumonia (IP) and pulmonary hypertension (PH). She was hospitalized for treatment. Based on the results of right heart catheterization, we considered that PH was mainly a Nice's group 3 condition and started treatment with prednisolone (PSL) for IP. After the start of treatment, PH showed some improvement. In this case, Raynaud's phenomenon and positive anti-RNP antibodies were observed, and when combined with pulmonary arterial hypertension, the diagnostic criteria for mixed connective tissue disease (MCTD) were also met. However, the lack of mixed findings on the diagnostic criteria of MCTD and the DLH/LIP pattern with multiple cyst formation on CT images suggest that the pathophysiology of this case is PH caused by IP associated with SS. We consider this an interesting case and report it here.

## P2-050

**A case of pulmonary arterial hypertension complicated by Sjögren's syndrome with smooth conversion from continuous intravenous epoprostenol to oral selexipag**

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Conflict of interest: None

[Patient] 67-year-old female [Present illness] At the age of 48, she was diagnosed with SjS based on sicca syndrome and anti-SS-A antibody positive. Right heart catheterization (RHC) revealed mean pulmonary artery pressure (mPAP) 40 mmHg and pulmonary artery wedge pressure (PAWP) 4 mmHg, and was diagnosed with PAH. Immunosuppressive therapy was ineffective, but the combination of ambrisentan, riociguat and epoprostenol (EPO) improved the disease but she had difficulty reducing the dose less than 60 ng/min/kg and also had repeated catheter-related blood stream infections. She was admitted to our hospital to switch from continuous intravenous therapy with EPO to oral treatment with SLX. [Clinical Course] Pre-switch RHC was mPAP of 25 mmHg, PAWP of 6 mmHg. SLX was started at the lowest dose and reached the maximum dose on day 22, and EPO was tapered to 12 ng/min/kg. Post-switch RHC showed mPAP 22 mmHg and PAWP 5 mmHg and EPO was subsequently discontinued. During the clinical course, there was no evidence of right heart failure or infections. [Clinical Significance] Continuous intravenous EPO carries the risk of serious infections. This case revealed the safety of switching to SLX to maintain PAH associated with connective tissue disease, which could reducing its risk of infections.

## P2-051

**The association of T cells between peripheral blood and local salivary glands in Sjogren syndrome**

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Conflict of interest: None

[Objective] Although the characteristics of T cells in the peripheral blood of Sjogren syndrome (SS) are reported to be different from those of healthy controls, it remains unknown if they reflect the local immune responses. The purpose of this study is to elucidate the association of T cells between peripheral blood and local salivary glands. [Methods] We examined two patients with primary SS who admitted to our department in 2023. Both salivary glands and peripheral blood were collected from the same patients. Salivary glands were digested with collagenase and $Dead^{-}CD19^{-}CD14^{-}CD3^{+}$T cells were sorted from peripheral blood mononucleolar cells. They were applied to single cell RNA-seq (scRNA-seq) with TCR-seq. [Results] We detected total 30063 cells from the integrated datasets. Salivary glands had six clusters (gland cells, epithelial cells, endothelial cells, plasma cells, T cells and NK cells) and about 20% were occupied with T cells, of which $CD8^{+}$ T cells were dominant. We could also detect $CD4^{+}$ T cells and $CD8^{+}$ T cells in blood clearly. [Conclusions] We established scRNA-seq datasets from both peripheral blood and salivary glands in SS. We will decipher cell-cell interactions and moreover, clarify the association of T cells between blood and salivary glands deeply.

## P2-052

**Examination of anti-thyroid peroxidase antibodies, anti-mitochondrial M2 antibodies, and anti-centromere antibodies in anti-SS-A antibody-positive cases and the relationship between these antibodies and RF, ACPA, and the development of RA**

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Conflict of interest: None

[Objective] Sjögren's syndrome is associated with a variety of autoimmune diseases. We investigated autoantibodies in anti-SS-A antibody (SSA) positive cases. [Method] The subjects were 243 women who were positive for SSA and measured thyroid peroxidase antibodies (TPO), anti-mitochondrial M2 antibodies (AMA), and anti-centromere antibody (ACA). [Results] The positive rate was significantly higher for TPO (37%) than for AMA (19%) and ACA (16%). RF was observed in 60% cases, ACPA in 20% cases, and RA occurred in 12% cases. 47% cases were negative for all 3 antibodies, 38% cases were positive for 1 antibody, 13% cases were positive for 2 antibodies, and 2% cases were positive for 3 antibodies. ACPA was significant higher 30% in all antibody-negative cases than 12% of any antibody-positive cases ($p<0.01$). Among the antibody-positive cases, 65% of the cases were positive for one antibody in TPO, 46% in AMA, and 23% in ACA; there were many single-positive cases in TPO (65%), and many other antibody-positive cases in ACA (77%) ($p<0.0001$). [Conclusion] Among SSA-positive cases, those who were negative for 3 antibodies had a higher risk of developing RA, and more than half of the SSA-positive cases had 3 antibodies, demonstrating the clinical significance of measuring 3 antibodies.

## P2-053

**A case of TAFRO syndrome which was treated with combination therapy of glucocorticoid, tocilizumab and ciclosporin may be effective**

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Conflict of interest: None

[Clinical Significance] We had experienced a case of TAFRO syndrome which was treated with combination therapy of glucocorticoid, tocilizumab (TCZ) and ciclosporin (CYA). [Case] 59 year-old woman [Course] She was admitted to our hospital in October, X due to continous fever and edema. She had CRP 32.07 mg/dl, CRE 1.20 mg/dl and platelet count of $2.2x10^{3}/\mu l$. We diagnosed her with TAFRO syndrome from her left axillary lymph node biopsy. We had started predonisolone (PSL) 60 mg/day (1 mg/kg) with biweekly drip of TCZ 400 mg/time. PSL was tapered. Her symptoms and data began to improve except low platelet counts and edema. In November X, we had started CYA 140 mg/day (two times/day after meal). Edema had begun to decrease. In January X+1, her platelet counts were slowly amerliorated. In March X+1, we discharged her with CYA 120 mg/day (Trough 0hr 115, 2hr 571 ng/ml), PSL 10 mg/day and TCZ. In August X+1, she had again low platelet counts and edema. We had increased the amount of CYA to 160 mg/day (Trough Ohr 165, 2hr 640 ng/ml). We had increased amount of TCZ 400 mg/time to every week, but we had kept amount of PSL 10 mg/day. Her platelet counts are still low, but other parameters are slowly recovering. [Conclusion] We assumed adequate amount of CYA was essential in our case with other drugs.

## P2-054

**Successful Treatment of Tocilizumab in TAFRO Syndrome with Liver Injury: Case Report and Review of the Literature**

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Conflict of interest: None

A 66-year-old woman was admitted to a previous hospital due to high inflammatory response. Antibacterial drugs were administered, but after two weeks, she developed hypoalbuminemia, enlarged lymph nodes, and ascites effusion, prompting her transfer to our hospital. An axillary lymph node biopsy revealed histological findings similar to Castleman's disease, and a subsequent bone marrow biopsy led to the diagnosis of TAFRO syndrome. Treatment with tocilizumab and concurrent steroid therapy was initiated, but the patient experienced rapid worsening of renal impairment, thrombocytopenia, and fluid retention, necessitating hemodialysis. Subsequently, the emergence of liver damage was observed during the disease course, with elevated levels of direct bilirubin. A liver biopsy showed nonspecific inflammatory findings. Continued administration of tocilizumab and a gradual tapering off of steroids led to a progressive improvement in the patient's general condition, enabling the discontinuation of hemodialysis. Hypoalbuminemia, thrombocytopenia, and hepatic impairment also improved. She was transferred to a rehabilitation hospital four months after the commencement of treatment. While complications of liver disorders linked to TAFRO syndrome are uncommon, we present a valuable case report.

## P2-055

**Two cases of TAFRO syndrome refractory to steroids and tocilizumab were successfully treated with rituximab**

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Conflict of interest: None

[Case 1] 66-years-old man was admitted to the previous hospital with fever and cough, and was found to have decreased platelets, abnormal coagulation, renal disorder, pleural effusion, and ascites. The patient was transferred to our hospital for further examination due to worsening renal disorder. He was diagnosed TAFRO syndrome (grade 5). He was started on continuous dialysis and was treated with high-dose steroids and tocilizumab, but there was no improvement. The patient responded well to rituximab. The patient is an outpatient on a low dose of steroids only. [Case 2] 57-years-old woman was treated with antimicrobial agents for pyelonephritis, but there was no improvement. Pleural effusion, dyspnea, and acute renal failure occurred, and the patient was transferred to our hospital. The patient was diagnosed with TAFRO syndrome (grade 4) and treated with high-dose steroids and tocilizumab, but the edema did not improve, and thrombocytopenia worsened. Rituximab was added to the treatment, which was successful. The patient is now drug-free. [Clinical Significance] TAFRO syndrome is sometimes a severe case with rapidly worsening hemodynamics and death as the outcome. Rapid treatment selection is necessary, especially in cases of prolonged thrombocytopenia.

## P2-056

**A case of TAFRO syndrome with fever and eosinophilia that was difficult to diagnose and treat**

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Conflict of interest: None

A 60-year-old man had acute onset fever, vomiting and diarrhea, and was admitted to the previous hospital as a case of bacterial enteritis. He developed pleural effusion, ascites, and eosinophilia during antibiotic treatment, but he recovered spontaneously, and was discharged. The following day, he developed fever again with respiratory circulatory failure, and required to be managed in the intensive care unit. Worsening of renal function were also observed. Close examination for infection, malignancy, and collagen disease showed no findings leading to a diagnosis. Prednisolone (PSL) 60 mg/day was initiated and immediately improved. However, after the dose was reduced to PSL 50 mg/day, he repeated relapsed. Because of high-dose steroid dependence, he was transferred to our hospital. Although a definitive diagnosis had not been made, the PSL dose was reduced with cyclosporine, but he repeated relapsed with PSL 30 mg/day, along with thrombocytopenia. Additional lymph node biopsy showed no findings, but the clinical course led to a diagnosis of TAFRO syndrome other than iMCD-TAFRO. Finally rituximab was given and remission was achieved. There has been no previous report of a patient diagnosed with TAFRO syndrome with hypereosinophilia, so we discuss the pathogenesis of the disease.

## P2-057

**Renal pelvic involvement in multicentric Castleman disease**

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Conflict of interest: None

Castleman disease (CD) is a lymphoproliferative disorder first described by Castleman in 1954. Clinically, it is classified into a unicentric (UCD) or multicentric (MCD) type. In computed tomography (CT) findings of MCD, systemic lymphadenopathy or lung lesions are well-known ones, and few studies have described imaging findings of urological lesions in MCD. In the present report, soft tissue masses were observed surrounding the bilateral renal pelvises on contrast-enhanced CT. Treatment with oral prednisolone and intravenous tocilizumab was begun, and follow-up CT demonstrated significant improvement in the lesions, suggesting that the lesions were associated with MCD.

## P2-058

**A case of idiopathic multicentric Castleman disease associated with neuromyelitis optica spectrum disorder**

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Department of Rheumatology and Applied Immunology, Saitama Medical University Hospital

Conflict of interest: Yes

A 52-year old woman was diagnosed with neuromyelitis optica spectrum disorder (NMOSD) in year X-4 due to paralysis, sensory disturbance, longitudinal spinal cord involvement, and positive anti-aquaporin 4 (AQP4) antibody. Treatments of triple-course of methylprednisolone-pulse and three times of plasma exchange were performed and followed by high-dose prednisolone (PSL) and tacrolimus (TAC). Her symptoms except lymphadenopathies improved. The patient was admitted to our Department in year X because of suspicion of Castleman disease (CD) by lymph node biopsy. [Clinical Course] A diagnosis of idiopathic multicentric CD was made by multiple lymphadenopathies, high levels of CRP, IgG and IL-6 and histology (plasma cell type). After discontinuing TAC and introducing tocilizumab, CRP, IgG and lymphadenopathies significantly improved. The dosage of PSL has been reduced and symptoms of NMOSD and CD have been under control. [Discussion] Anti-AQP4 antibodies produced from plasmablast (PB) are important as a cause of NMOSD. IL-6 is involved in the differentiation of PB from B cells and production of anti-AQP4 antibody. Because CD could be implicated in the onset of NMOSD and because the association of both diseases is rare, we will report the case and discuss the pathological mechanisms.

## P2-059

**Two cases of successful tocilizumab monotherapy in multicentric Castleman disease with concomitant autoimmune disease**

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Conflict of interest: None

[Case 1] A 75-year-old female presented with bilateral elbow and knee joint pain. She had elevated CRP levels, hypergammaglobulinemia and lymphadenopathy. Lymph node biopsy led to a diagnosis of multicentric Castleman disease (MCD). At the same time, polyarthritis and dryness in the mouth, with positive anti-CCP, rheumatoid factor (RF) and anti-SSA, resulting in a diagnosis of rheumatoid arthritis and Sjogren syndrome. Tocilizumab monotherapy led to improvement in both MCD and rheumatoid arthritis. [Case 2] A 64-year-old female presented with exertional dyspnea. She had elevated CRP levels, hypergammaglobulinemia, and lymphadenopathy. Lymph node biopsy led to a diagnosis of MCD. Additionally, she had anemia, elevated indirect bilirubin, low haptoglobin levels, and positive direct and indirect Coombs tests, leading to a diagnosis of autoimmune hemolytic anemia. Tocilizumab monotherapy led to improvement in both diseases. [Clinical Significance] While the pathogenesis of MCD remains unclear, there is a clinical phenotype of concomitant autoimmune diseases, and IL-6 commonly contributes to disease pathogenesis. Interestingly, IL-6 inhibition did not correct the aberrant production of autoantibodies, suggesting that autoantibody-producing B cells are upstream in the pathogenesis.

## P2-060

**A case of Castleman's disease diagnosed by paratracheal lymph node biopsy about 1 year after prior elevation of biliary enzymes and treated as primary sclerosing cholangitis**

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Conflict of interest: None

[Case] Male 20s [Past History] Neutropenia from ages 5-12 [Current History] From X-2 years, the patient was noted to have elevated biliary enzymes and was referred to our hospital in X-1 year. The patient's CRP was 10.29 mg/dL, ALP 722 U/L, γGTP 225 U/L, Imaging tests and a liver biopsy led to a diagnosis of suspected primary sclerosing cholangitis. Treatment with 40 mg of PSL was initiated leading to a reduction in CRP and biliary enzymes. However, with a PSL dose of less than 20 mg, CRP increased again. The patient was referred to our department. At the initial visit, CRP was 11.5 mg/dL, ALP 65 U/L, IL-6 120 pg/mL, Bone marrow examination was performed, but no abnormalities were found. The patient continued with 7.5 mg of PSL, While the patient's overall condition was good, CRP remained high at 7-9 mg/dL. In December of X+1 year, CT revealed worsening of sclerosing cholangitis, as well as enlargement of the right parasternal lymph nodes. A biopsy of the lymph node led to a diagnosis of mixed-type Castleman's disease (CD). After starting TCZ, CRP normalized [Discussion] Reports of cholangitis in CD are rare, but when symptoms of cholangitis precede, it's necessary to consider other diseases including CD for differential diagnosis when prednisone reduction is difficult.

## P2-061

**A male case of multicentric reticulohistiocytosis developed followed by arthritis during the course of Sjogren syndrome**

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Conflict of interest: Yes

Multicentric reticulohistiocytosis (MRH) is a rare disease characterized by generalized papulonodular skin lesions and polyarthritis. We describe a case of a male patient with Sjögren's syndrome whose arthritis and skin rash led to the diagnosis of MRH. [Case] A male in his fifties had been diagnosed with Sjögren's syndrome based on positivity of anti-SS-A Ab and salivary gland biopsy. He presented with arthralgia. He was positive for RF but negative for anti-CCP Ab. ANA were x640 (Sp.) and IgG was elevated at 2365 mg/dL. Ultrasonography (US) showed no synovitis; however, he developed persistent arthralgia. Six months later, multiple papules appeared on his body. Skin biopsy revealed diffuse infiltration of tissue with eosinophilic spores and CD68-positive histiocytes and multinucleated giant cells, and therefore we diagnosed MRH. At the same time, joint swelling became apparent in his fingers and hands, and synovitis was observed on US. He is currently receiving MTX 10 mg/week for arthritis. [Discussion and Conclusion] We have experienced a case in which MRH symptoms appeared more than 10 years after the diagnosis of Sjögren's syndrome. A case of MRH in a male patient with Sjögren's syndrome has not been reported in Japan.

## P2-062

**Time-course analysis from the first wave to early 2023 in critically ill patients with novel coronavirus infection in rheumatoid arthritis**

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Conflict of interest: None

[Objective] We analyzed the risk factors of severe COVID-19 in patients with rheumatoid arthritis by calendar time. [Methods] We analyzed the clinical characteristics of severe COVID-19 in each calendar period. [Results] During the period, of 2,631 RA patients, 553 (21.0%) were diagnosed with COVID-19 (21.0%, mean age 57.8 ± 12.8 years, 84.4% female). There were 9 cases (1.6%) of severe COVID-19. Severe COVID-19 cases decreased over calendar time ($p < 0.0001$). The rate of severe cases during the early stage of COVID-19 (March 1, 2020 to November 30, 2021) was 16%, but after that (December 1, 2021 to September 30, 2023) it was 0.9%. In the early stage of COVID-19, older people ($p=0.0054$), hypertension ($p=0.0021$), diabetes ($p=0.0291$), and rheumatoid comorbidity score RDCI (1.5+/-1.3 vs. 0.4+/-0.7, $p=0.0388$) was associated with severe COVID-19. After December 2021, the elderly ($p=0.0292$), hypertension ($p=0.0006$), RA-ILD ($p< 0.0001$), RDCI (4.0+/-2.6 vs. 0.4+/-0.8, $p=0.0002$)) were associated with severe COVID-19. [Conclusions] Among RA cases, the proportion of severe COVID-19 cases has decreased after December 2021 compared to the early stage of COVID-19, but the clinical characteristics of severe COVID-19 are different between the two groups. It was similar.

## P2-063

**Did COVID-19 pandemic affect therapeutic decision making of rheumatologists in Japan? Assessment of changes over time using NinJa registry**

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Conflict of interest: None

[Objective] To assess changes of therapeutic decision of bDMARDs or tsDMARDs (molecular targeted therapy (MTT)) by rheumatologists between before under COVID-19 pandemic. [Methods] Two groups are compared: from NinJa2018 to 2019 (before pandemic (BP); 12965 cases) and from NinJa2019 to 2020 (under pandemic (UP); 12195 cases). Three situations were set up. New indication of MTT; the patients who have not ever used MTT were extracted from two groups and compared on the proportion of initial induction of MTT. Changes or discontinuation of MTT; the patients who have already used MTT were extracted from two groups and compared on the proportion of changes or discontinuation of MTT. [Results] New indication of MTT; 5.4% of BP group and 4.3% of UP group were newly started MTT ($p<0.0001$). Changes or discontinuation of MTT; MTT were changed in 12.5% of BP group and 8.9% of UP group ($p<0.0001$). The proportion of discontinuation of MTT in two groups was comparable. [Conclusions] Under COVID-19 pandemic, therapeutic decision making of MTT became passive.

## P2-064

**A case of idiopathic multicentric Castleman disease (iMCD) diagnosed after COVID-19 infection**

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Conflict of interest: None

A woman in her 50s with a 16M history of fatigue contracted COVID-19 11M ago. She was hospitalized on the 8th day due to pneumonia and an 8 kg weight loss. Post-discharge, she continued to experience fatigue, palpitations, high CRP levels, anemia, and elevated immunoglobulins. 7M later, although her symptoms improved, abnormal blood test results persisted. Despite elevated SSA antibodies, Sjögren's syndrome was not suspected with no sympton and negatice lip biopsy. 14 days ago, she was hospitalized for palpitations and dizziness, with sinus tachycardia and somehow palpable lymph nodes. Lab results showed low albumin, LDH, elevated CRP, soluble IL-2 receptor and IL-6 and immunoglobulin. A biopsy confirmed MCD with plasmacytic features. Discussion: MCD is a non-clonal lymphoproliferative disorder associated with excessive IL-6. The cause of HHV-8-negative MCD remains uncertain, possibly involving an unknown virus. SARS-CoV-2 can lead to prolonged infections, contributing to "long COVID." Reports exist of MCD occurring after COVID-19 and MCD patients having prolonged COVID-19. It's unclear which condition preceded in this case, but an association is apparent. Undiagnosed MCD may reduce QOL, emphasizing the importance of considering hidden cases of MCD among "long COVID" patients.

## P2-065

**Two cases of autoimmune encephalitis with status epilepticus after the COVID-19 vaccination**

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Conflict of interest: None

Case 1; A 24-year-old woman admitted to our hospital due to convulsions 9 days after the Covid-19 vaccination. Her cerebrospinal fluid showed pleocytosis with IL-6 elevation. She was resistant multiple anticonvulsants. The examinations of infection were negative. Autoimmune encephalitis was suspected. She was treated with PSL50 mg, plasma exchange and IVIG. Her seizures gradually disappeared. She was transferred on the 78th hospital day. Case 2; A 74-year-old woman admitted our hospital due to convulsions 9 days after the Covid-19 vaccination. Her cerebrospinal fluid showed normal cell count with IL-6 elevation. She was resistant multiple anticonvulsants and autoimmune encephalitis was suspected. PSL50 mg was started and her condition was improved. On the 10th day of hospitalization, hemorrhagic shock and NOMI occurred due to retroperitoneal hematoma. She died of multiple organ failure on the 37th day of hospitalization. Clinical significance is follows; Because two cases had no underlying disease and developed acutely after Covid-19 vaccination, a relationship with the vaccination was suspected. Autoimmune encephalitis after Covid-19 vaccination is rare, however, could be fatal, and we are going to discuss our two cases with literature review.

## P2-066

**SARS-Cov-2 mRNA vaccination-induced new-onset seronegative rheumatoid arthritis**

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Conflict of interest: None

[Case] An 83-years-old woman developed polyarthritis 9 days after 6th dose of SARS-Cov-2 mRNA vaccination and treated as unexplained adverse reaction including functional somatic syndrome (FSS). Serologies revealed elevated CRP, ESR and MMP-3 of 9.37 mg/ dL, 81 mm/h and 478 ng/mL, respectively. RF and ACPA were negative. The SJC and TJC were 3 and 8, respectively. Ultrasound demonstrated synovial thickness in multiple joints. Her DAS28-CRP, DAS28-ESR and MHAQ were 5.82, 6.30 and 2.875, respectively. Under the diagnosis of seronegative RA, she was started on 10m/day of prednisolone (PSL). PSL was reduced to 6 mg/ day and 4 mg/week of MTX was introduced 1 week later. Her RA symptoms still remained after 3 weeks. Therefore, MTX was discontinued and 200 mg/2 weeks of sarilumab was introduced. Complete remission was achieved after 4 weeks with CRP of 0.02 mg/ dL, ESR of 2 mm/h, SJC of 0, and TJC of 0. [Clinical Significance] Several adverse reactions of SARS-Cov-2 mRNA vaccination have been reported recently. FSS is one of the unexplained adverse reactions and usually treated by only symptomatic therapy. RA may be among these unexplained adverse reactions after this vaccination. This case is in remission after appropriate diagnosis and treatment. Therefore, careful diagnosis is important.

## P2-067

**Case Report: 4 cases of COVID-19 with rheumatoid arthritis showing different prognosis (Follow-up reports)**

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Conflict of interest: None

Case 1: A 74-year-old female treated by PSL and MTX. She was infected with COVID-19 during the hospitalization. She was commenced NRV/RNV and finished quarantine on Day 7. Case 2: A 68-year-old female treated by TOF. She was infected with COVID-19 during the hospitalization. She has started NRV/RNV but suspended on Day 3, due to epigastric distress. She finished quarantine on Day 15. Case 3: A 76-year-old male treated by PSL3 mg, MTX6 mg and SASP1000 mg. He was infected with COVID-19 during the hospitalization. He was commenced MPV. But on Day 8, pneumonia deteriorated and was initiated on RDV. However, on Day 15, DEX was started because of the decreased oxygenation. Since the symptoms improved markedly, DEX was reduced. Case 4: A 75-year-old male treated by PSL, IGU and SASP. He was found to be positive for COVID-19 during the hospitalization. Although he was treated symptomatically, pneumonia developed on Day 9. RDV was started but found to be refractory. DEX was started due to dyspnea. Since the symptoms improved, the dose of DEX was reduced. Clinical significance: Even that COVID-19 has been classified as a Class 5 infectious disease, the severity rate in RA patients is high. We will report on four cases experienced at our hospital, including a literature review.

## P2-068

**Analysis of the incidence of herpes zoster and the risk of administered drugs in daily medical care of rheumatoid arthritis patients who have not received the inactivated herpes zoster vaccine**

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National Hospital Organization Sagamihara National Hospital

Conflict of interest: None

[Background] JAKi are known to have a high incidence of HZ in Japan, based on data from clinical trials for RA. In Japan, the frequency of HZ onset is unknown in detail without the use of inactivated vaccines. [Objective] We will clarify the risk of developing HZ and RA treatment drugs during the period from 2015 to 2020. [Methods] We analyzed 2858 RA patients (11148Person-year) who were treated at our hospital during the 5-year period and investigated the presence or absence of HZ onset and the drugs administered. [Results] 67 years (mean age), 82.3% (women). The number of HZ cases were 206, of which 11 were generalized. 9 cases of HZ itself were affected twice during the same period. The incidence of HZ: 1.77/100 person-years. Using Medications of HZ onset MTX 50.5%, TAC10.2%, biologics [TNF-αi. 8%, IL-6i 3.4%, CTLA-4i 3.4%], and JAKi 10.7%. PSL 39% (Ave: 4.5 mg). Between HZ onset and drugs used, (multivariate analysis) odds ratio PSL use: 1.53 [95% CI: 1.16-2.03]) and JAK i use: 3.22 [95% CI: 1.99- 5.21]) was significant. MTX, TAC, Biologics were not significant. [Conclusions] Treatment with JAKI or PSL in RA patients in clinical practice without vaccination poses high risk of developing HZ. It is thought that sufficient care should be taken when using them.

## P2-069

**Evaluation of safety and efficacy of recombinant zoster vaccine in patients with collagen disease attending our department**

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Conflict of interest: None

Objective: To evaluate the safety and efficacy of recombinant zoster vaccine in patients with collagen diseases treated at our department. Methods: To evaluate patients with collagen diseases (rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis, palmoplantar pustular osteoarthritis, ankylosing spondylitis, dermatomyositis/polymyositis, etc.) who were vaccinated with RZV between May 2021 and March 2024. Results: Up to September 2023, 58 patients were inoculated with RZV. The number of patients was 36 with rheumatoid arthritis, 7 with systemic lupus erythematosus, 7 with psoriatic arthritis, 4 with palmoplantar pustulosis osteoarthritis, 2 with ankylosing spondylitis, and 2 with dermatomyositis/ polymyositis. Patients with systemic lupus erythematosus often had a history of herpes zoster (5/7 patients), and the age of onset was younger than that of other diseases. No relapse of the primary disease was observed in any of the 58 patients vaccinated with RZV. Side effects were swelling and pain at the vaccination site, but none of them led to discontinuation. Herpes zoster was not observed in any of the patients after RZV vaccination. Conclusion: RZV was administered relatively safely, and there were no cases of flare-ups of the primary disease.

## P2-070

**Usefulness of neutrophil-lymphocyte ratio as a predictive marker of herpes zoster in rheumatoid arthritis**

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Conflict of interest: None

[Objective] We investigated whether the NLR and PLR are useful as predictors of the onset of HZ in RA. [Methods] Among 1687 RA patients attending our hospital, randomly selected the RA-VZV group who developed HZ and the RA-nonVZV group who did not at a ratio of 1:5. For the RA-nonVZV group, blood test taken within 1 month of onset was examined using blood test from the same period. [Results] 27 patients in the RA-VZV group (6 men, 21 women, median age 76 years) and 135 patients in the RA-nonVZV group (38 men, 97 women, median age 66 years) were eligible and developed the disease. Treatments in the RA-VZV group included MTX in 13 cases (48.1%), SASP in 7 cases (26%), PSL in 9 cases (33.3%), TAC in 3 cases (11.1%), bDMARDs in 4 cases (14.8%), and tsDMARDs in 1 case. In the RA-nonVZV group, 86 patients received MTX (63.7%), 41 patients with SASP (30.4%), 23 patients with PSL

(17%), 3 patients with TAC (2.2%), and 30 patients with bDMARDs (22.2%), 7 cases (5.2%) of tsDMARDs. The mean NLR values were 4.94±4.01 and 2.54±1.91, respectively, and the mean PLR values were 176.1±103.2 and 155.6±78.3, with NLR being significantly higher in the RA-VZV group. ($p<0.01$) [Conclusions] High NLR in RA patients may predict the onset of shingles, and may lead to recommendations for shingles vaccination.

## P2-071

**Two cases of varicella-zoster virus meningitis during treatment of systemic lupus erythematosus**

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Conflict of interest: None

Case 1: A 30-year-old woman who was diagnosed as systemic lupus erythematosus (SLE) and was treated with steroids, tacrolimus, and mycophenolate mofetil (MMF). She developed herpes zoster in the trigeminal area and was treated with valacyclovir. On the 19th day of onset, a CSF test was positive for varicella-zoster virus (VZV)-DNA, and a diagnosis of VZV meningitis was made. She was hospitalized and treated with acyclovir, and was discharged on the 15th day of admission. Case 2: A 49-year-old woman who was diagnosed as SLE, and was treated with steroids and MMF. She developed herpes zoster in the trigeminal nerve area and was treated with amenamevir. On the 34th day of onset, she visited our hospital. A CT scan of the head showed capsular hemorrhage, and VZV-DNA in the CSF were positive. The diagnosis of VZV meningitis combined with vasculopathy was made, and she was hospitalized and treated with acyclovir and steroids. On the 14th day of admission, she became unconscious, and a head CT scan showed aggravated capsular hemorrhage. Craniotomy was performed to remove the hematoma. On the 43rd day of admission, she was transferred to the hospital for rehabilitation. We report the importance of early diagnosis, treatment, and prevention, including a review of the literature.

## P2-072

**A case of disseminated herpes zoster during treatment for systemic lupus erythematosus, leading to cysto-rectal damage**

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Conflict of interest: None

[Case] 84 years old, female [History] She was diagnosed with systemic lupus erythematosus (SLE) in X-2 years. She was in remission with prednisolone, tacrolimus, and belimumab, and remained in remission thereafter. [Progress] On the third day of admission, a blood test showed pancytopenia with marked neutropenia, and a red skin rash with blisters appeared on the whole body. The diagnosis of disseminated herpes zoster was made. Acyclovir 500 mg/day intravenous infusion was immediately started, and abdominal pain gradually improved. On the other hand, she developed urinary retention. The urologist noted significant dysuria, which necessitated the placement of a urethral catheter. By the 12th day of hospitalization, all blisters had crusted over, and the patient was judged to have healed from herpes zoster. Pancytopenia and abdominal pain improved with the healing of herpes zoster. However, urinary retention persisted after healing, and the patient was discharged from the hospital with an indwelling urinary catheter. [Discussion] We have experienced a case of herpes zoster that developed from abdominal pain and was accompanied by neuropathy. Herpes zoster is an unavoidable disease in the treatment of collagen disease, and we report this highly suggestive case here.

## P2-073

**Frailty as an Important Indicator for Difficult-to-treat rheumatoid arthritis from the T-FLAG study**

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Conflict of interest: None

[Objective] In the treatment of RA, difficult-to-treat RA (D2T RA) is a condition that can be difficult to treat. No clear definition has been provided regarding the part of the D2T RA definition that states “RA symptoms that are causing a reduction in quality of life”. The aim of this study was to clarify the indicators that cause “ reduction in quality of life. [Methods] 696 RA patients (T-FLAG study) were included in the study. As indicators of “reduction in quality of life”, we used the HAQ-DI, the Kihon Checklist (KCL), and the SARC-F. Using the four models, factors associated with D2T RA were determined by multivariate logistic analysis. [Results] 38 patients (5.5%) had D2T RA. There were significant differences in D2T RA vs. non-D2T RA in women (87 vs. 71%), disease duration (17 vs. 12 years), DAS28-ESR (4.22 vs. 2.72), HAQ-DI (1.04 vs. 0.49), KCL (10.7 vs. 6.9 points), SARC-F (4.1 vs. 2.3 points) but not for age (70 vs. 69 years). Adjusting for age, gender, disease duration, and BMI, HAQ-DI (OR1.21), KCL (OR1.08), and SARC-F (OR1.07) were associated. [Conclusion] In the assessment of “reduction in quality of life”, KCL, a comprehensive concept of frailty assessment that includes not only physical function assessment but also psycho-social factors, is considered to be useful.

## P2-074

**Risk factor to become difficult-to-treat rheumatoid arthritis in our hospital**

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Conflict of interest: None

[Objective] When patients were diagnosed with rheumatoid arthritis (RA), they were treated with methotrexate (MTX) and whose doses reached maximum 16 mg within one month in our hospital. The aim of this study was to investigate the characteristics of difficult-to-treat RA (D2T RA) patients under this treatment. [Methods] 97 patients were diagnosed as RA and started the treatment between 2014 and 2022. Patients who failure of ≧ 2 biological disease modifying antirheumatic drugs (DMARDs) / targeted synthetic DMARDs were defined as D2T RA. Several factors to become D2T RA were picked up and they were performed with Logistic regression analysis. [Results] The number of D2T RA were 5 (male 2, female 3/ ACPA positive 3, RF positive 4) whose rate was 5.2% and their average age was 62.6 years. The disease activities were DAS28 (ESR) 4.95 and SDAI 19.7. The average duration from RA onset to start the treatment was 107 days. 4 patients were treated by MTX16 mg in one month. In our study, there were no factors to predict the DT2 RA when they were started the treatment. [Conclusions] There were no factors to predict the DT2 RA but the rate wasn’t so much compared with other reports. It was important to treat with MTX when patients were diagnosed as RA and this treatment may decrease the D2T RA.

## P2-075

**Clinical characteristics of patients with difficult to treat rheumatoid arthritis**

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Conflict of interest: None

[Objective] The aim of this study was to investigate the characteristics of patients with difficult-to-treat rheumatoid arthritis (D2T RA). [Methods] We reviewed RA patients treated at our hospital from April 2021 to March 2022. We defined D2T RA according to the EULAR definition. We compared the clinical information between D2T RA and Non-D2T RA

groups. [Results] We enrolled 277 patients (mean age 67.4 ± 24.4 years, 240 females). We classified 14 patients (mean age 64.6 ± 24.4 years, 13 females) as D2T RA and 263 as Non-D2T RA (mean age 67.5 ± 24.6 years, 227 females). The mean age of disease onset was significantly lower in the D2TRA group (37.2 years) than the Non-D2T RA group (47.2 years). DAS28-ESR was higher in the D2T RA group (4.4) as compared to the Non-D2T RA group (2.6). Although there was no significant difference in positive RF rate between 2 groups, we found significantly elevated RF titer in the D2T RA group (310.5 IU/mL) than the Non-D2T RA group (50 IU/mL). The optimal cut-off value of RF was determined by ROC analysis to be 144.0 IU/mL (area under curve = 0.79, $p$ = 0.0032). There was no significant difference in other clinical data between 2 groups. [Conclusions] Young age of disease onset, high DAS28-ESR and high RF levels were clinical characteristics of D2T RA.

## P2-076

**Risk factors for transition from monoarthritis to Polyarthritis of the knee**

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Conflict of interest: None

[Objective] Patients with monoarthritis of the knee often progress to polyarthritis. We investigated the risk factors of rheumatoid arthritis (RA) patients who developed polyarthritis during the course of their disease. [Methods] Twenty-three patients (7 males and 16 females) with RA seronegative monoarthritis of the knee underwent surgery and pathologic examination of the synovial membrane. A comprehensive differential diagnosis was performed, including pathologic examination, and either osteoarthritis (OA) or RA was diagnosed. Age, disease duration, and blood tests (CRP, MMP-3) were examined. Among RA patients, those who developed polyarthritis (polyarthritis group) and those who remained monoarthritis (monoarthritis group) were divided into two groups for comparison. [Results] The diagnosis was RA in 11 cases and OA in 12 cases. Five (45.4%) of the 11 patients in the RA group developed polyarthritis during the course of the disease. The change in MMP-3 before and after surgery was +60.1 ng/dl in the polyarthritis group and -295.9 ng/dl in the monoarthritis group, with a significantly smaller decrease in MMP-3 after surgery in the polyarthritis group (p=0.015). [Conclusion] Patients with a lack of decrease in MMP-3 even after surgery may develop polyarthritis.

## P2-077

**Investigation of the clinical significance of anti-MAC antibodies in rheumatoid arthritis treatment**

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Conflict of interest: None

[Objective] Since 2011, anti-MAC antibody serum testing has been used as an auxiliary diagnosis for pulmonary MAC disease. In this study, we attempted to evaluate whether anti-MAC antibody positivity is a poor prognostic factor for RA treatment. [Methods] 150 cases diagnosed with RA and measured for MAC antibodies at our hospital from 2014 to 2020 were analyzed. Background factors and changes in disease activity were extracted from the medical records. 14 MAC-positive patients were defined as P group and 134 MAC-negative patients were defined as N group, and a retrospective comparative analysis was performed. [Results] Regarding background factors, there were no significant differences in age, gender, BMI, steroid use history, and the positive rate of ACPA and RF, but the MTX use rate was significantly lower in the P group (p=0.001). In the comparison of DAS28ESR trends from the start of treatment to 3 years later, the median values were significantly higher in the P group except at the start of treatment (p<0.03). Multiple regression analysis with DAS28ESR as the dependent variable after 3 years of treatment identified anti-MAC antibody positivity as a factor. [Conclusions] The results suggest that patients with positive anti-MAC antibodies may have a poor course of RA treatment.

## P2-078

**Predictors of frailty in patients with rheumatoid arthritis: ~multicenter observational study T-FLAG using data from 2020 to 2023~**

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Conflict of interest: None

[Objective] This study examined predictors of frailty progression after 3 years in RA patients. [Methods] 434 patients were included using the Japanese Frailty Diagnostic Criteria (J- CHS) from June 2020 to August 2023. 338 robust and pre-frail patients with J-CHS of 0 to 2 were analyzed. Based on J-CHS score in 2023, patients were divided into 3 points or more (56 in the frailty group) and 2 points or less (282 in the non-frailty group). Using baseline data in 2020, predictive factors of frailty were examined by logistic regression analysis. [Results] The frailty group was older than the non-progression group (71.2 years vs. 63.6 years), had a longer disease duration (15.6 years vs. 9.9 years), and had a higher DAS28- ESR (3.17 vs. 2.53), higher HAQ-DI (0.67 vs. 0.20), lower usage rate of Methotrexate (MTX) (47.3% vs. 71.9%), higher usage rate of steroid (40.0% vs. 24.1%). Predictors for frailty progression (adjusted odds ratio, 95% confidence interval) were DAS28-ESR (1.48, 1.03-2.13), HAQ-DI (3.73, 1.89-7.49), and MTX use (0.34, 0.16-) 0.71) and steroid use (2.41, 1.17-4.99). [Conclusions] Using MTX without relying on steroid is important to prevent the progression of frailty. Examining why treatment has not been strengthened for patients without basic treatment is necessary.

## P2-079

**Analysis of predictive factor of clinical backgrouind including patient reported outcome in rheumatoid arthritis patient at first visit**

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Conflict of interest: None

[Objective] To clarify the association between clinical background including Patient reported outcome and remission achievement in rheumatoid arthritis first visit patients [Methods] Our rheumatoid arthritis outpatient who had not been treated, 42 cases. Their age, gender, stage, class, disease activity, rheumatoid factor, anti-CCP antibody titer, HAQ-DI, Short Form 36, analyzed with DAS-28 ESR remission achievement by logistic regression analysis. [Results] Our patients was 42 cases, 19 male, 23 female, median age was 71, median value of DAS-28 ESR, CDAI, SDAI, HAQ-DI were 4.75, 18.2, 19.9, 0.625, respectively. Remission case was 16 at 6 months, 30 at 12 months. Bodily pain, General health, Mental Component Score in Short-Form 36 was associated with 6 month remission (Odds ratio, 95% C.I., p, was 0.81, 0.69-0.95 0.01, 0.87, 0.79-0.99, p<0.05, 0.92, 0.85-0.90, <0.05, respectively). Bodily pain was still associated with 12 months remission achievement. Other composite measure association was not evident. [Conclusions] SF-36 bodily pain score was associated with remission achievement in early rheumatoid arthritis patients.

## P2-080

**Joint Destruction in Patients with Seronegative Rheumatoid Arthritis**

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Conflict of interest: None

Objective: To investigate the prognosis of joint destruction in patients with seronegative rheumatoid arthritis. Methods: Newly diagnosed with rheumatoid arthritis (RA) according to the 2010 ACR/EULAR classification criteria in our hospital were selected. Patients who could be observed for at least 52 weeks were then divided into seropositive and seronegative cases. Results: Of 225 patients with new-onset arthritis, 90 patients who fulfilled the above criteria were selected, 69 of whom were seropositive and 21 of whom were negative. The seronegative cases were older at the time of diagnosis than the positive cases, and had higher RA disease activity in all indices, and these differences were statistically significant. Regarding treatment, seronegative cases had a higher rate of concomitant steroid use at diagnosis, but at 52 weeks, the two groups used similar amounts of steroids. DAS28CRP, DAS28ESR, SDAI, and CDAI at 52 weeks were similar, and ΔTSS was also similar in both groups. Conclusion: Although seronegative rheumatoid arthritis patients have more active disease at the time of diagnosis, it is possible to expect suppression of disease activity and bone destruction with the same treatment as for positive patients.

## P2-081

**The effectiveness of biological DMARDs and JAK inhibitors in patients with rheumatoid factor and anti-CCP antibodies positive/negative**

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Conflict of interest: None

[Purpose] It is unclear which molecular target drug is preferable to use for autoantibody positive/negative cases. [Method] This analysis was included 270 patients with TNF inhibitors, 215 patients with IL-6 inhibitors, 86 patients with CTLA4-Ig preparations, and 183 patients with JAK inhibitors. The improvement rate of CDAI was examined for each of them based on RF positive/negative and CCP positive/negative. We also investigated the combination of RF±/CCP±. [Results] In RF-negative cases, the improvement rate was high with TNF inhibitors and IL-6 inhibitors, and in RF-positive cases, there was a tendency for early improvement with JAK inhibitors. In CCP-negative cases, TNF inhibitors had the highest improvement rate, and in CCP-positive cases, IL-6 inhibitors had the highest improvement rate. In cases with both RF/CCP negative, TNF inhibitors and IL-6 inhibitors were highly effective, while the improvement rate of CTLA4-Ig preparations was low. In cases with both RF/CCP positive, there was a tendency for early improvement with JAK inhibitors, but the improvement rate was highest with IL-6 inhibitors. [Conclusion] There were trends in drug efficacy depending on whether RF/CCP was positive or negative.

## P2-082

**Factors determining the degree of DAS28-CRP improvement 3 months after b/tsDMARD administration in patient with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Biological or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs) are important phase II drugs in treating rheumatoid arthritis (RA). It is a known fact that it affects prognosis. We analyzed the factors influencing the therapeutic efficacy of patients treated at our hospital. [Methods] We investigated the changes in 28-joints disease activity score using C-reactive protein (DAS28) from the time of administration (@BL) 3 months after administration, targeting patients who received b/tsDMARDs from August 2010. The dependent variable, the patient's gender, age at the time of administration, and other clinical indicators were used for statistical evaluation. [Results] A total of 312 patients were included. As independent factors, there was a significant correlation between positive anti-citrullinated polypeptide antibodies, whether or not methotrexate was taken, history of b/tsDMARDs administration, degree of pain, degree of fatigue, physician evaluation, prognostic nutritional index (PNI), and DAS28@BL. [Conclusions] The short-term effects after b/tsDMARD administration are influenced by various factors. Among these, PNI is attracting attention as a new standard.

## P2-083

**IL-6 inhibitors and JAK inhibitors, inhibiting a common pathway, which is better at suppressing bone destruction in RA?**

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Conflict of interest: Yes

[Objective] To estimate the effects on the bone immune system after IL-6i and JAKi treatment, which inhibit common pathways, based on peripheral blood gene expression. [Methods] Peripheral blood gene expression changes in 38 RA patients (Tocilizumab (TCZ)=13, Tofacitinib (TOF)=15, Baricitinib (BAR)=10) were analyzed before and 3 months after the initiation of treatment using next generation sequencing. Changes in gene expression of molecules involved in bone immunity were analyzed before and after each treatment. [Results] Comparison of L-6i and JAKi showed that JAKi treatment significantly suppressed RANKL expression in peripheral blood. At the same time, significant suppression of RANK, ETS1, and IL-34 gene expression was also observed with JAKi treatment. Comparison of TOF and BAR treatment showed significant suppression of IL-4 expression in TOF and significant suppression of MMP-2 and IL-12 expression in BAR. [Conclusions] The results showed that the effects of each drug on the bone immune system were heterogeneous. Assuming that the promoter regions of RANK in osteoclastic progenitor cells and of ETS1 gene in fibroblasts are common in peripheral blood, JAKi, which significantly suppressed RANKL expression, may be more favorable than IL-6i for suppressing bone destruction.

## P2-085

**A petit consideration regarding renal dysfunction based on cystatin-C in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Estimated glomerular filtration rate (eGFR) based on cystatin-C (CysC) as an index of renal dysfunction in patients with rheumatoid arthritis (RA) was evaluated. [Methods] Patients with RA who measured eGFR based on CysC and creatinine (Cr) simultaneously when first consulted (BL) and one year after (1Y) were picked up. (1) Clinical parameters influencing eGFR based on CysC were evaluated. (2) The chronic kidney dysfunction (CKD) stage using eGFR based on CysC and Cr were compared, and the matching rate and change from BL to 1Y were evaluated. (3) The control group with non-RA patients (nRA) was picked up, and the change from BL to 1Y for each CKD stage was compared to those in the RA group. [Results] A total of 353 for RA and 344 for nRA were picked up. (1) eGFR correlated significantly with age, serum albumin level, rheumatoid factor, and hemoglobin. (2) The eGFR matching rate decreased as age increased and the CKD Stage worsened. eGFR at 1Y was significantly lower than that at BL. This tendency was more significant as age increased, and the change from G2 was significantly more sensitive with CysC than with Cr. (3) There was no significant difference in the

change of eGFR between the RA and nRA. [Conclusions] eGFR based on CysC could catch more sensitive than on Cr.

## P2-086

**Features and the initial treatment response in the late-onset rheumatoid arthritis patients ~Comparison with the younger-onset rheumatoid arthritis patients~**

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Conflict of interest: None

[Objective] To compare the features of patients with rheumatoid arthritis whose onset was over 65 years of age (LORA) and patients whose onset was under 65 years of age (YORA), and to investigate the initial treatment response through T2T practice. [Methods] From January 2021 to July 2022, 74 cases of LORA (mean age 74.5 years, male/female 28/46) and 59 cases of YORA (50.7, 10/49) visited our hospital. Clinical data at diagnosis and one year after the initial treatment were compared. [Results] The mean period from onset to diagnosis of RA was 25 weeks. At diagnosis, shoulder pain was more common in LORA, and CRP, DAS28-ESR, RF, and ACPA were higher in LORA. Osteoarthritis grade 3 or higher according to the Kellgren-Lawrence classification was more common in the knee joint, thumb CM joints, and finger PIP/DIP joint in LORA, and the frequency of knee joint swelling was higher. HAQ7, 18, 19, 20 in LORA and HAQ-DI in LORA 12 weeks or more after the onset of RA were higher. Among anti-rheumatic drugs, SASP was used most often in LORA and MTX in YORA. Almost all clinical data improved to the same extent in both groups one year after starting treatment. [Conclusion] In the initial treatment of LORA, T2T practice resulted in clinical and functional remission comparable to that of YORA.

## P2-087

**5-year treatment continuation rate for early-stage and late-stage elderly patients with rheumatoid arthritis**

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Conflict of interest: Yes

[Objective] As the baby boomer generation reaches the age of 75 or older in 2025, the number of elderly patients with rheumatoid Arthritis (RA) is increasing. As systemic function declines with age, we are faced with the challenge of determining drug therapy to maintain clinical remission. [Methods] Of the 195 RA, 70 cases (36%) were in the elderly aged 70 years or older, 35 cases in the early elderly (70-74 years) and 35 cases in the late elderly (75 years or older). They were divided into two groups and the 5-year treatment continuation rate was investigated. [Results] The rate of continuation of hospital visits was significantly lower in late elderly patients than in early elderly patients (71% in 25 cases in the early vs. 34% in 12 cases in the late, p = 0.0019). The reasons for discontinuation were 8 cases of death, 12 cases of transfer or nursing home, 2 cases of malignant tumor, 2 cases of stroke, and 1 case of pneumonia. The incidence of complications was higher in the later elderly (51% in the early vs. 74% in the late). [Conclusion] Late elderly patients with RA are more likely to develop complications than early elderly patients, and difficulty in visiting hospitals.

## P2-088

**Changes in mHAQ and fracture occurrence in rheumatoid arthritis (RA) patients**

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Conflict of interest: None

[Objective] In this study, we examined the change in mHAQ in RA patients over 2 years and the occurrence of fractures in the following year. [Methods] Patients enrolled in NinJa for 4 consecutive years in 2002-2020 were sampled, and the change in mHAQ in the 1st-3rd year was classified according to whether or not it increased, and the fracture incidence rate in the 4th year was calculated. [Results] Classified by the change in mHAQ at 2-3 years, the number of fractures/cases was 298/17,474 in the ascended group and 433/50,677 in the non-elevated group of 68,151 cases, with significantly higher fractures occurring in the elevated group ($p<0.0001$). The number of cases was 88/4,163 in the group that increased for two consecutive years, 187/13,023 in the group that increased only in 1- 2 year, 205/13,018 in the group that increased only in 2-3 year, and 251/37,947 in the group that did not increase for two consecutive years. In the group that increased for 2 consecutive years, fractures were significantly higher than in the group that increased only in 1-2 year ($p=0.0038$) and in the group that increased only in 2-3 year ($p=0.0314$). [Conclusions] Patients with increased mHAQ for two consecutive years were significantly more likely to develop fractures the following year.

## P2-089

**Long-term changes in physical function of patients with rheumatoid arthritis-Comparison between elderly onset and young onset rheumatoid arthritis-**

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Conflict of interest: None

[Objective] At our hospital, we have been treating rheumatoid arthritis (RA) according to Treat to Target (T2T). The purpose of this study is to examine the long-term changes in physical function of patients with RA and to compare between elderly onset (EO) and young onset (YO) RA. [Methods] The subjects were 52 patients with RA who started treatment at our hospital and were able to be followed up for more than 3 years. There are 36 females and 16 males and the average age was 60.3 years old. The study was divided into two groups: those over 65 years old (EO) and those under 65 years old (YO). There were 21 patients (15 females and 6 males) in EO group, and 31 patients (21 females and 10 males) in YO group. We studied Health Assessment Questionnaire (HAQ) and Simplified Disease Activity Index (SDAI), and retrospective evaluations were performed until 3 years. [Results] The median values of HAQ at the start of treatment are 0.5 for EO group and 0.375 for YO group. After 3 years, the median values of HAQ are also 0 for both groups. Regarding disease activity, SDAI improved markedly in both groups after 6 months and was maintained for 3 years. [Conclusions] HAQ in the EO group was slightly higher than that in the YO group, but improved equivalently and was maintained for 3 years.

## P2-090

**Effect of concomitant use of statins on treatment outcomes of b/tsDMARDs: ANSWER cohort study**

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Conflict of interest: Yes

[Objective] We investigated the effect of concomitant statin therapy on the outcome of b/tsDMARDs. [Methods] We investigated RA patients naive to b/tsDMARDs. Those with a history of statin prescription were considered concomitant statin users. The blood lipid profile, disease activity, and the drug persistence rate due to treatment failure were examined. [Results] 3208 RA patients (2009 TNF inhibitors, 526 CTLA4-Ig, 494 IL6 receptor inhibitors, 179 JAK inhibitors) were analyzed. Of these, 482 were concomitantly treated with statins. There were no differences in disease activity or retention rate based on pretreatment lipid profiles. There was no difference in disease activity after initiation in b/tsDMARDs overall, with or without statins, but the drug persistence was significantly worse in the statin group. In comparison by mode of action, the statin group had a significantly worse retention rate with TNF inhibitors and IL6 receptor inhibitors, while the statin group had a significantly better retention rate with CTLA4-Ig and JAK inhibitors. Disease activity after induction by mode of action did not differ by statin use. [Conclusion] There was no difference in disease activity after b/tsDMARDs with or without statins, but there was a significant difference in drug persistence.

## P2-091

**Consider the use of biological DMARDs and JAK inhibitors in elderly rheumatoid arthritis and treatment goals**

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Conflict of interest: None

[Objective] We evaluated the use of biological DMARDs (bDMARDs) and JAK inhibitors (JAKi) in RA patients over the past 5 years and discussed future issues in the elderly. [Methods] 901 RA patients began treatment with either TNFαinhibitor (TNFi: n=226) or IL6 inhibitor (IL6i: n=294) or Abatacept (Abata: n=208) or JAKi (n=173). These patients were divided into 4 groups: A:250 patients (<65 years), B:259 (65≦years<75), C:224 (75≦years<85), D:68 (85≦). The discontinuation rates, and concomitant medications were examined. Disease actibity was also examined in patients who started treatment within 2 years of disease onset. [Results] As the transition from 2017 to 2023, patients treated with Abata decreased in groupB, C andD, and with JAKi increased remarkably. The discontinuation rates of TNFi were 51.3% (more in groupA), Abata: 47.6% (more in group C), IL6i: 23.1%, and JAKi: 26%. The rate who had difficulty of getting to hospital or transferred to a different hospital was higher in Abata (19.3%). [Conclusions] It will be important to concider the social background, including the hospital visit enviroment, drug and formulation selection, and collaboration with local hospitals in order to continue treatment.

## P2-092

**Outcome and rate of progression to Difficult-to-treat RA (D2T RA) in our department's first-time rheumatoid arthritis patients**

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Conflict of interest: None

[Objective] To investigate the clinical characteristics of patients with RA who first presented to our department, treatment, disease activity and progression to D2TRA. [Methods] Retrospectively, we analysed patient characteristics with RA who had a first visit to our department between April 2022 and October 2023. We defined D2TRA as RA with over moderate disease activity (CDAI > 10) despite the use of two or more different mechanism b/tsDMARDs. [Results] We analysed 103 patients. The median age was 69.0 years, female was 64.0%, RF-positive was 61.1%, ACPA-positive was 60.1%, and the median CDAI was 18.0. We evaluated 95 patients over 3 months, and the median observation period was 11 months. 33 (34.7%) patients were used 1st b/tsDMARDs: 7TNF-i, 13 IL-6-i, 7 ABT and 6 JAK-i patients. 8 (5.9%) patients transferred to 2nd b/tsDMARDs: 2 IL-6-i, 1 ABT and 5 JAK-i. The median CDAI at recent visit was 3.0, and 78 (82.1%) were controlled below low disease activity with CDAI. But, 14 patients (16.7%) remained at or above moderate disease activity, and 2 (2.1%) had progression to D2TRA. [Conclusions] About 80% of patients with RA who initially presented to our department were controlled below low disease activity. But in two cases (2.1%), progression to D2TRA during one year.

## P2-093

**Regarding the relation between bird-specific IgG antibodies and lung lesions with RA**

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Conflict of interest: None

[Objective] In patients with rheumatoid arthritis (RA), not only joint symptom but also lung lesions are often observed. In recent, Chronic hypersensitivity pneumoniti (CHP) has been reported among collagen lung diseases. The incidence rate of CHP is reported to be 0.3-0.9 per 100,000 people, the prevalence is reported to be 1.67-2.71 per 100,000. 60% of causative antigen is bird antigen. Chest CT in CHP typically shows fibrosis predominantly in upper lobes, mosaic pattern, and so on. We will focus on the relation between bird-specific IgG antibody (avian antibody) and lung lesions with RA (RA lung), and clarify whether the presence or absence of avian antibody causes differences in imaging patterns, clinical features, etc. [Methods] 55 RA patients with lung lesions in the medical record of our hospital are divided into two groups: avian antibody positive and avian antinody negative, analyzed retrospectively for clinical symptoms and image distribution on chest CT. [Results] 24 (43.6%) are found to be positive for avian antibody, indicating RA lung people have very high prevalence of avian antibody compared to the general. [Conclusions] There is trend toward mosaic pattern in RA lung with avian antibody. The avian antibody may play a role in defining the imaging pattern of RA lung.

## P2-094

**Association of serum anti-aminoacyl-transfer ribonucleic acid synthetase antibody levels with interstitial lung disease in rheumatoid arthritis**

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Conflict of interest: None

[Objective] Interstitial lung disease (ILD) is frequently complicated

with rheumatoid arthritis (RA). Anti-aminoacyl-transfer ribonucleic acid synthetase (ARS) antibodies (Abs) are associated with ILD in idiopathic inflammatory myopathies. However, there are few studies on anti-ARS Abs in RA. We investigated whether anti-ARS Abs are associated with ILD in RA. [Methods] Anti-ARS Abs were measured in sera from RA patients by enzyme-linked immunosorbent or line blot assay. [Results] Anti-ARS Ab levels were higher in RA patients with ILD ($P$=5.58×10$^{-12}$), usual interstitial pneumonia ($P$=3.14×10$^{-12}$), and nonspecific interstitial pneumonia ($P$=5.07×10$^{-5}$) than without chronic lung disease. The area under the curve (AUC) value of the receiver operating characteristic curve for anti-ARS Ab was not sufficiently high to discriminate between RA patients with or without chronic lung disease (0.608). Multiple logistic regression analyses of anti-ARS Abs, age, Steinbrocker stage, and smoking status generated an ARS-index with a higher AUC value (0.707). [Conclusions] Anti-ARS Abs were associated with ILD in RA. Anti-ARS Abs might be involved in the pathogenesis of ILD in RA.

## P2-095

**A case of interstitial pneumonia with acute exacerbation after SARS-Cov-2 vaccination during treatment of rheumatoid arthritis**

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Conflict of interest: None

[Case] 75 years old male The patient developed rheumatoid arthritis 13 years ago and was currently in remission. He was injected with SARS-Cov-2 mRNA vaccine in June X. Six days later, he developed dyspnea and was urgently admitted to our hospital. He was hypoxic with SpO2 around 90%, and a CT scan showed new frosted and reticular shadows in both lungs. We treated him with antibacterial drugs, but he did not improve. We considered it as an acute exacerbation of interstitial pneumonia (ILD) and treated him with steroid pulse therapy for 3 days. On the sixth day, his dyspnea improved. He was treated with prednisolone (PSL) 60 mg/day (1 mg/kg/day), and his oxygen demand disappeared on the 13th day. He continued to do well after that, and PSL was tapered down to 40 mg/day, and he was discharged from the hospital on the 38th day of his illness. [Discussion and Clinical Significance] Acute exacerbation of RA-ILD is considered to be refractory to treatment and has a poor prognosis. However, the patient's response to steroid therapy was good. Existing reported cases of ILD after SARS-Cov-2 vaccination show a relatively good response to steroids. The vaccination may have contributed to ILD exacerbation in this case as well, and we report this case with a discussion of the literature.

## P2-096

**Survey on the current status of rheumatoid arthritis with lung disorder at our hospital**

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Conflict of interest: None

[Objective] We conducted a retrospective study using real-world data to clarify the current status of how monitoring methods and treatments differ between RA-ILD and non-RA-ILD groups. [Methods] The subjects were 311 RA patients treated by 8 collagen disease internists at our hospital on August 2023. Divided into two groups: RA-ILD group (n=57) and non-RA-ILD group (n=254), data on test frequency, type, and treatment details were extracted from medical records for 5 years from 2019 to 2023, and statistics were conducted. [Results] Number of chest X-rays (9±10 times VS 4±4, P<0.0001), number of respiratory function tests (2±3 times VS 0±1 times, P<0.0001), amount of prednisolone used (3±5.25 mg/day VS 0±2 mg/day, P<0.0001) was higher in the RA-ILD group. There was no difference in number of hospitalizations (0 ± 1 times/5 years for both groups, P = 0.635), JAK inhibitor usage rate (7.0% VS 3.9%, p = 0.31), bDMARDs usage rate (27.4% VS 7.8%, P = 0.18), and the annual forced vital capacity change (-0.03±0.11 L/year VS -0.01±0.32 L/year, P=0.44) between the two groups. [Conclusions] Although RA-ILD patients are monitored more frequently than non-RA-ILD patients, it has become clear that there is a difference in treatment only in the amount of prednisolone used.

## P2-097

**Questionnaire on Adverse Events for Rheumatoid Arthritis Patients Taking Oral Methotrexate**

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Conflict of interest: None

[Objective] Methotrexate (MTX) is the primary conventional synthetic disease-modifying antirheumatic drug (csDMARD) used as a first-line treatment for Rheumatoid Arthritis. However, there is limited knowledge regarding adverse events associated with oral MTX in real-world settings, particularly in clinical practice. To address this, we administered several questionnaires to 331 RA patients. [Methods] In this study, we utilized the MISA questionnaire (Japanese-translated version) to assess gastrointestinal events related to oral MTX. [Results] Among the 220-240 patients surveyed, no adverse events were reported in any of the main questionnaire items concerning oral MTX. Specifically, 35 patients reported experiencing nausea after taking the drug, 39 reported stomach discomfort, 21 reported appetite loss or abnormal taste, 47 reported fatigue or lethargy, 17 reported irritation or anxiety, and 14 reported diarrhea or fever. In an additional questionnaire, 33 patients reported stomatitis, and 67 reported loss of hair. Notably, 42 patients expressed interest in subcutaneous MTX, which is known to reduce gastrointestinal symptoms. [Conclusions] This questionnaire system reveals that 20-30% of patients taking oral MTX experience some form of adverse event.

## P2-098

**Clinical reality of MTX dose reduction and discontinuation in RA patients**

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Conflict of interest: None

[Objective] To clarify the actual situation of MTX dose reduction and discontinuation in RA clinical practice. [Methods] In 61 RA patients under follow-up, we investigated the previous MTX treatment, continuation status, dose change, treatment modification, current disease activity, and adverse events. [Results] MTX was introduced in 40 patients (66%), with a maximum dose ranging from 4 to 16 (mean 10.5 ± 4.2) mg/W and a maintenance dose ranging from 0 to 16 (mean 5.2 ± 4.9) mg/W. Of these, 12 patients (30%, group C) continued on the maximum dose, 20 (50%, group AD) had dose reduction/stop due to adverse events, and 8 (20%, group RD) had dose reduction/stop due to remission. 13 (65%) of patients in group AD had treatment modification. At the last observation, SDAI was predominantly higher in the AD group than in the C group (7.6±7.2 vs 1.8±1.7, P=0.012). SDAI remission/low disease activity or less was achieved in 75/100% of patients in the C group, 40/70% in the AD group, and 75/100% in the RD group. The adverse events were resolved in all patients after MTX dose reduction or discontinuation. [Conclusions] MTX was reduced or discontinued as necessary to ensure safety after induction of therapy, and treatment was changed as necessary.

## P2-099

**A case of rheumatoid arthritis (RA) with other iatrogenic immunodeficiency-associated lymphoproliferative disorders (OIIA-LPD) found as iliac and sacral tumor**

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Conflict of interest: None

OIIA-LPD in RA is said to be more likely to occur in patients who are older, have had a long illness, have high disease activity, or are taking

immunosuppressive drugs such as methotrexate (MTX) at high doses or for a long period of time. The patient is a 72-year-old man who developed RA 1 year and 10 months ago. He had high disease activity from early onset and the arthritis persisted even after taking small doses of steroids and multiple conventional synthetic disease modifying anti-rheumatic drugs (bucillamine 200 mg/day, MTX 10 mg/week, tacrolimus 2.5 mg/day), so abatacept 125 mg/week subcutaneous injection was added 1 year ago to maintain low disease activity. About 2 weeks before the scheduled outpatient visit, he noticed pain in his right buttock for no apparent trigger and had multiple orthopedic visits for X-rays and MRI, the cause was not found. However, blood tests revealed elevated levels of CRP and LDH, and a CT scan and a MRI revealed tumorous lesions in the ilium and sacrum, and biopsy results of the sacrum ultimately led to the diagnosis of diffuse large B-cell lymphoma (DLBCL). Although the disease duration is not long and the site is rare as an extranodal lesion, it is clinically significant to know the pathology of the disease as in this case.

## P2-100

**A case of death with rapidly progressive glomerulonephritis at the onset of methotrexate-associated lymphoproliferative disease**

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Conflict of interest: None

[Case] An 87-year-old woman was diagnosed with rheumatoid arthritis (RA) in X-10 and received oral methotrexate (MTX) 10 mg/week, leading to clinical remission. In January X, she was admitted to an orthopedic department for treatment of a fracture and continued rehabilitation. In April X, she developed fever, thrombocytopenia, and elevated creatinine and was referred to our department. We suspected a side effect of MTX and had her stop taking it. She had red blood cell casts in urinary findings and was diagnosed with rapidly progressive glomerulonephritis (RPGN). Further examination revealed a positive fecal occult blood test, and lower gastrointestinal endoscopy revealed multiple neoplastic lesions, which were determined to be diffuse large B-cell lymphoma. Although steroids were started as preliminary treatment for lymphoma, there was no response, and she died in the end. Her pathological autopsy revealed lymphoma infiltration all over her body. [Discussion] It is known that some patients using MTX develop lymphoproliferative disease (MTX-LPD). While it is known that RPGN occurs in LPD patients, it is rare for RPGN to occur in MTX-LPD patients. We report them together with the microscopic findings of the pathological autopsy.

## P2-101

**Underlied Vitamin B12 metabolic abnormality is related to AE of MTX**

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General Internal Medicine, Tenri Hospital

Conflict of interest: None

A 50 y.o. female came to our hospital because of cough and fever. She had been treated as RA by csDMARDs including MTX for 13 years in our hospital. On August of certain year she went back to her hometown, where she complaint high grade fever and transferred to nearest hospital and prescribed some antibiotics under the diagnosis of pneumonia. When she returned to her house, again high fever recurred and pneumonia still on-going and therapy continued. There blood test showed thrombocytopenia and elevation of LDH level to 497, and macrocytic anemia. The physician thought that adverse effect of MTX became apparent by pneumonia. She was referred to our hospital after cessation of MTX. Thereafter she was treated by using several biologics with moderate effect. Two years after, she was pointed out to have macrocytic anemia again but this time without MTX. Blood level of vitamin B12 was low and gastrointestinal fiberscope revealed atrophic gastritis with positive intrinsic factor antibody, which showed she had “autoimmune gastritis”.

## P2-102

**A study of rheumatoid arthritis patients with tocilizumab for more than 10 years**

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Conflict of interest: None

[Objective] To evaluate the outcomes of patients with tocilizumab (TCZ) for rheumatoid arthritis (RA) more than 10 years after initiation of treatment. [Methods] 15 RA patients with TCZ for more than 10 years were included in our department. Patient demographics, disease activity, methotrexate (MTX) and prednisolone (PSL) combination rates, TCZ continuation rates after 10 years, reasons for changing TCZ, and drugs changed were evaluated. [Results] Patient demographics at the start of treatment was as follows: mean age 60.4 years, mean duration of RA 8.9 years, 1st bio 0 cases, 2nd bio 13 cases, and 3rd bio 2 cases. Mean SDAI improved from 26.80 at start, 7.71 at 1 year, 5.40 at 3 years, 4.08 at 5 years, 3.65 at 7 years, and 2.33 at 10 years. Mean DAS28-ESR improved from 4.80 at start, 2.12 at 1 year, 1.81 at 3 years, 1.59 at 5 years, 1.39 at 7 years, and 1.36 at 10 years. 12 patients used MTX at start and 6 at 10 years. 6 patients used PSL at start and 2 at 10 years. The average duration of TCZ use was 11.8 years. At the time of observation, 4 patients were still on TCZ, 2 were switched to JAK inhibitors due to inadequate response, 1 patient discontinued TCZ due to adverse events. [Conclusions] Long-term clinical results with TCZ were good, but caution is needed regarding adverse events.

## P2-103

**Characteristics of clinical test values before the administration of sarilumab in our clinic and its impact on disease activity**

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Conflict of interest: None

[Objective] Here, we investigated the influence of pre-administration laboratory test values on salimumab (SAR) on disease activity, and will present its characteristics and potential for increasing efficacy. [Methods] In 38 cases treated for SAR at our hospital, we investigated pre-administration laboratory test values and investigated the influence of these values on subsequent disease activity. Morning stiffness time, fatigue (Pt. VAS), and SDAI were used to evaluate disease activity. [Results] The clinical test values before administration exhibited certain trends, including low Hgb, high platelet counts, low ALB, high CRP, and IgG levels in many cases. These values were scored: low Hgb (<13.7 for men, <11.6 for women), high platelet count (≧348,000), low ALB (<3.9), low AST (<16), low ALT (<15), high CRP (≧0.3), and high IgG (≧1,300). Patients with scores of 0 to 2 points had lower continuation rates, while those with scores of 6 to 7 points or more tended to show better SDAI improvement. [Conclusions] This time, we investigated the influence of clinical test values before SAR administration on subsequent disease activity, but we would like to add more cases and investigate whether there are any other effective markers other than those mentioned above.

## P2-104

**Outcome of Salirumab in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To evaluate the continuation rate of patients with rheumatoid arthritis treated with sarilumab (SAR) in terms of efficacy and adverse events. [Methods] Of the RA patients who started treatment with SAR at our hospital, 44 patients who could be followed up for at least 1 year after the start of SAR were included. We investigated the continuation rate of SAR, and whether discontinuation due to inadequate efficacy or adverse events was associated with background factors. [Results] The 1-year con-

tinuation rate of SAR was 68%. At the last observation, 8 patients discontinued due to inadequate response and 12 patients discontinued due to adverse events. There were no discontinuations due to inadequate response and only one discontinuation due to an adverse event among the 15 patients who received SAR as their first line. AE discontinuations were associated with platelet count (p=0.02) and white blood cell count (p=0.03) at the time of SAR induction. No significant differences were found for other items. [Conclusion] Patients who used SAR as their first Bio were more effective and had fewer adverse event discontinuations. There was a trend toward more discontinuations due to adverse events in patients with low platelet counts at induction and in those without high WBC.

## P2-105

**Efficacy and Safety of Sarilumab in Patients with Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] To investigate the efficacy and safety of sarilumab (SAR) in RA patients in our department. [Method] Clinical data were reviewed retrospectively from their medical records of RA patients who received SAR and were observed for 104 weeks in our department and Ogawa Red Cross Hospital. [Results] Forty patients were eligible. mean age; 61.0 years, mean disease duration; 7.25 years, mean CDAI; 19.10. Biologics (Bio) or JAK inhibitors (JAKi) were used in 28 cases (1 drug: 11 cases, 2 drugs: 7 cases, 3 or more drugs: 10 cases), and of the 40 patients 20 (50%) continued SAR for 104 weeks. The reason of discontinuation included five adverse events (hair loss, rash, itching, anorexia and malaise, liver dysfunction), 14 inadequate response, and 1 economic reason. Of the 20 patients who were able to continue SAR for 104 weeks, 13 had a history of using Bio/JAKi (1 drug: 5 patients, 2 drugs: 4, 3 or more: 4). After 104 weeks, mean CDAI significantly improved from 19.47 to 4.26, it also significantly improved from 13.36 to 5.13 among 13 patients who had used other Bio/JAKi. The rate of low disease activity increased from 38.5% to 92.3%. [Conclusion] The continuation rate of SAR for 104 weeks was 50%. Despite switching from other Bio/JAKi, SAR remained effective after 104 weeks.

## P2-106

**Retrospective study of clinical efficacy differences between non-TNF inhibitors, abatacept and sarilumab in our cases**

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Conflict of interest: Yes

[Objective] To clarify if there is a difference in clinical efficacy between selective T-cell co-stimulation modulators and IL-6 inhibitors, we retrospectively examined abatacept (ABT) and sarilumab (SAR) groups. [Subjects/Methods] RA patients who had received ABT or SAR at Dept. of Rheumatology and Applied Immunology, Saitama Medical University and Dept. of Rheumatology, Red Cross Ogawa Hospital were included in the study. Patients who had begun treatment with either drug within 4 years of insurance coverage were chosen, and the continuation rate and treatment efficacy after 52 weeks were evaluated. Treatment efficacy was evaluated by DAS28-4/ESR and CDAI. [Results] Within 4 years of insurance coverage, ABT was administered to 29 patients and SAR to 40. 20 patients in ABT group and 28 in SAR group remained in the study for 52 weeks. DAS28 and CDAI improved from 4.88/21.24 to 2.89/3.14 in ABT group and from 4.99/18.61 to 2.16/3.60 in SAR group respectively with significant differences. However, there was no significant difference between ABT and SAR groups. [Conclusions] The efficacy of ABT and SAR in RA was confirmed, but the difference in clinical efficacy was not clarified. Further, we will increase analysis cases and stratify them by other drug use, etc. for discussion.

## P2-107

**The Treatment Outcomes of Sarilumab for Rheumatoid Arthritis at Our Institution**

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Conflict of interest: None

[Objective] IL-6 is a promising therapeutic target for rheumatoid arthritis (RA). In this study, we assessed the utility of sarilumab (SAR) in patients undergoing treatment at our hospital. [Methods] We conducted a retrospective investigation of patient backgrounds, disease activity changes, the use of methotrexate (MTX) and prednisolone (PSL), and SAR continuation rates for 35 RA patients who initiated SAR from April 2019 to April 2023. [Results] The average age was 65.5 years, and 85.3% of the patients were female, with an average RA duration of 109 months. There were 11 cases (31.4%) with no history of biological agents or JAK inhibitors. The average SDAI was 22.2 at baseline, which decreased to 11.9 at one month, and 4.18 at six months. The SDAI remission rate at six months was 53.1%. The average MTX dose and usage rate decreased from 8.27 mg/week at the beginning to 6.67 mg/week in 42.9% at six months, 34.3%. The average PSL dose and usage rate decreased from 5.48 mg/day at baseline to 3.82 mg/day in 72.2% at six months, 45.7%. The SAR continuation rate was 82.9% at six months and 74.3% at one year. [Conclusions] SAR exhibited a rapid onset of efficacy, and there were numerous discontinuations in the early stages of treatment.

## P2-108

**Examination of the inhibitory effect on finger and medium-large joint destruction by Sarilumab**

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Conflict of interest: None

[Purpose] To investigate the clinical effectiveness, joint destruction inhibition effect, and safety of Sarilumab in 27 cases of progressive joint disease over the course of one year." [Methods] Clinical effectiveness was assessed using DAS28-CRP, patient VAS, Pain VAS, and joint destruction inhibition effect was evaluated using the mTSS method (small joints) and Larsen method (medium and large joints). Additionally, MRI assessments included OMERACT criteria for bone marrow edema. Adverse events were also examined. [Results] At the time of treatment and at 1, 3, 6, and 12 months, DAS28-CRP values were 4.63, 3.10, 2.92, 2.60, and 2.42, respectively. PainVAS scores were 64.4, 43.8, 35.1, and 27.4, showing significant improvement from baseline at all time points ($P<0.01$, Paired t-test). Clinical improvement was observed in both small joint and medium-large joint involvement cases, with most cases showing improvement in joint destruction on X-rays and bone marrow edema on MRI. No serious adverse events leading to discontinuation were observed. [Conclusion] Sarilumab was confirmed to be effective in cases with rapid progression and bone marrow edema.

## P2-109

**The efficacy and safety of tocilizumab against elderly onset RA**

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Conflict of interest: None

[Object] To clarify the efficacy and safety of tocilizumab (TCZ) against elderly onset RA (EORA). [Methods] The response to TCZ was evaluated in 58 patients (female 46, male 12) who developed RA at 65 years old or over. TCZ treatment was initiated after mean disease duration of 3.3 years in female and 4.9 years in male, with no less than 1 year of TCZ treatment completed between May 28, 2008, and August 31, 2023. TCZ efficacy was evaluated using the DAS28-ESR, C-reactive protein levels, and matrix metalloproteinase 3 (MMP-3). [Results] The mean DAS28-ESR decreased from 4.66 at baseline to 2.44 and 1.49 at 1 month and 1 year, respectively in female. Similarly, it decreased from 4.56 at baseline to 2.47 and 1.36, respectively, at 1 month and 1 year, respectively in male. There were no "no response" cases. Swollen joint count decreased to 1 or less within 6 months in all patients. The value of MMP-3 decreased from 283.7 ng/ml to 75.1 ng/ml at 1 year in female. It also decreased from 296.9 ng/ml to 129.6 ng/ml at 1 year in male. Corticosteroids were administrated in 15 patients at baseline and the amount of corticosteroid could be reduced in all of them. The adverse event was not increased. [Conclusions] TCZ demonstrates high efficacy and a favorable safety profile even in EORA patients.

## P2-110

**Clinical usefulness of sarilumab at24 weeks in 43 patients**

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Conflict of interest: Yes

[Objective] Clinical usefulness and treatment continuation following 24 weeks of Sarilumab (SAR) in rheumatoid arthritis (RA) patients were investigated. [Methods] Subjects were 60 analyzable patients introduced to SAR at the author's institution from Dec. 2018 to Sep. 2022. Mean age was 60.1 years, mean duration of illness 11.6 years. Most of the patients (55 patients) were switched from patients inadequate response to TNF inhibitors. 34 patients were treated with MTX and 26 patients were not treated with MTX. The course of DAS28 (ESR), HAQ and remission rate were analyzed. [Results] Overall DAS28 (ESR) remission rate showed clinical remission in 61% of patients from 4 weeks, and achieved 83% from 12 weeks, after that this condition continued. Overall HAQ remission rate at 24 weeks was 63%, which is considered a good result considering the average disease duration of 11.6 years, and the large number of Stage4 and switch cases. [Conclusions] SAR is effective even in patients without MTX and with inadequate response to TNF inhibitors, and the time to onset of effect is rapid.

## P2-111

**The efficacy of sarilumab at 1 year in patients with rheumatoid arthritis in our institution**

Masayuki Murai[1], Kota Imaizumi[1], Yayoi Hashiba[1], Kazuyoshi Kubo[1], Atsushi Matsuoka[2], Hiroshi Kuroda[2], Toshihiko Hidaka[1]
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Conflict of interest: None

[Objective] We assessed the efficacy and safety of sarilumab (SAR) in patients with rheumatoid arthritis. [Methods] Sixty-nine RA patients were initiated SAR in our institution from June 2018 to July 2023, and 62 of them were continued SAR over three months. DAS28-ESR and CDAI were assessed at the point of 0,1,2,3,6,12 months. We investigated about adverse events within 1 year. [Results] The mean DAS28-ESR/CDAI was 5.57/26.89 at start, 3.36/11.57 at 1 month, 2.63/9.80 at 2 months, 2.32/7.70 at 3 months, 2.15/6.80 at 6 months and 2.12/6.70 at 1 year, with significant differences 1 month later onward ($p<0.001$/$p< 0.001$). DAS28-ESR/CDAI remission rates were 3.2%/1.6% at start, 64.5%/33.9% at 3 months, 71%/45.2% at 6 months, 74.2%/43.5% at 1-year, low disease activity or less was 4.8%/6.5% at start, 75.8%/72.6% at 3 months, 83.9%/75.8% at 6 months and 82.3%/79% at 1 year. Serious adverse events requiring hospitalization were 1 lung abscess, 2 community-acquired pneumonia, 1 disseminated herpes zoster, 1 pyelonephritis, 1 cholecystitis, 1 cellulitis, 1 subcutaneous hematoma, and 1 malignant lymphoma. [Conclusions] SAR reduced RA patients' disease activity early in the initiation phase and the effect was sustained. The majority of serious adverse events were infections.

## P2-112

**The clinical outcome of abatacept in patients with RA from Niigata Orthopedic Surgery Rheumatoid Arthritis Database (NOSRAD)**

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Conflict of interest: None

[Objective] To examine efficacy and safety of abatacept (ABT) for patients with rheumatoid arthritis (RA). [Subjects and Methods] Fifty-two cases with RA who were administered with ABT from Niigata Orthopedic Surgery RA Database (NOSRAD) were registered in this study. The average age on administration was 68 years old. The average RA disease duration was 13.7 years. Time courses of DAS28 at the administration, 3 months, 6 months, and 12 months after the administration were analyzed. In addition, the 1-year retention rate and adverse event were examined. [Results] MTX was used in 21 cases and its dose was 7.1 mg/week on average. PSL was used in 25 cases and its dose was 5.8 mg/day on average. The average DAS28 was 3.20 at the administration, and significantly decreased to 2.44 ($p<0.001$) at 6 months, and to 2.17 ($p<0.001$) at 12 months after the administration. DAS28 was also significantly improved even with or without MTX, and even with more than 65 years old or under 65 years old. One-year retention rate of abatacept was 66.7%. No severe adverse events occurred but SLE was observed in 1 case. [Conclusion] ABT showed good efficacy in spite of MTX and age without severe adverse events.

## P2-113

**A case of mycosis fungoides that developed while using MTX and improved after switching to TCZ**

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Conflict of interest: None

[Objective] Methotrexate (MTX) is considered an anchor drug for the treatment of rheumatoid arthritis (RA), but attention should be paid to serious adverse events such as MTX-associated lymphoproliferative disease (MTX-LPD). We report a case of mycosis fungoides that developed during MTX therapy. The patient's symptoms improved after initiation of tocilizumab (TCZ). [Case Description] A 50-year-old woman was diagnosed with RA in X-8 and started treatment with MTX. The disease activity was in remission, but in March X-1, non-remitting skin rash appeared on her upper limbs. She visited our dermatology department. MTX was discontinued on suspicion of MTX-LPD, and after remissions and flare-ups of skin findings, mycosis fungoides was finally diagnosed. During the course of the disease, worsening of RA activity was observed, and she was referred to our department in June of X year. Her symptoms improved after initiation of tocilizumab (TCZ). [Conclusion] In this case, the skin rash that developed during MTX treatment was suspected to be MTX-LPD, and MTX was discontinued, but the skin rash repeatedly improved and worsened, eventually leading to a diagnosis of mycosis fungoides. The patient's joint symptoms worsened after discontinuation of MTX, and TCZ was started to stabilize the symptoms.

## P2-114

**The Therapeutic Efficacy of Sarilumab for RA in Juntendo Koshigaya Hospital**

Kazuhisa Nozawa[1,2], Shihoko Nakajima[1,2], Issei Kida[1], Shigeto Kobayashi[1], Ken Yamaji[2], Naoto Tamura[2]
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Conflict of interest: None

(Objective) IL-6 has a pivotal role for pathogenesis of RA. The blockade of IL-6 by administration of biologics plays an important role for the treatment with RA. At the moment, the 2 type of biologics for IL-6 blockade were available and Sarilumab has been known as a strong inhibitor for IL-6 signal mediated by powerful binding to IL-6 receptors. Therefore, we investigated the therapeutic effects of Sarilumab in 42 RA patients treated with Sarilumab in our hospital (observation period from 3 to 54 months) by evaluating the persistence rate and the efficacy in addition to analyzing the clinical profile with the patients. (Results) The persistence rate was 73.9%. The efficacy was evaluated by CDAI at 24 weeks after the treatment and CDAI decreased from 26.1 (baseline) to 7.5 (24 weeks after). The remission rate was 14.8%. Salilumab treatment was effective not only Biologics naïve patients but also Biologics switched patients even the patients switched from Tocilizumab. (Conclusions) Salilumab was useful and sustainable biologics for the treatment with RA if the patients overcome early withdrawal such as primary invalid response and adverse events of Salilumab.

## P2-115

**Application of sarilumab for patients with rheumatoid arthritis**

Masashi Aso[1], Yuya Takakubo[1], Jun Nagai[1], Yoshihiro Wanezaki[1], Yang Suran[1], Ryusuke Honma[1,2], Michiaki Takagi[1]
[1]Yamagata University Faculty of Medicine Department of Orthopaedic, [2]Department of Orthopaedic Surgery, Okitama Public General Hospital

Conflict of interest: None

[Background] Sarilumab has spread its use since it was approved in 2017 in Japan. We investigated the use of sarilumab for patients with RA who received sarilumab at our hospital. [Methods] Nine patients with RA who received sarilumab at our hospital were included from 2017 to 2022. All patients were female, mean age was 58.7 (38-74) years, and mean follow-up period was 21.2 (1-65) months. Evaluation items encompassed CRP, ESR, C-DAI, and the occurrence of complications. [Results] During the follow-up period, sarilumab could be continued in 5 patients. The mean value of CRP decreased from the mean 0.9 (0-3.3) mg/dL before induction to negative within 4 weeks. The mean ESR decreased from 42.0 (2-84) mm/h to 10.4 (2-23) mm/h after 4 weeks. The mean C-DAI improved from 22.7 (13-35) to 6.3 (0-12) at final observation. Because complications manifesting as skin rash, thrombocytopenia, and hepatic dysfunction occurred in 4 patients, sarilumab was quitted after them. [Discussion] In this study, CRP and ESR improved immediately after induction. On the other hand, there were 4 cases of discontinuation due to skin rash, decreased white blood cell counts, and liver dysfunction. These are typical adverse events of sarilumab, and caution should be exercised during administration.

## P2-116

**Sarilumab Drug Survival: A Real-World Analysis at St. Luke's International Hospital in Japan**

Hiromichi Tamaki[1], Sho Fukui[1,2], Masato Okada[1]
[1]Immuno-Rheumatology Center, St. Luke's International Hospital, St. Luke's International University, [2]Department of Emergency and General Medicine, Kyorin University Faculty of Medicine

Conflict of interest: Yes

[Objective] Sarilumab, an interleukin-6 receptor inhibitor for Rheumatoid Arthritis (RA) treatment, is examined in our Japanese real-world experience at St. Luke's International Hospital. [Methods] We retrospectively reviewed Sarilumab-treated patients at St. Luke's International Hospital, Tokyo [Results] A total of 62 patients were identified, with one patient excluded due to lack of consent for data use. We analyzed data from 61 patients, of which 84% were women. The median disease duration was 6 years (2-9). Seventy-five percent were Rheumatoid Factor positive, 75% anti-CCP antibody positive, and 15% had Interstitial Lung Disease (ILD). Concurrently, 24 used methotrexate, 87% used a conventional synthetic DMARD, and 26 used glucocorticoids. Moreover, 52 had prior biological (b) or targeted synthetic (ts) DMARD experience. We assessed drug survival and factors using Kaplan-Meier curves and log-rank tests. No prior b or ts DMARD usage associated with superior drug survival, followed by one or two modes of action (MOA), with three MOAs showing the lowest survival. Sarilumab survival was lower if patients used abatacept or JAK inhibitors before. [Conclusions] Sarilumab exhibited relatively good continuation. Previous b or ts DMARD use impacted Sarilumab drug survival.

## P2-117

**Comparative Study of Abatacept and IL-6 Inhibitors in Rheumatoid Arthritis with Interstitial Lung Disease**

Akiko Kitagawa[1], Rinko Katsuda[1], Masayuki Azukizawa[2], Kohei Miyake[3], Misuzu Fujimori[1]
[1]Rheumatology, National Hospital Organization Himeji Medical Center, [2]Orthopedics, National Hospital Organization Himeji Medical Center, [3]Pulmonary Medicine, National Hospital Organization Himeji Medical Center

Conflict of interest: None

[Objective] This study aims to compare the effectiveness and safety of abatacept (ABT) and IL-6 inhibitor (IL-6i) treatments in patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD), as limited reports have examined non-TNF inhibitors against each other. [Methods] Twenty-five patients with RA with ILD treated at our department from 2012 to 2022 who received ABT or IL-6i (ABT: 7 patients, IL-6i: 18 patients) were included. Data before and 1 year after treatment were extracted from medical records. [Results] All 7 patients in the ABT group and 13 (72%) in the IL-6i group remained on treatment at 1 year. 5 (71.4%) in the ABT and 11 (84.6%) in the IL-6i had moderate or good improvement in disease activity based on EULAR criteria by DAS28. ILD on chest CT improved in 3 patients (42.9%) in the ABT and 4 (30.8%) in the IL6i. ILD worsened in 0 patients in the ABT and 3 (23%) in the IL-6i. Only 1 patient (14.3%) in the ABT and none in the IL-6i was hospitalized within 1 year due to infectious pneumonia. [Conclusion] In RA with ILD, ABT and IL-6i showed no significant difference in improvement of RA disease activity, improvement or worsening of ILD, or hospitalization for infectious pneumonia. Further studies with a larger number of patients are warranted.

## P2-118

**Efficacy and corticosteroid dose reduction effect of tocilizumab in patients with elderly-onset rheumatoid arthritis in real clinical practice**

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Conflict of interest: None

[Objective] To clarify the clinical efficacy and corticosteroid dose reduction using tocilizumab (TCZ) in patients with EORA in clinical practice. [Methods] This retrospective observational study enrolled EORA patients who received TCZ from January 2019 to February 2022. The clinical efficacy and the effect of corticosteroid dose reduction of TCZ with and without MTX up to 52w were evaluated. [Results] This study was comprised consecutive 34 EORA patients treated with TCZ (12 with MTX, median age 71 y. o and 22 without MTX, median age 75 y. o, at onset). The remission rates of SDAI (0w, 52w) were 0.0%, 50.0% in the MTX group and 0.0%, 45.5% in the MTX non-combination group, respectively. The HAQ remission rate at 52w increased (33.3% vs 58.3% in the MTX group, 31.8% vs 59.1% in the MTX non-combination group, 0w vs 52w). The rate and dose of corticosteroid were significantly lower at 52w compared with at the baseline (31/34 (91.2%) vs 22/31 (71%), 9.2 mg vs 3.6 mg a day on average, 0w vs 52w, $p<0.05$), and 7/31 (22.6%) patients were able to discontinue corticosteroids at 52w. [Conclusions] TCZ for

EORA is effective with or without MTX, and the ability to reduce the dose of corticosteroids suggests the possibility of safer treatment.

## P2-119

**Efficacy of sarilumab in rheumatoid arthritis and its efficacy in reducing the dose of glucocorticoid and methotrexate**

Yoichiro Haji[1], Sho Higuchi[1], Mirai Hozumi[1], Yukina Yokoyama[1], Yui Amari[1], Mizuki Kato[1], Mitsuru Watanabe[1], Tatsuo Watanabe[2], Takanori Ito[1]
[1]Rheumatology, Daido Hospital, [2]Rheumatology, Daido Hospital

Conflict of interest: Yes

[Objective] To evaluate the efficacy and safety of sarilumab (SAR) in the treatment of rheumatoid arthritis (RA) and the effect of reducing the dose of concomitant glucocorticoids (GC) and methotrexate (MTX). [Methods] RA patients aged 18 years or older who had received SAR by July 31, 2023, were included in the study. Disease activity was evaluated from the start of SAR to 4, 8, 12, and 24 weeks, as well as on the date of the last visit. Also, concomitant GC and MTX on the last visit was evaluated. [Results] 37 patients used SAR, median age 73.0 years, disease duration 2.6 years, seropositivity 78.6%, 67.6% had been treated with bDMARD, disease activity at the start of treatment was DAS28CRP 4.0, CDAI 17.0. 38.2% (13 patients) used MTX, 26.5% (9 patients) used GC. Complications were interstitial pneumonia in 9 patients and malignancy in 6 patients. Efficacy was DAS28CRP 2.3, CDAI 5.5 at 4 weeks, and DAS28CRP 1.1, CDAI 2.0 at last visit. The number of patients who continued SAR with MTX was reduced from 9 to 3, and the number of patients who continued SAR with GC was reduced from 7 to 1. [Conclusions] SAR showed clinical efficacy at an early stage, and the effect on the reduction of MTX and GC was also observed.

## P2-120

**The efficacy of Tocilizumab therapy in D2T rheumatoid arthritis**

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Department of Orthopedics Surgery, Chuno Kosei Hospital, Seki City, Japan

Conflict of interest: None

[Objective] To evaluate the efficacy in tocilizumab therapy with rheumatoid arthritis (RA) and tapering of methotrexate. [Methods] This study comprised 45 patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received tocilizumab therapy with methotrexate for 12 months. The outcomes were assessed with the disease activity during 12 months study period, using the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28 ESR) and Clinical Disease Activity Index (CDAI). [Results] DAS28ESR (from 3.3 to 1.4) and CDAI (from 4.6 to 0.3) decreased significantly from baseline to Week 52. DAS28ESR Remission achieved in 43 cases at Week 52. Tocilizumab monotherapy was also effective with RA patients of in adequate response to antiTNF inhibitor therapy. The retension rate of tocilizumab at 52 weeks was 89%. The average dose of methotrexate tapered from 5.6 mg to 3.2 mg. The average dose of glucocorticoid also tapered from 1.4 mg to 0.1 mg. [Conclusions] These results suggested that tocilizumab therapy is effective in patients with RA of an inadequate response to other biologic DMARDs.

## P2-121

**Treatment of Sarilumab for elderly-onset rheumatoid arthritis difficulted to differentiate from Polymyalgia Rheumatica**

Atsunori Murase
Orthopedics Surgery, Kasugai Joint & Sports, Pain, Orthopedics Clinic, Kasugai, Japan

Conflict of interest: None

[Objective] Problems with elderly-onset rheumatoid arthritis (EORA) include the need for adjustment of MTX due to decreased renal function, complications of osteoporosis, and cases that are difficult to distinguish from polymyalgia rheumatica (PMR). In this study, we report the treatment for EORA patients who were difficult to differentiate from PMR using sarilumab, a human-type IL-6 receptor monoclonal antibody. [Methods] 4 patients (1 male and 3 female: mean age 74.0 ± 3.7 years) were evaluated at the start of treatment of Sarilumab and 6 months. [Results] At the start of treatment, C-reactive protein (CRP) level was 6.8 ± 3.6, ESR (1 hour) was 49.8 ± 18.4, and maximum prednisolone was 8.8 ± 2.2 mg at the average. At the last observation, CRP level was 0.1 ± 0.1, ESR (1-hour value) was 7.0 ± 6.4, prednisolone dose was1.0 ± 1.2 mg, and MTX dose was 2.5 ± 2.6 mg at the average. No adverse events were observed. [Conclusions] If differentiation from PMR is difficult, prednisolone may be used for initial treatment. However, early use of sarilumab may reduce MTX and steroids. These results suggest that sarilumab may be a useful treatment for EORA which is difficult to distinguish from PMR.

## P2-122

**Efficacy and safety of sarilumab in rheumatoid arthritis patient**

Ryujiro Okado, Takatomo Mine
National Hospital Organization Kanmon Medical Center, Yamaguchi, Japan

Conflict of interest: None

[Objective] The aim was to evaluate efficacy and safety of sarilumab in RA patient in our department. [Methods] Twenty-four patients used sarilumab at our hospital since November 2018, including 7 males and 17 females. The continuation of sarilumab and the side effects, and complications after its administration were assessed. [Results and Discussion] Sarilumab was the first biological DMARDS administered in 11 patients, and 13 biologic DMARDS were used prior to sarilumab. 10 patients were able to continue the drug administration. Complications were observed in 11 cases, including 3 cases of malignancy and 2 cases each of herpes zoster, interstitial pneumonia, and infection. About these cases, we examine its treatment and its subsequent course.

## P2-123

**Clinical effect of sarilumab in patients with rheumatoid arthritis from data registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA)**

Shun Igarashi[1,2], Yusuke Sugimura[2], Moto Kobayashi[2], Natsuo Konishi[2], Masakazu Urayama[2], Hiroki Ito[2], Takeshi Kashiwagura[2], Tsutomu Sakuraba[2], Takayuki Tani[2], Toshiaki Aizawa[2], Hidekazu Abe[2], Norio Suzuki[2], Keiji Kamo[2], Hiroshi Aonuma[2], Nozomi Kaga[2], Yosuke Iwamoto[2], Takanori Miura[2], Rena Wakabayashi[2], Naohisa Miyakoshi[3]
[1]Omori Municipal Hospital, [2]Akita Orthopedic Group on Rheumatoid Arthritis (AORA), [3]Department of Orthopedic Surgery, Akita University Graduate School of Medicine

Conflict of interest: None

[Objective] To analyze the efficacy of sarilumab (SAR) in patients with rheumatoid arthritis (RA). [Methods] SAR was used in 13 patients with RA treated at the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) from 2021. Eight patients who were followed for at least 52 weeks of treatment with SAR were included in this study. We evaluated persistence rate, DAS28-CRP, SDAI, CDAI, and reasons for discontinuation at 52 weeks. [Results] There were 2 males and 6 females, mean age was 67.3 years and mean disease duration was 17.1 years. One patient was biologic naïve while 7 were biologic switched. MTX was administered to 4 patients (50%) at a mean dose of 6.5 mg/week, PSL to 4 patients (50%) at a mean dose of 5.3 mg/day and csDMARD to 2 patients (25%). Four patients (50%) were treated continuously for 52 weeks. At 0, 12, 24, and 52 weeks after initiation, mean DAS28-CRP was 4.12, 3.09, 2.82, and 2.94, mean SDAI was 23.5, 14.2, 13.7, and 14.3, and mean CDAI was 23.5, 14.2, 13.7, and 14.3, respectively. The reasons for discontinuation were insufficient effect in 2 cases and adverse events in 2 cases. [Conclusions] These data suggest that SAR improves disease activity at 12 weeks after initiation and may become an option for the treatment of patients with biologic switched RA.

## P2-124

**Clinical Outcome of Abatacept in Rheumatoid Arthritis Patients at our Hospital**

Shigeto Kanda, Kiichiro Ando
Department of Orthopedic Surgery, JA-Gifu Chuno Kosei Hospital

Conflict of interest: None

[Objective] In recent years, the number of elderly RA patients has been increasing due to improvements in the treatment of rheumatoid arthritis (RA). Treat to Target (T2T)" has been practiced in the daily practice of RA. Abatacept has been reported in post-marketing surveillance to have a higher average patient age and fewer serious adverse events than other biologic agents. The purpose of this study was to confirm the use and therapeutic efficacy of Abatacept in rheumatoid arthritis patients and to investigate its usefulness. [Methods] 9 RA patients attending our outpatient clinic were introduced to Abatacept between April 2012 and October 2023, and were observed for at least 1 year. [Results] DAS28CRP was well managed with 2.41 (1.5-3.87). The patients were managed in the outpatient clinic without any major problems such as pulmonary complications. There were no drop-outs during the course of the treatment in patients who continued the treatment for more than one year. [Conclusions] Abatacept has a good continuation rate in elderly RA patients, suggesting that it is effective as a treatment for elderly RA patients.

## P2-125

**Investigation of association between efficacy of filgotinib and patient background, concomitant drugs, and treatment drug history in a rheumatoid arthritis cohort, FIT-RA**

Ichiro Mizushima[1], Masahiro Konishi[1], Hajime Sanada[1], Akira Sakata[1], Satoshi Nakazaki[2], Takashi Murayama[2], Hiroshi Fujinaga[3], Hiraku Motomura[4], Isao Matsushita[5,6], Yasunori Iwata[1], Mitsuhiro Kawano[1], Kazunori Yamada[7]
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Conflict of interest: None

[Objectives] To clarify the association between efficacy of filgotinib for rheumatoid arthritis (RA) and patient background, concomitant drugs, and treatment drug history. [Methods] From 48 filgotinib (FIL)-treated RA cases in the Fukui Ishikawa Toyama Database of RA, we extracted 16 cases who switched from one JAKi to FIL (JJ group), 25 who switched from biologics to FIL (BJ group), and 6 who were biologics/JAKi-naïve (NJ group). We compared the baseline factors, treatment response, and FIL continuation rate among the three groups. Association between efficacy of FIL and ACPA status, concomitant MTX use, and past JAKi use were also evaluated. [Results] No significant differences were found among the three groups in treatment response and FIL continuation rate, except for the 3-month and 6-month treatment response between the JJ and NJ groups. In the 48 cases, neither ACPA status, concomitant MTX use, nor past JAKi use significantly influenced the efficacy and retention rates of FIL during the 12-month observation. [Conclusions] Although the response to FIL treatment was partially poor in JAKi switching patients compared to biologics/JAKi naive patients, the efficacy of FIL was suggested to be independent of patient background, concomitant drugs, and treatment drug history.

## P2-126

**Filgotinib (200 mg/day) in combination with methotrexate may represent a valuable therapy for preventing rapid radiographic progression by reducing bone edema**

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Conflict of interest: None

[Objective] Filgotinib (FIL) is well-known for its ability to inhibit bone destruction in patients with RA, especially those with poor prognostic factors. On the other hand, it has been demonstrated that extensive MRI-detected bone edema (BE) in the hand is a prognostic factor for rapid radiographic progression (RRP). To investigate FIL's impact on inhibiting RRP, we analyzed radiographic joint destruction in 10 patients with extensive BE in their hands or moderate to large joints out of a total of 32 patients treated with FIL+MTX. [Methods] We measured BE in their most painful joints before treatment using MRI (Canon, 1.5T). Additionally, we conducted RA disease activites and yealy mTSS. [Results] The majority of patients received FIL 200 mg/day + MTX and exhibited extensive BE in their hands and RRP at baseline. Ultimately, RRP improved in all patients, and BE almost disappeared. Patients who initially had extensive BE in the mid-tarsal area, toes, and shoulders also experienced a reduction in BE and related symptoms. Finally, most of the patients displayed clinical improvement, as evidenced by changes in DAS28-ESR, VAS, and mHAQ scores. [Conclusions] The combination of FIL (200 mg/day) and MTX shows promise as a therapy for reducing RRP by decreasing bone edema.

## P2-127

**Efficacy and Safety of Filgotinib in Patients with Rheumatoid Arthritis in clinical Practice**

Hiroyuki Ide[1], Yukitaka Ueki[1], Toshiyuki Aramaki[1], Ayuko Takatani[1], Tohru Michitsuji[1], Kaoru Terada[1], Katsumi Eguchi[1], Toshimasa Shimizu[2], Tomohiro Koga[2,3], Takahisa Suzuki[4], Naoki Iwamoto[2], Atsushi Kawakami[2]
[1]Rheumatic Disease Center, Sasebo Chuo Hospital, Hakujyujikai Foundation, sasebo, Japan, [2]Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan, [3]Internal Medicinre, Matsuoka Hospital, [4]Department of Rheumatology, Nagasaki Atomic Bomb Hospital

Conflict of interest: None

Purpose: Filgotinib (FIL) is the fifth JAK inhibitor approved in Japan for rheumatoid arthritis (RA). We report on the efficacy and safety of this drug in post-marketing studies in actual clinical practice. Methods: Safety and efficacy were evaluated up to 6 months after the start of FIL. Efficacy was evaluated by DAS28-ESR, DAS28-CRP, SDAI, and CDAI at 1, 2, 3, and 6 months after the start of FIL, and safety was evaluated by the incidence of adverse events. Results] The study population consisted of 44 patients. The median duration of disease was 13.4 years, and the median age at initiation of FIL was 66.3 years. 18 patients were treated with MTX and 38 patients were treated with bio/ts DMARDs. 85.3% of patients continued treatment at 6 months. Efficacy was significantly reduced from 1 month to 3 months after the start of treatment, especially in naive patients. There was no effect of prior therapy on efficacy in the switch group. Safety: Adverse events (pneumonia, liver function abnormality, and spinous cell carcinoma) were observed in 3 out of 44 patients. Conclusion: FIL showed efficacy as early as 1 month after initiation, and the frequency of adverse events was relatively low, indicating the need for further case accumulation.

## P2-128

**Efficacy of Filgotinib in rheumatoid arthritis patients with poor prognostic factors**

Kazuya Kishimoto[1], Rika Fukuda[1], Hirotaka Yamazawa[1], Kaori Ishimura[1], Chisato Ashida[1], Hiroki Akazawa[1], Akinori Okada[2], Daisuke Tomita[1], Tetsu Itami[1], Toshihiko Shiga[1], Shoichi Hino[2], Yuji Nozaki[1], Koji Kinoshita[1], Itaru Matsumura[1]
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Conflict of interest: None

[Objective] PPF in early RA include RF or anti-CCP antibody positivity, elevated CRP, high disease activity, and the presence of bone erosions, and clinical trials of filgotinib have reported efficacy in patients with PPF. In this study, we investigated the efficacy of figotinib in patients with PPF

in real world. [Methods] 76 patients who could be followed up for at least 6 months were included in the study. We compared the change in DAS28ESR and CDAI and the remission rate after 24 weeks of treatment in all patients, in patients with all four PPFs (4PPF group), and in patients with each PPF. [Results] The change in DAS28ESR and CDAI for all patients showed improvement of -1.9 and -12.7, and the remission rate of DAS28ESR and CDAI was 38% and 37%. The change in DAS28ESR and CDAI in the 4PPF group was -2.3 and -16.2. For each PPF, there was a significant difference in the change in patients with CRP ≧0.6 mg/dl and DAS28ESR ≧5.1. The remission rates of DAS28ESR and CDAI were 40% and 42% in patients with CRP ≧0.6 mg/dl, and 35% and 45% in patients with DAS28ESR ≧5.1. [Conclusions] The results suggest that filgotinib is effective in patients with PPF, especially in those with an increased inflammatory response or high disease activity.

## P2-129

**Five-year changes in upper cervical spine lesions in 46 patients with rheumatoid arthritis treated with tofacitinib for 5 years at our hospital**

Keio Ayabe, Akira Inoue, Wataru Iriyama, Yurina Iwasaki
Keiyu Orthopedic Hospital

Conflict of interest: None

[Objective] In this study, we report the changes in upper cervical spine lesions in 46 patients treated with Tofacitinib (TOF) for 5 years at our hospital. [Methods] 46 patients who started receiving TOF at our hospital from December 2013 to May 2018 and continued for 5 years. The mean age at the start of TOF treatment was 67.0 years, the mean disease duration was 15.0 years and The mean DAS28ESR was 4.4, the mean CDAI was 17.4, and the mean anti-CCP antibody was 523.7 IU/mL. The conditions of axial subluxation (ASS) and vertical subluxation (VS) were atlanto-dental interval (ADI) > 3 mm and Ranawat value < 13 mm, respectively. The conditions of progression of upper cervical lesions were evaluated as ADI increase > 2 mm and Ranawat value decrease > 2 mm over 5 years. [Results] There were no cases of progression of ASS and 11 cases of progression of VS that met the conditions. [Conclusions] Although the progression of ASS was not so great after 5 years by controlling disease activity with TOF, 23.9% of patients had progression of VS. Even if the progression of osteoarticular destruction such as ΔmTSS is controlled, careful observation of the upper cervical spine is still necessary.

## P2-130

**Five-year changes in lymphocyte counts in 46 patients with rheumatoid arthritis treated with tofacitinib for 5 years at our hospital**

Keio Ayabe, Akira Inoue, Wataru Iriyama, Yurina Iwasaki
Keiyu Orthopedic Hospital

Conflict of interest: None

[Objective] Lymphocyte counts are important as a marker of infectious diseases and for the evaluation of susceptibility to infection. In the present report, we examined the 5-year lymphocyte counts of 46 patients who were treated with TOF for 2 years. [Methods] The mean age at the start of TOF administration: 67.0 years, disease duration: 15.0 years, switch cases: 67.4% (mean number of biologic agents before administration: 2.0), MTX cases: 63.0% Lymphocyte counts at the beginning of TOF administration, 3 years after administration, and 5 years after administration were compared. [Results] The mean lymphocyte counts of A: 1655/μL, B: 1328/μL, and C: 1475/μL at the beginning, 3 years, and 5 years after TOF administration, respectively, showed a decreasing trend in B as in the previous report, but an increasing trend in the following 2 years. However, the percentage of easily infected cases with lymphocyte counts of 1000/μL or less still exceeded 20% (A: 10.9%, B: 21.7%, C: 23.9%). [Conclusion] Although the number of patients who continue to receive JAK inhibitors is increasing due to their efficacy, it is necessary to pay close attention to the presence of cases with low lymphocyte counts in the increasing number of elderly patients.

## P2-131

**Comparison of efficacy and safety of bDMARDs and tsDMARDs for elderly patients with rheumatoid arthritis**

Rina Watanabe, Hiroshi Kanazawa
Department of Rheumatology, Aomori Prefectural Central Hospital

Conflict of interest: None

[Objective] The aim of this study is to compare the efficacy and safety of bDMARDs and tsDMARDs for elderly patients with rheumatoid arthritis (RA). [Methods] Medical records of patients with RA who were over 75 years old and treated with bDMARDs or tsDMARDs for the first time between January 2018 and September 2022 were reviewed. [Results] There were 33 patients treated with bDMARDs (ETN: n=1, GLM: n=15, CZP: n=1, TCZ: n=7, SAR: n=4, ABT: n=5) and 16 patients treated with tsDMARDs (TOF: n=2, BAR: n=6, PEF: n=4, UPA: n=3, FIL: n=1). Both groups showed similar efficacy; DAS28 (starting time, 1-year, mean±SD) improved 4.95±0.95 to 2.59±1.01 in bDMARDs group and 4.76±1.29 to 2.57±0.93 in tsDMARDs group. There was no difference in 1-year continuation rates (60.6% vs 75.0%). The reasons of discontinuation were ineffective (n=11) and adverse event (n=2) in bDMARDs group, and adverse event (n=2) in tsDMARDs group. The rate of ineffective case was significantly lower in tsDMARDs group (33.3% vs 0.0%, *P=0.0093*). [Conclusion] There was no significant difference in efficacy and safety of bDMARDs and tsDMARDs for elderly RA. The rate of ineffective case was significantly lower in tsDMARDs group; therefore, tsDMARDs may be a treatment option for elderly RA after being careful about side effects.

## P2-132

**The effect of MTX on efficacy and retention rate of JAK inhibitors in elderly patients**

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Conflict of interest: None

[Objective] JAK inhibitors (JAKi) are recommended in combination with methotrexate (MTX) but they can be administered as monotherapy. There are concerns about the risk of long-term MTX administration to elderly patients because of adverse reactions. In this study, we compared the efficacy and the retention rate of JAKi with and without MTX in elderly patients. [Methods] The subjects were 70 patients over 65 years old who administered JAKi from March 2019 to March 2023. We evaluate the retention rate at 12 months and disease activity up to 56 weeks. [Results] There were 55 patients in the non-MTX group and 15 in the MTX group. The non-MTX group had significantly higher disease activity at the start of treatment (DAS28-CRP 4.03: 3.08, P<0.01). DAS28-CRP was higher in the non-MTX group at 4 weeks but there was no difference after 12 weeks (12 weeks (2.53: 2.41, P=0.71), 24 weeks (2.03: 1.63, P= 0.13), and 56 weeks (1.74: 1.30, P=0.09)). The retention rate at 1 year was 72.0% in the non-MTX group and 72.7% in the MTX group, showing no significant difference (P=0.402). [Conclusion] In the elderly patients treated with JAKi, MTX use was not associated with the efficacy and the retention rate. In elderly patients with safety concerns, JAKi without MTX may be recommended.

## P2-133

**The study of rheumatoid arthritis treatment for the elderly patients**

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Conflict of interest: None

[Introduction] Rheumatoid arthritis (RA) in the elderly can be difficult to treat because it has comorbidity and it is to increase the dose of medication. [Purpose] We investigated the disease activities, medications, and comorbidities of elderly RA patients. [Materials and Methods] Materials were 109 RA patients aged over 65 years included and followed up for more than two years since January 2020. Methods were prospectively con-

ducted from medical records for distribution by age group, age of onset, disease activity, and medications. [Results] By age group, the population was 18.3% aged 65~69, 40.4% aged 70~74, 20.2% aged 75~79, 12.8% aged 80~84, and 8.3% aged 85 more than. The ages of onset were 39.4% in their 60s, 18.3% in 70s and 17.4% in 50s. In disease activities were remission in 28.4%, low disease activity in 26.6%, and moderate disease activity in 45.0%. Medications were used methotrexate (MTX) in 28.4%, biologics in 26.6%, JAK inhibitors in 1.8%, tacrolimus in 32.1%, and other drugs in 14.7%. Complications were respiratory problems in 25.7%, renal disorder in 13.8%, cancers in 9.2%, and liver disorder in 7.3%. [Conclusions] There are management of treatment adherence, mental health of disease activity, and complications in elderly RA patients.

## P2-134

**Inhibition of Joint Destruction by JAK Inhibitors in Patients with Rheumatoid Arthritis with Bone Marrow Edema in the Hand**

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Conflict of interest: None

[Objective] Investigate the inhibitory effect of JAK inhibitors on joint destruction in RA patients with MRI confirmed bone marrow edema (BE) in the hand. [Methods] Twenty-four RA patients showing extensive BE in the hand by MRI (BE (+) group) and 30 patients without BE (BE (-) group) were studied for DAS28-ESR and ΔmTSS/y after 1 year JAK inhibitor treatment. BE score was measured using T1 or STIR images of hand MRI (1.5T) through the RAMRIS method. [Results] The pre-treatment mTSS/y values for the BE (+) and BE (-) groups were 6.76 and 3.21 respectively (P = 0.0000582, t-test), with the BE (+) group showing significantly higher values. DAS28-ESR values at 1 year of treatment decreased significantly in both groups: from 4.82 to 3.39 (P<0.01) in the BE (+) group and from 4.83 to 3.45 (P<0.01) in the BE (-) group. In terms of the inhibitory effect on joint destruction, RRP was observed in 5 individuals in the BE (+) group, but not in the BE (-) group. No significant differences were observed between JAK1 inhibitors and JAK1/3 inhibitors. The annual progression of destruction ΔmTSS/y decreased in both groups: from 6.39 to 1.59 (P=0.000003) in the BE (+) group and from 3.21 to 0.16 (P= 0.000545) in the BE (-) group. [Conclusions] BE may be a predictive factor for RRP in JAK inhibitor treatment.

## P2-135

**Predictors of clinical remission in rheumatoid arthritis patients treated with JAK inhibitors**

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Conflict of interest: Yes

[Objective] This study aimed to investigate predictors of clinical remission in patients with rheumatoid arthritis (RA) treated with JAK inhibitors. [Methods] Among RA patients enrolled in a multicenter registry, 396 patients who initiated treatment with JAK inhibitors (baricitinib, peficitinib, upadacitinib, and filgotinib) and were followed for at least 24 weeks were included. [Results] Patients' characteristics at the initiation of JAK inhibitor therapy (mean±SD or %) were as follows: age 64±14 years, 80% female, disease duration 13±12 years, 83% anti-CCP antibody positive, 68% with b/tsDMARD, 55% with methotrexate, and 39% with glucocorticoids. SDAI remission rates were 5% at baseline, 23% at 4 weeks, 31% at 12 weeks, and 37% at 24 weeks. Multivariate Logistic regression analysis revealed that anti-CCP antibody positivity [odds ratio (OR): 2.09, 95% confidence interval (CI): 1.05-4.15], glucocorticoid use (OR: 0.40, 95% CI: 0.24-0.67), and SDAI score (OR: 0.96, 95% CI: 0.94-0.98) were independent predictors of SDAI remission at 24 weeks. [Conclusions] In clinical practice, RA patients who are anti-CCP antibody-positive, not using glucocorticoids, and have a lower SDAI score at the initiation of JAK inhibitor therapy are more likely to achieve clinical remission.

## P2-136

**The effect of JAK inhibitors on pain visual analogue scale (VAS) in patients with CRP-negative and CRP-positive rheumatoid arthritis**

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Conflict of interest: Yes

[Objective] JAK inhibitors exert antirheumatic effects by controlling inflammation. We investigate the effect on pain visual analogue scale (VAS) in patients with CRP-negative and CRP-positive rheumatoid arthritis (RA). [Methods] In RA patients with pain VAS more than 30 mm at the start of JAK inhibitors (tofacitinib, baricitinib, peficitinib, upadacitinib, filgotinib), improvement of more than 20 mm or 20% of pain VAS was compared between CRP-negative (less than or equal to 0.3 mg/dL) and CRP-positive (more than 0.3 mg/dL) patients. The statistical analysis was performed by chi-square test. [Results] In 114 patients with pain VAS more than 30 mm, 38 were CRP-negative and 76 were CRP-positive. Pain VAS improved in 26 of 38 (68.4%) CRP-negative patients and 61 of 76 (80.2%) CRP-positive patients (p=0.17). In patients with tofacitinib, baricitinib, or upadacitinib, there were no significant differences in pain VAS improvement between CPR-negative and CRP-positive patients, but in patients with filgotinib, improvement rate was higher in CRP-positive patients than CRP-negative patients (92.3% vs. 55.5%, p=0.02). [Conclusions] JAK inhibitors are effective in CPR-negative patients, indicating that there are certain mechanisms other than controlling inflammation for pain.

## P2-137

**The treatment of osteoporosis in patients with rheumatoid arthritis in the real world**

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Conflict of interest: None

[Objective] The actual status of osteoporosis treatment in patients with rheumatoid arthritis (RA) were investigated in Kyushu Medical Center. [Methods] We surveyed 320 patients with RA who visited from January to December 2022, and investigated medical information related RA and osteoporosis. Lumbar spine X-ray was analyzed for diagnosing vertebral fracture including asymptomatic morphological fracture. Risk factors for fracture were analyzed by comparing patient backgrounds with fracture to ones without fracture. [Results] The mean values of patient were age 69

years, disease duration 15.8 years, DAS28-CRP 2.23, HAQ-DI 0.76, bio/ts DMARDs use 34.4%, and prednisolone (PSL) use 44.7% (mean 3.72 mg). Bisphosphonates (29.7%), denosumab (11.3%), teriparatide (1.3%), romosozumab (0.6%), and others (13.7%) were used as a treatment for osteoporosis, while 43.4% were untreated. Existing fracture accounted for 49.4%, of which 39% had untreated osteoporosis. PSL use, increased dose of PSL, high value of TRAP-5b, and low YAM value in the proximal femur were significant fracture risks. [Conclusions] Half of patients with RA had existing fracture, but 40% of these were untreated. Regular examinations for morphological fractures and aggressive treatment for patients with risk factors are considered.

## P2-138

**The relationship between locomotive syndrome and bone mineral density in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] It has been reported that patients with rheumatoid arthritis are prone to locomo, which is a decline in mobility due to musculoskeletal disorders. Rheumatoid arthritis is also said to be a risk factor for osteoporosis, but the relationship between locomo and bone density, an indicator of osteoporosis, has not been fully reported. [Methods] One hundred and thirty rheumatoid arthritis patients (42 males and 88 females) were included in this study, of whom locomo tests and BMD (lumbar spine, proximal femur) were measured by DEXA. The mean age was 70.5 (22-91) years, the mean duration of disease was 10.4 (0.2-44) years, and the mean DAS28-CRP was 2.33 (1.03-4.76). Multiple regression analysis was performed using the degree of locomo as the objective variable. [Results] 5%, 40%, 21.7%, and 32.5% had degree 0, degree 1, degree 2, and degree 3 of locomotion, respectively. The mean BMD (YAM value) was 85.4% (40-169%) for the lumbar spine and 72.8% (37-127%) for the proximal femur. BMD at both the lumbar spine and the proximal femur was not correlated with the degree of locomo. [Conclusions] The correlation between the degree of locomo and BMD was low, suggesting that physical function assessment and bone mineral density assessment should be conducted separately.

## P2-139

**A case of adult hypophosphatasia with serum ALP within the reference range for a long period due to peripheral arthritis with pencil-in-cup deformity in the fingers**

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Conflict of interest: None

[Case] 58-year-old woman [Chief complaint] At the age of 41, she noticed stiffness in his fingers, numbness from the index finger to the ring finger on both sides, and pain in the PIP joint. At the age of 49, she presented to our hospital with bilateral finger PIP, MCP, hand, elbow, shoulder, and knee joint pain, as well as neck pain. Hand X-rays showed subluxation of the PIP joint with pencil in cup deformity. When we started denosumab 60 mg/3 months as a DMARD and added tocilizumab 162 mg/2 weeks at the age of 56 years, the disease activity of peripheral arthritis improved and ALP was low. At the age of 58, the urine PEA/CRE level was as high, and hypophosphatasia was suspected. A heterozygous p. Phe327Leu variant was detected in the ALPL gene, and the diagnosis of hypophosphatasia was confirmed. After administering Asfotase alfa, her neck pain and PIP joint pain have improved. [Discussion] Hypophosphatasia is an inherited metabolic disease caused by mutations in the ALPL gene, resulting in decreased tissue-nonspecific alkaline phosphatase activity. This is a case in which co-administration of denosumab and tocilizumab improved the disease activity of peripheral arthritis and revealed a low serum ALP level, which led to the diagnosis.

## P2-140

**Japanese diet patterns may be associated with changes in frailty status in outpatients with osteoporosis**

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Conflict of interest: None

[Objective] Frailty can be a risk for falls and fractures, so its prevention and treatment is important in patients with osteoporosis (OP). This study aimed to examine the relationship between changes in frailty status and dietary intake status assessed based on Japanese dietary (JD) patterns in OP patients. [Methods] A prospective cohort study of OP outpatients at a single medical center was conducted and surveyed at baseline (BL) and one year later. Frailty status was assessed using the Kihon Check List. The dietary intake status was assessed by Brief-type self-administered Diet History Questionnaire. JD patterns were scored based on intake of 12 dietary components. The association between change in frailty status over time and JD score was analyzed by logistic regression analysis. [Results] A total of 264 patients (4% female, mean age 78 y) were included in the analysis. Of the 92 patients who were pre-frail at BL, 17 (18%) had improved to robust at 1 year, and of the 129 patients who were frail at BL, 33 (26%) had improved to robust or pre-frail at 1 year. A JD score at or above the median for this cohort was a factor significantly associated with improved frailty status (OR: 2.89, 95%CI: 1.35-6.18). [Conclusions] JD patterns may be associated with frailty in patients with OP.

## P2-141

**Preoperative low serum 25 (OH)D levels may influence falls within 1 year after surgery in patients undergoing primary total knee arthroplasty**

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Conflict of interest: None

[Objective] We conducted a cross-sectional survey of patients who fall within 1 year after TKA. [Methods] Patients with end-stage osteoarthritis of the knee who underwent primary TKA at our hospital for July 2020 to July 2022 and who gave written consent for this study were included. Preoperative and 1 year postoperative locomotive syndrome, presence of sarcopenia, presence of frail, History of osteoporosis, functional assessment (JOA score, KSS, EQ-5D), quadriceps strength, knee range of motion, femoral YAM value, serum 25 (OH)D levels, and bone turnover markers (TRACP-5b, total P1NP) were measured and a comparison was made between the two groups based on the presence or absence of a history of falls within 1 year postoperative TKA. [Results] The subjects consisted of 155 patients with 155 knees, 21 with falls and 134 no falls. Preoperative serum 25 (OH)D levels were 12.9 ng/ml in fall group and 15.2 ng/ml in no fall group, which were significantly lower in fall group ($p=0.036$). The rate of preoperative severe sarcopenia was significantly higher in fall group ($p=0.007$). No significant differences were found for the other items. [Conclusions] We hypothesize that the effect of low serum 25 (OH)D levels may be related to fall within 1 year postoperative TKA.

## P2-142

**Insufficiency fracture of the ankle with rheumatoid arthritis; three case report**

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Conflict of interest: None

[Objective] The incidence of Insufficiency fracture at distal tibia is not low. However, the absence of a history of trauma, the physical findings suggesting an inflammatory process, and the presence of arthritis make it

difficult to consider fracture as the primary diagnosis in patients with rheumatoid arthritis (RA). We experienced three RA cases with late-diagnosed insufficiency fracture with around the ankle. [Case Presentation] Three patients with establish RA who sustained ankle insufficiency fractures which were not detected on X-ray. Two patients were on biologic treatment, all patients were on methotrexate and predonisone for RA, and diagnosed between two weeks and 8 weeks after onset. Two of three patients required surgery for this fracture. [Conclusions] Juxta-article insufficiency fractures might be easily misdiagnosed in patients with RA, because X-ray imaging is often normal. when patients have juxta-articular pain durring RA treatment, we should to consider the possibility of insufficiency fracture and carefully take the physical examination around the joint.

## P2-143

**A case of rheumatoid arthritis with a subclinical fracture of the proximal tibia following minor trauma while receiving Denosumab**

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Keiyu Orthopedic Hospital

Conflict of interest: None

[Objective] We report a case of rheumatoid arthritis in which the patient sustained a fracture of the proximal end of the right tibia due to minor trauma while receiving denosumab. [Cases and Course] The patient is a 79-year-old woman. Duration of disease was 16 years. After about 5.5 years of treatment, her condition was good and she became drug-free. Denosumab was started about 5 years before the right proximal tibia fracture, and bone mineral density measurements taken 5 months before the injury showed that YAM values were 77.66% for the femur, 81.29% for the lumbar spine, and 32.3 for urinary NTX. After being injured as if she twisted her right knee joint this time, she was able to walk normally but an MRI performed one month and 10 days after the injury confirmed a fracture of the proximal end of the tibia. The knee brace was removed 2.5 months after the injury, and the knee brace was replaced with a full-load knee brace. [Conclusions] Even rheumatoid arthritis patients who are undergoing treatment for osteoporosis and seem to be doing well may suffer subclinical fractures in elderly patients, and it is important to observe physical findings such as severe local pain and tenderness.

## P2-144

**Internal fixation using Ender nail for the treatment of atypical femoral fracture with excessive lateral bowing**

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Conflict of interest: None

[Objective] As one of the minor features of atypical femoral fracture (AFF), delayed union is well known, therefore that demands ever rigid internal fixation. Thereby, the intramedullary long nail is usually used. However, it's controversial how to fix for the case whose femoral form is unadaptable to the ready-made intramedullary long nail. We report the case suffered from AFF with excessive lateral bowed femur who was treated by Ender's nails. [Case] The female patient who was 85 years old felled and couldn't move because of the right thigh pain, and carried to our institute. By X-ray examination, right AFF with excessive lateral bowed femur were detected. For internal fixation, we selected Ender's fixation nail because of the inadaptation among the femoral form and ready-made intramedullary long nail. Postoperatively, the callus was formed strongly, and at 5 months later of index surgery she had become to be able to gait by full-weighted bearing using walker. [Conclusions] AFF is classified two groups by its backgrounds; one caused by bone resorption inhibitor and another caused by excessive lateral bowing of femur. In former, it's considered ever rigid internal fixation is needed, however in latter Ender's nail can be candidate for the treatment for AFF.

## P2-145

**Examination of the usefulness of ultrasound echo in knee osteoarthritis**

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Conflict of interest: None

[Objective] Regarding joint echocardiography (US) findings in KOA, there are reports on the relationship between synovitis findings and pain, but details regarding US findings in patients scheduled for TKA are unknown. We investigated preoperative joint ultrasound findings in patients scheduled for TKA. [Methods] Patients scheduled for TKA and who requested joint ultrasound were targeted. The thickness of the thickest part of the synovial membrane and the degree of PD were observed and recorded. The degree of progression of KOA was also evaluated using the KL classification. [Results] The subjects were 7 patients with 14 joints. Evaluation of the synovium in the medial joint space was difficult in 5 joints due to osteophyte formation, and the average thickness of the suprapatellar capsule synovium was 2.09 mm, and the lateral joint synovium was 2.73 mm. PD had a wide range and none of these had any correlation with the degree of KL. [Conclusions] By performing an additional ultrasound of the knee joint before surgery, we were able to visualize differences in the degree of synovitis. It is possible to evaluate the state of synovitis, which cannot be determined from XP or symptoms.

## P2-146

**The effects of obesity on the knee lesions of the patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The effects of obesity on the knee lesions of the patients with rheumatoid arthritis were studied. [Methods] Sixteen patients with rheumatoid arthritis (RA) and 135 patients with arthritis of the knee joint (OA) were performed total knee arthroplasty. Body mass index (BMI) was 25.5±3.7 kg/m$^2$ (range, 20.1-32.1) in RA patients and 26.4±3.6 kg/m$^2$ (range, 17.7~38.0) in OA patients. [Results] Obesity (25≦BMI) was 50.0% in RA and 63.0% in OA patients respectively. [Conclusion] In RA patients, knee lesions were progressed by obesity as well as OA patients.

## P2-147

**Factors associated with walking speed one year after total knee arthroplasty for patients with end-stage knee joint disorders**

Syuji Yamada, Shingo Maeda, Shunya Yamashita, Eriki Yanagi, Kentaro Inui
Osaka Saiseikai Nakatsu Hospital

Conflict of interest: None

Background and Purpose: Mobility is impaired due to knee joint disorders. The purpose of this study was to determine the gait speed of patients who underwent initial TKA at 1 year postoperatively and to examine the factors that correlate best with this gait speed. Subjects and Methods: Patients with end-stage knee arthroplasty who underwent initial TKA at our hospital between July 2020 and June 2022 were included, and their gait speed was measured before and one year after surgery. Results and Discussion: A total of 159 subjects showed significant improvement in gait speed at 1 year after TKA compared to preoperative gait speed. Results showed that age, gender, skeletal muscle mass of both lower extremities, KSS, quadriceps strength, and range of motion (extension) were significantly and independently associated with walking speed. Conclusion: One year after TKA, the patient's gait speed improved compared with the preoperative gait speed, suggesting that TKA improves flexion range of motion limitation, thereby reducing the load on the quadriceps muscle and improving the range of motion in extension, as well as the gait speed.

## P2-148

**Improvement in Physical Performance and Clinical Outcomes in Elderly Patients Undergoing Total Knee Arthroplasty**

Syuji Yamada, Shingo Maeda, Shunya Yamashita, Eriki Yanagi, Kentaro Inui
Osaka Saiseikai Nakatsu Hospital

Conflict of interest: None

Objective: The age range for TKA is expanding. We evaluated the preoperative physical and motor abilities and clinical outcomes of TKA patients aged 80 years or older, and compared them with those of patients aged less than 80 years to determine the degree of improvement. Subjects and Methods: Of the TKA patients who underwent TKA at our department between July 2020 and May 2023, 158 patients who had been evaluated for at least 1 year were included. Fifty-four patients were older than 80 years at the time of surgery (80+ group), and 104 patients were younger than 80 years at the time of surgery (<80 group). JOA score, Knee Society Score (KSS), Locomo 25, quadriceps muscle strength, walking speed, and skeletal muscle mass index (SMI) were measured preoperatively and postoperatively to evaluate motor function, and were statistically evaluated. Results: KSS score, quadriceps muscle strength, and Locomo 25, gait speed, SMI were all significantly lower than in the <80 group. Discussion: We have previously reported that the majority of patients with knee osteoarthritis have locomo. The results of this study indicate that even elderly patients with reduced mobility can achieve a certain level of improvement in exercise capacity and clinical outcomes.

## P2-149

**In total knee arthroplasty, improvement in Locomo 25 is better in cases of bilateral simultaneoussurgery than unilateral surgery**

Eriki Yanagi[1], Shingo Maeda[2], Syuji Yamada[2], Shunya Yamashita[2], Kentaro Inui[2]
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Conflict of interest: None

[Objective] The purpose of this study was to evaluate the improvement in locomo degree at 1 year postoperatively in patients who underwent bilateral TKA or unilateral TKA. [Methods] Patients who underwent primary bilateral TKA or unilateral TKAat our hospital between July 2020 and June 2022, and gave consent for this study were included. Locomotor function and functional assessment were measured preoperatively and one year postoperatively, and compared between the bilateral and unilateral groups. [Results] There were 116 patients in the unilateral group and 48 patients in the bilateral group. The mean age was 75.0 and 75.4 years, respectively, and the gender was 26 males and 90 females in the unilateral group and 41 males and 44 females in the bilateral group, with a predominance of females in both groups. There was no significant difference in the preoperative and postoperative scores of locomo 25 between groups, but the percentage of patients who improved was significantly higher in the bilateral group. There were no significant differences in the degree of locomotion, 2-step test/stand-up test, JOA score, and KSS score between groups. [Conclusions] The percentage of patients with improved Locomo 25 was significantly greater in the bilateral TKA group.

## P2-150

**Investigation of the safety of TKA with continuous antithrombotic medication using intra-articular administration of tranexamic acid**

Yukio Mikami
Matsudo City General Hospital

Conflict of interest: None

[Objective] We investigated whether total knee arthroplasty (TKA) could be safely attempted by administering tranexamic acid (TXA) intraoperatively while continuing antithrombotic drugs (Xa inhibitor, clopidogrel, aspirin). [Methods] The subjects were 106 knees that underwent initial TKA using intra-articular administration of TXA from 2018 to 2023. 52 knees in suspending group (group S) and 54 knees in continuation group (group C). The items examined were estimated blood loss, amount of change in Hb before and after surgery, rate of change in thigh circumference before and after surgery, and amount of drainage fluid. [Results] The average estimated blood loss (ml) was 247.9 in group S and 268.1 in group C. The average change in Hb (g/dl) before and after surgery was 0.6 in group S and 0.5 in group C. The mean rate of change in thigh circumference (fold) one week after surgery was 1.04 in group S and 1.05 in group C. The average amount of drain fluid (g) was 144.7 in group S and 140.4 in group C. There were no significant differences between the groups in all items. [Conclusion] Even if antithrombotic drugs were continued, there were no differences between the groups in terms of bleeding amount or complications.

## P2-151

**A case of catastrophic antiphospholipid syndrome requiring plasma exchange and steroid pulse therapy**

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Conflict of interest: None

A 34-year-old woman was diagnosed with primary antiphospholipid syndrome (APS) at the age of 27 following the onset of deep vein thrombosis and started taking warfarin. She had urinary protein and renal dysfunction, and a renal biopsy showed thrombotic microangiopathy at the age of 32. Next year, after cholecystectomy for acute cholecystitis, she had adrenal infarction and was treated with warfarin. She was admitted to the hospital with persistent back pain, Cre 1.88 mg/dl, CRP 8.94 mg/dl, and PT-INR 1.68. A contrast-enhanced CT scan showed no obvious thrombotic lesions, but after admission, renal function rapidly declined to Cre 2.50 mg/dl, and progressive anemia and thrombocytopenia were observed, leading to a diagnosis of catastrophic APS. After plasma exchange (PEX) and steroid pulse therapy, the patient was started on a maintenance dose of PSL 50 mg/day and aspirin in addition to warfarin. The patient was discharged from the hospital without recurrence of thrombosis. We experienced a case of catastrophic APS with thrombocytopenia and rapid renal dysfunction and successfully treated with PEX and steroids. The patient was considered to be at very high risk of thrombosis because of triple positivity of lupus anticoagulant, anticardiolipin antibody and anti-beta2GPI antibody.

## P2-152

**A case of cerebral hemorrhage secondary to nephrotic syndrome associated with lupus nephritis**

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Conflict of interest: None

[Case] A patient, a 37-year-old female with complaints of leg edema, fever, and arthralgia, was diagnosed with nephrotic syndrome. She suffered a left capsular hemorrhage and became unconscious. Ventricular drainage was performed, but she developed status epilepticus. She was diagnosed with systemic lupus erythematosus (SLE) and lupus nephritis based on antinuclear antibodies 640 times, hypocomplementemia, and pancytopenia. After undergoing steroid pulse therapy, she was transferred to our hospital. Treatment for lupus nephritis was initiated with intravenous cyclophosphamide therapy (IVCY) also considering NPSLE. The disease activity of SLE decreased, but her consciousness impairment and seizures persisted. CSF examination was negative for infection, malignancy, or autoimmune pathology. IVCY was terminated after two sessions, hydroxychloroquine was added, and PSL was tapered off. She was transferred to her previous hospital for continued treatment. [Discussion] Various mechanisms of cerebral hemorrhage in SLE are hypothesized, where lupus nephritis is complicated by cerebral hemorrhage, excluding NPSLE can be challenging. The treatment of NPSLE is acceptable. We report on the differentiation of NPSLE with a literature review.

## P2-153

**A case of juvenile-onset systemic lupus erythematosus (SLE) who relapsed as severe myelitis during maintenance therapy, treated with remission induction therapy of plasma exchange (PE), intermittent intravenous cyclophosphamide (IVCY) and rituximab (RTX)**

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Conflict of interest: None

[Case] 19-years old woman [Chief complain (CC)] Fever, headache, paraplegia [Present illness] In X-11 year (Y), she was diagnosed with SLE based on fever, hematuria, proteinuria, leukopenia, low CH50, positive anti-dsDNA and ANA. She was treated with PSL 50 mg/day (d). Although several immunosuppressants were added, she relapsed repeatedly. In X-6Y, renal biopsy revealed LN IV+V, and she was treated with mPSL pulse and subsequent PSL 45 mg/d which gradually decreased. When she was transitioned to our department from pediatrics in Aug X, her disease was active under treatment with PSL 10 mg/d, MMF, TAC, and HCQ. On Oct 18, she was admitted because of paresthesia of trunk, anesthesia of lower limbs in addition to CC. [Clinical Course] She was diagnosed as myelitis by NP-SLE based on elevated anti-DNA, low CH50, T2 high and swelling of C5-Th10 in spinal MRI, and elevated IL-6 in CSF. We started mPSL pulse and subsequent PSL 40 mg/d, and PE 8 times, IVCY, and RTX were added. Although myelitis improved, necrosis of Th9-12 occurred. Only paresthesia of trunk improved while other neurologic symptoms unchanged. PSL was tapered, and RTX in every 6 months was used for maintenance therapy. [Discussion] Our rare case complicated with severe myelitis by NP-SLE was treated with PE, IVCY, and RTX.

## P2-154

**A case in which a diagnosis of protein-losing gastroenteropathy led to a definitive diagnosis of systemic lupus erythematosus**

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Conflict of interest: None

[Case] A 64-year-old woman. She had arthritis from August X-1, from January X, had difficulty in moving due to fatigue, and in taking oral intake from April. In May, she hospitalized for pneumonia with remarkable emaciation. At this time, her antinuclear antibody level was high: x5120 (homogenous type, specific antibody-negative), and she had hematopenia, alopecia, and extensive blood clots in the left thigh vein, which suggested the possibility that she had systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome. She was transferred to our hospital for close examination. Despite re-nutritional therapy, she presented with marked hypoalbuminemia (1.8g/dL) and generalized edema. Proteinuria was not found. We suspected Protein-losing enteropathy (PLE), and indeed 99mTc Albumin (Alb) scintigraphy, it showed leakage into the gastrointestinal tract, leading to a diagnosis of SLE. After starting treatment with methylprednisolon div, Alb levels recovered dramatically in a few days. [Considerlation] Complication frequency of PLE in SLE is reported to be 1.8 to 3.2%. This is a case in which the diagnosis of PLE was significant because she had no other organ damage and was hesitant to undergo therapeutic intervention, so we report this case with consideration of the literature.

## P2-155

**A case of effective rituximab in a patient with lupus nephritis with refractory serositis and thrombocytopenia**

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Conflict of interest: None

A 23-year-old woman presented to our hospital with dyspnea, edema of the face and extremities, and cyanosis and was admitted for anemia, decreased platelets, and low complement. She presented with hemolytic anemia, thrombocytopenia, positive antinuclear, anti-ds-DNA, and anticardiolipin antibodies, elevated urine protein, pleural and ascitic effusions, and arthritis, and was diagnosed with systemic lupus erythematosus (SLE). In addition, the patient had an elevated PAIgG level and a bone marrow examination revealed immune thrombocytopenia (ITP). Prednisolone (PSL) 1 mg/kg was started on day 11, but pleural effusion and ascites tended to increase and thrombocytopenia did not improve. Then, due to elevated urine protein, rituximab (RTX) 375 mg/m2 was administered a total of 4 times at 1-week intervals starting on day 32, and the pleural effusion and ascites improved immediately, as did platelets and urine protein. The prevalence of serositis In SLE patients is reported to be 11-54%. Most patients respond to steroids, but severe or refractory cases may require the use of immunosuppressive drugs. In this case, thrombocytopenia and serositis improved with RTX for lupus nephritis. In conclusion, RTX may be an option for refractory serositis associated with SLE.

## P2-156

**Feasibility of glucocorticoids as "bridging therapy" therapy for systemic lupus erythematosus**

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Conflict of interest: None

[Objective] To investigate feasibility of glucocorticoids (GCs) used as bridging therapy during periods of disease activity in systemic lupus erythematosus (SLE) [Methods] Disease activity was assessed with the British Isles Lupus Assessment Group (BILAG) index, and medications in the remission induction phase and maintenance phase were retrospectively analyzed. [Results] Thirty-five patients (female 33) were enrolled. The average age and disease duration was 52.7±16.2 yr., 10.9±11.2 yr., respectively. Including 10 patients with lupus nephritis (LN), 25 patients had organ domain scores of ≥1A, and 26 patients had severe disease activity in one or more organs or moderate disease activity in two or more organs measured by the BILAG index as organ domain scores of ≥1A or ≥2B, respectively. Remission induction therapy with glucocorticoids was administered in 29/35 patients, and 24/29 (83%) patients maintained remission without glucocorticoids. Of the 26 patients with BILAG ≥1A or ≥2B, 24 patients had remission induction therapy with glucocorticoids, and 21 patients (81%) including 8 patients with LN maintained remission without glucocorticoids. [Conclusions] It was feasible that GCs are used as "bridging therapy" only during periods of disease activity in SLE.

## P2-157

**Switching to anifrolumab improved skin lesions with a reduction in anti-double-stranded DNA antibody titer in systemic lupus erythematosus refractory to belimumab**

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Conflict of interest: None

Case: A 51-year-old woman was diagnosed with systemic lupus erythematosus (SLE) 17 years ago on the basis of facial erythema, psychiatric symptoms, and positivity for antinuclear and anti-double-stranded (ds) DNA antibodies complicated by Sjögren's syndrome. She achieved remission with prednisolone (PSL) 40 mg/day and intravenous cyclophosphamide, and PSL was discontinued. Cyclosporine, mizoribine, hydroxychloroquine, and azathioprine were attempted to maintain remission, but all were discontinued due to drug eruption or inadequate response. At the age of 40 years, she suffered from a stroke with antiphospholipid antibody positivity, leading to a diagnosis of antiphospholipid antibody syndrome. As she had shown lymphadenitis and erythema of the face and neck since she was 46 years old, berilimumab (BEL) was initiated. The lesions on lymph and skin had been getting better with a decrease in anti-dsDNA

antibodies. After the temporary discontinuation of BEL, the erythema relapses. Switching BEL to anifrolumab (ANF) significantly improved skin lesions just 1 month later with a reduction of anti-DNA antibodies. Conclusion: Although there are only a few reports of the benefits of switching BEL to ANF, ANF may be a treatment option for skin lesions in SLE refractory to BEL.

## P2-158

**The case of new-onset SLE that developed after vaccination**

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Conflict of interest: None

Exacerbation of underlying autoimmune diseases after COVID-19 vaccination is often experienced. We herein report a case of new-onset SLE that developed after vaccination. The patient was a 73-year-old woman who had never been diagnosed with autoimmune diseases. 7 days after receiving the third COVID-19 vaccine, she developed numbness in her extremities, vomiting and weight loss. 17 days after vaccination. Clinical findings included edematous erythema on her forehead and cheeks, non-scarring hair loss, and right axillary lymph node enlargement. Laboratory test results showed hemolytic anemia, leukopenia, hypocomplementemia and positive antinuclear antibody. Both anti-Sm antibody, anti-RNP antibody and Lupus anticoagulant were positive. She was diagnosed with SLE. Methylprednisolone 500 mg/day x 3 days was started 27 days after vaccination, followed by prednisolone (PSL) 40 mg/day. Azathioprine (AZT) 50 mg/day was added 38 days after vaccination. After the treatments, the symptoms improved rapidly, and complement levels returned to normal on the 29th day. AZT was discontinued on the 29th day of treatment due to elevated hepatobiliary enzymes. PSL could be tapered rapidly and PSL was 10 mg/day on the 111th day. There was no recurrence of symptoms after PSL and AZT were discontinued.

## P2-159

**Autopsy case of systemic lupus erythematosus with refractory macrophage activation syndrome that could not be saved**

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Conflict of interest: None

[Case] A 33-year-old woman with systemic lupus erythematosus (SLE) of 22 years of age was treated with prednisolone (PSL) 5 mg and tacrolimus (TAC). The patient was referred to our department because of difficulty in induction of remission due to flare-up of symptoms during PSL dose reduction. Bone marrow examination revealed hemophagocytosis. Steroid pulse therapy and TAC 3 mg were started, as well as tocilizumab and later etanercept, but the fever continued, and during the course of the disease, posterior reversible encephalopathy syndrome also developed and MAS progressed, and the patient died. Postmortem examination revealed hemophagocytosis and macrophage activation in the bone marrow, spleen, and lymph nodes. [Discussion] There is no consensus in Japan on the treatment of MAS associated with SLE, but EULAR/ACR has published recommendations for HLH/MAS in 2023. Glucocorticoids, immunoglobulin therapy, and anakinra, are recommended, as well as calcineurin inhibitors. In this case, the patient was refractory to high-dose steroids and TAC, and despite the use of tocilizumab and etanercept, the patient could not be saved. Although anakinra is not covered by insurance in Japan at this time, there is a need for other drugs that can be used to treat refractory MAS.

## P2-160

**Effective treatment with intravenous cyclophosphamide for refractory myopathy: a case report of anti-Ku antibody positive juvenile SLE**

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Conflict of interest: None

[Backgrounds] Systemic lupus erythematosus (SLE) occasionally causes lupus myopathy. However, characteristics of myopathy in SLE remain unknown. We report a case of anti-Ku antibody positive juvenile SLE in which intravenous cyclophosphamide (IVCY) was effective for myopathy. [Case] 13-year-old girl had Raynaud's phenomenon and arthritis. Physical examination showed proximal muscle weakness. Laboratory tests revealed antibodies to dsDNA/SS-A/Ku, low complement, elevated CK, proteinuria, hematuria. Muscle and renal biopsy were performed. They showed necrotizing myopathy and lupus nephritis. Methylprednisolone pulse therapy, mycophenolate mofetil, tacrolimus, hydroxychloroquine, belimumab, and intravenous immunoglobulin were not effective, however additional treatment with IVCY was effective for nephritis and myopathy. [Discussion] Lupus myopathy is relatively rare. Some of them are positive for anti-Ku antibody with high SLE disease activity. Pathological findings are similar to those of necrotizing myopathy and dermatomyositis. Lupus myopathy should be considered as a cause of elevated CK in SLE patients. It is important to treat refractory lupus myopathy with immunosuppression including IVCY for better outcome of myopathy.

## P2-161

**Safety and Efficacy of Belimumab for Systemic Lupus Erythematosus: A Real-World Observational Study of Single Center**

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Conflict of interest: None

Objectives: We aimed to evaluate the efficacy and safety of belimumab (BEL) for systemic erythematosus (SLE) in our department. Methods: We included the patients with SLE who was started the treatment with BEL in our department between February 2018 and September 2022. We retrospectively analyzed general background, clinical course and disease activities after 52 weeks. Results: Among 21 patients, 21 patients (100%) were female. At the baseline, the median age of patients was 54 (46-60) years old, duration of disease was 18 (9-25) years. The median SLEDAI was 4 (2-8) and the median titer of anti-DNA antibody was 13 (2-26) IU/mL. The median dosage of prednisolone (PSL) was 9 (6-12) mg. The retention rate of BEL over 52 weeks was 95% (21/22 patients). One patient discontinued BEL in line with her requests. At 52 weeks, serum C3 (86 [68-103] mg/dL vs 103 [83-110] mg/dL, $p<0.01$), serum C4 (17 [9-23] mg/dL vs 19 [14-24] mg/dL, $p<0.05$), SLEDAI (4 [2-8] vs 2 [0-2] $p<0.01$) and anti-DNA antibody titer (13 [2-26] IU/mL vs 4 [2-11] IU/mL, $p<0.01$) were significantly improved. The dosage of PSL was significantly decreased (9 [6-12] mg vs 6 [4-8] mg $p<0.01$). There were no serious adverse events. Conclusion: BEL might be one of the safe and effective treatment options for SLE.

## P2-162

**Efficacy and safety of using belimumab at acute and stable phase in systemic lupus erythematosus**

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects a variety of tissues. Of approximately 200 patients with SLE, Juntendo University Urayasu Hospital, a cumulative total of 53 patients had received Belimumab (BLM). 46 patients were included in the study to evaluate patient background, treatment response, and glucocorticoid (GC) dose reduction. Of the 46 patients, 41 were female, age 36.3 (±11.8) years, anti-DNA antibody 33.8 (±39.9) IU/ml, SLEDAI 4.41 (±2.11), and GC use 16.2 (±14.5) mg. At induction, lupus nephritis was the most common co-

morbidity (52%), arthritis and only positive serology each accounted for 10%, and skin rash and cytopenia each accounted for 8%. 52 weeks later, anti-DNA antibodies, CH50, and SLEDAI all improved significantly, and GC use was also reduced. The results showed that SLEDAI, and GC use decreased significantly in the relatively stable group that was introduced for GC reduction. To improve the long-term prognosis of SLE, it is important to reduce the risk of drug-related adverse events in addition to controlling disease activity, and it is highly significant to actively introduce biologic agents.

## P2-163

**Clinical characteristics, therapeutic efficacy in 10 patients with anifrolumab for systemic lupus erythematosus**

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Conflict of interest: None

[Objective] Anifrolumab (ANF) is a biological drug that is expected to improve symptoms of SLE and reduce glucocorticoid by inhibiting type I IFN signaling. We clarify the actual use of ANF in SLE treatment. [Methods] 10 SLE patients treated with ANF in our hospital between Septemper 2021 and June 2023 were evaluated for clinical characteristics and treatment efficacy. [Results] All patients were female, the median age was 27 years (21-80), the median disease duration was 10 years (3 months-22 years), and 7 patients were cSLEDAI≧4. All patients used hydroxychloroquine and prednisolone (PSL), median PSL use was 6 mg/day (4-40), and 9 patients were treated with tacrolimus, 3 with mycophenolate mofetil, 3 with azathioprine, and 5 with cyclosporine. 5 patients were switched from belimumab (BLM). 6 patients were started on ANF for skin rash, 2 each for PSL reduction and arthritis, and 1 each for thrombocytopenia, lupus nephritis flares, low complement, and fatigue. 1 patient was switched to BLM for lupus nephritis flares. 2 patients had COVID-19 (not severe), and none had herpes zoster. PSL reduction was possible in 8 out of 9 patients continuing ANF. [Conclusion] We often used ANF as maintenance treatment in relatively young patients. 9 patients were able to improve symptoms and reduce PSL.

## P2-164

**Analysis of Risk Factors for Hydroxychloroquine-Induced Drug Eruptions in Patients with Systemic Lupus Erythematosus**

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Conflict of interest: None

[Objective] To investigate risk factors for drug eruptions due to hydroxychloroquine (HCQ) in systemic lupus erythematosus (SLE) patients. [Methods] Among SLE patients with a history of HCQ administration, we analysed 117 patients who continued HCQ and 14 patients who had to discontinue HCQ due to drug eruptions. Age, duration of the disease, disease activity and treatment at the initiation of HCQ, major organ involvements, autoantibodies and a history of drug allergies were retrospectively compared between the two groups. [Results] The median age at the initiation of HCQ was 42 (IQR 33.3-51.5) years, and the median duration of the disease was 87 (16.3-193) months. The HCQ dosage was 5 mg/kg ideal body weight/day. Drug eruptions occurred 26.5 (21.5-34.5) days after the initiation of HCQ. In the drug eruptions group, the presence of anti-SS-B antibodies (p=0.004) and a history of drug allergies (p=0.046) were significantly higher. In the multivariate analysis, the presence of anti-SS-B antibodies (odds ratio: 5.2, 95% CI 1.58-17.2) was identified as a risk factor of drug eruptions. [Conclusions] The most common reason for discontinuing HCQ was drug eruptions, and SLE patients with positive anti-SS-B antibodies need to be carefully monitored during the early periods of HCQ administration.

## P2-165

**Clinical features of systemic lupus erythematosus who treated with anifrolumab at our institution**

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Conflict of interest: None

[Objective] To clarify clinical features of systemic lupus erythematosus (SLE) for which treatment with anifrolumab was initiated. [Methods] Patients with SLE who received anifrolumab until October 2023 (ANI group) and who did not as of October 2023 (non-ANI group) at our department were enrolled. Continuous values were compared by Wilcoxon rank sum test, and categorial values were by Pearson's chi-square test. [Results] Seven patients were classified into the ANI group (7 females) and 44 into the non-ANI group (42 females). Median age was 41.0 years old vs. 42.5 years old (p=0.29), and median disease duration was 7.0 years vs. 10.5 years (p=0.12). The proportion of glucocorticoids (GCs) administration was 100% vs. 86.4% (p=0.30), and the median dose of GCs of prednisolone equivalent was 12.9 mg/day vs. 3.0 mg/day (p=0.0003). The proportion of the usage of hydroxychloroquine was 85.7% vs. 72.7% (p=0.46), that of mycophenolate mofetil (MMF) was 57.1% vs. 27.3% (p=0.11), that of tacrolimus was 14.3% vs. 34.1% (p=0.29) and that of belimumab was 28.6% vs. 43.2% (p=0.47). [Conclusions] Anifrolumab was more likely to be initiated in patients with shorter disease duration, higher doses of GCs and who was treated with MMF at our institution.

## P2-166

**Efficacy of belimumab in patients with systemic lupus erythematosus: retrospective single center experience**

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Conflict of interest: None

[Objective] The aim of this study was to examine the efficacy of belimumab therapy in the patients with systemic lupus erythematosus (SLE). [Methods] Thirty-one patients with SLE who underwent belimumab treatment were examined. We examined disease activity of SLE, dose of prednisolone, and drug retention rate. [Results] Thirty patients were females, the average age was 44.7±18.9 years, and the mean disease duration was 8.6±11.8 years. The mean prednisolone dose was 13.8±13.6 mg/day. Tacrolimus was used as concomitant therapy in 20 patients, hydroxychloroquine in 13 patients, and mycophenolate mofetil in 5 patients, and azathioprine in 3 patients. Twenty-four patients were used due to ineffectiveness of previous treatments. Belimumab treatment significantly decreased titer of ds-DNA antibody (36.6±58.6 IU/mL at baseline, to 15.8±25 IU/mL at 3 months, and to 7.9±3.0 mg/day at 12 months (p<0.0001, and p<0.0001, respectively)), and reduced dose of prednisolone to 11.0±5.4 mg/day at 3 months (p<0.001), and to 7.9±3.0 mg/day at 12 months (p<0.001). The retention rate of belimumab was 89.5% at 1 year, and 87.5% at 2 years. [Conclusions] Belimumab treatments are effective and safety in SLE patients.

## P2-167

**A review of clinical features of patients treated with Anifrolumab for Systemic Lupus Erythematosus in our hospital**

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Conflict of interest: None

[Background] Recently, evidence has accumulated that type I interferon (IFN) plays important roles in the pathophysiology of systemic lupus erythematosus (SLE). We report our experience of anifrolumab (ANI), a monoclonal antibody against the type I IFN receptor. [Methods] We retrospectively analyzed the clinical course of 16 SLE patients treated with

ANI in our hospital from 2022 June to 2023 September. [Results] 13 patients were female. The median age was 48 years. In the entire course from onset, 12 patients were positive for anti-ds-DNA antibody at least once, 3 for anti-Sm, and 6 for anti-RNP. The median SLEDAI-2K at induction was 5. The main symptoms were joint symptoms in 10 patients, skin symptoms in 3, serological abnormalities in 3, and malaise in 1. The median prednisolone dose was 7 mg/day. 12 patients switched from belimumab. 5 patients discontinued ANI within 28 weeks. 8 patients received ANI for more than 24 weeks. In 7 patients of them, SLEDAI-2K improved in the 24 weeks after induction (median from 6 to 4). In 5 patients, corticosteroid dose decreased (median of prednisolone equivalent from 8 mg/day to 6 mg/day). [Conclusion] For SLE patients with difficulty reducing corticosteroid, ANI may be effective in terms of corticosteroid reduction and symptom improvement.

## P2-168

**A study of patients with SLE treated with concomitant medications including berylumab at our hospital**

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Conflict of interest: None

[Objective] To determine the use of concomitant medications in patients with SLE at our hospital and to determine the contribution of biologics and other concomitant medications to therapeutic efficacy. [Methods] We analyzed the clinical characteristics of 67 patients with SLE at our hospital, for each concomitant medications, and posttreatment SLEDAI-2K, BILAG, SRI4 attainment, and LLDAS attainment, retrospectively. [Results] Background: 60 female patients, 7 male patients. As of March 2023, LLDAS achievement rate was 67%, and concomitant medications included Tac in 39 cases, followed by HCQ and MMF in 20 cases each, and BEL in 17 cases. 31% of patients were initially severe cases and 44% were intensified treatment for relapse as the reason for BEL introduction. All BEL users are still using BEL as of March 2023. [Conclusions] In our practice, biologic agents were introduced in many patients who did not achieve LLDAS. Early introduction of biologics in patients who are refractory to initial therapy may contribute to PSL reduction.

## P2-169

**Two cases of severe pancreatitis with an unusual course after systemic lupus erythematosus treatment**

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National Center for Global Health and Medicine

Conflict of interest: None

[Objectice] To investigate the difference between pancreatitis that develops immediately after the start of treatment for SLE and other forms of pancreatitis. [Cases] Both cases were 38-year-old women with first-episode SLE and SLEDAI scores of 19 (case 1) and 47 (case 2). Case 1 was treated with 1 mg/kg/day of water-soluble prednisolone and Case 2 with 500 mg/day of methylprednisolone pulse. They developed acute pancreatitis on day 3 after starting steroids. At the onset, the amylase levels of case 1 and case 2 were 705 U/L and 1350 U/L and both were grade 1 on contrast-enhanced CT. However, their status worsened within a week of the start of infusion therapy, and ventilator management was required. Furthermore, the severity score of pancreatitis was either severe II or the most severe. In the end, they were extubated in about two weeks, their SLE activity stabilized, and they were discharged on their own. [Conclusions] However, they developed severe pancreatitis requiring ventilator, which is considered to be the difference between lupus pancreatitis and other forms of pancreatitis. This study suggests that acute pancreatitis immediately after the start of SLE treatment, even in the absence of laboratory or imaging findings, can be severe and should not be taken lightly.

## P2-170

**Longitudinal Observation of Thrombotic Events in Obstetric Antiphospholipid Syndrome: Clinical Characteristics of Four Cases**

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Conflict of interest: None

[Objective] In this study, we investigated the clinical characteristics of four patients with obstetric antiphospholipid syndrome (OAPS) who developed thrombosis following over two decades of observations. [Methods] Among the 87 APS patients who visited our department, we focused on OAPS patients with more than 20 years of observations and several antiphospholipid antibody (aPL) assessments. [Results] The mean age at the time of OAPS diagnosis was 33.8 ± 8.9 years. All patients had multiple aPL positivity and high titers of aPL. Although all patients underwent primary antiplatelet prophylaxis during an observation period averaging 23.6 ± 2.6 years, three patients developed cerebral infarction and one experienced deep vein thrombosis. The mean interval to the onset of thrombosis was 19.2 ± 2.9 years after OAPS diagnosis. Among them, two patients had hypertension and dyslipidemia, whereas the other two had no thrombosis risk factors. [Clinical Significance] Prolonged observation confirmed that the patients with consistently high aPL titers had increasing thrombotic risks as patients got older. Even in OAPS patients without prior thrombosis, thrombotic risk assessment and preventive measures are necessary.

## P2-171

**A case of systemic lupus erythematosus (SLE) with large granular lymphocyte (LGL) proliferation**

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Conflict of interest: None

[Case] A 69-year-old woman was referred to our department for further evaluation of progressive interstitial pneumonia and ANCA positivity. The detailed physical examination and laboratory tests showed arthritis, thrombocytopenia and anti-nuclear antibody (ANA) and anti-double stranded DNA antibody (anti-dsDNA antibody) positivity. Bone marrow test for the evaluation of thrombocytopenia suggested T-cell large granular lymphocytic leukemia (T-LGLL), while TCR gene rearrangement analysis didn't detect monoclonality. She was diagnosed with SLE on the basis of ANA and anti-dsDNA antibody positivity, interstitial pneumonia, thrombocytopenia and arthritis. The administration of high-dose corticosteroids, hydroxychloroquine and intravenous cyclophosphamide (IVCY) improved her symptoms and thrombocytopenia. The treatment decreased the number of LGL transiently, while the gradual tapering of corticosteroids slightly increased its number without any signs of SLE flare. [Clinical Significance] T-LGLL is frequently associated with autoimmune diseases, while SLE can cause reactive LGL proliferation. Standard treatment of T-LGLL is immunosuppressive therapy, which can improve autoimmune disorder.

## P2-172

**A case of elderly-onset idiopathic thrombocytopenic purpura (ITP), who had SLE-like blood test abnormalities (pancytopenia, positive anti-nuclear antibody, hypocomplementemia, high anti-DNA antibody), and primary eradication of H. pylori (HP) not only improves the platelet count but also improves the SLE-like condition**

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Conflict of interest: None

[Case] 87-year-old male was followed by cardiologist for atrial fibrillation. On Sep. 6, the platelet count was low at 34,000 (185,000 on Jun. 28). No bleedings. WBC was low, he had anemia, a bone marrow aspira-

tion was performed on Oct. 19. HIs BM was normal to hyperplastic, and megakaryocytes was within normal range. Three lines were maintained and no atypical cells. ANA 1280x (Homo), hypocomplementemia, anti-DNA Ab positivity, and high PAIgG were observed, and he was admitted on Dec. 1. He met the diagnostic criteria for ITP. SLE doesn't meet the 1997 ACR criteria. He was positive for Helicobacter pylori antibody 29, the eradication was performed. The platelet count increased from end of Dec. and remained stable at 200,000. WBC rose from 1,000 to 3000. 6 months after eradication, the effect was evaluated and HP antibody was 22. PAIgG 20400→215, C3 28→49, C4 ≦1→2, anti-ds-DNA Ab 159→80, anti-ss-DNA Ab ≧800→97, improving hypocomplementemia and reducing ITP/SLE-related antibodies. [Discussion] HP eradication not only showed remission of ITP but also improvement of SLE-like abnormalities. Suggesting that HP may be involved in some immune abnormalities in SLE. Previous reports shows the relationship between HP and SLE is controversial, we hoped this relationship will be pursued.

## P2-173

**A case of fatal autoimmune hemolytic anemia that appeared during the course of stable SLE and took a violent course in a few days**

Shunsuke Tsuge, Kiyoaki Ito, Anri Mori, Hiromitsu Akamatsu, Kaho Hayashi, Megumi Ikeda, Akira Sakata, Hiroaki Saito, Fumitaka Yamamori, Hiroyosh Yanagisawa, Daiki Hayashi, Hajime Sanada, Yoshinori Takahashi, Takahiro Yuasa, Akihiko Koshino, Taichiro Minami, Ryo Nishioka, Takeshi Zoshima, Megumi Oshima, Satoshi Hara, Ichiro Mizushima, Tadashi Toyama, Shinji Kitajima, Akinori Hara, Norihiko Sakai, Miho Shimizu, Yasunori Iwata, Mitsuhiro Kawano
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Conflict of interest: None

[Background] Autoimmune hemolytic anemias (AIHAs) are rare and heterogeneous disorders characterized by the destruction of red blood cells by warm or cold antibodies and are associated with 10% of SLE cases. [Case Presentation] A 77-year-old female patient with SLE had been stable for the past 20 years. She presented with fatigue and severe anemia. She was admitted to the hospital with a diagnosis of severe warm AIHA based on hemolytic findings and a direct Coombs test that was strongly positive for IgG and C3d. The patient underwent intensive care including steroid pulse and multiple acute hemodialysis therapies, but multiple organ failure with acute liver failure progressed rapidly, and was difficult to save his life. The autopsy revealed extensive sinusoidal obstruction of the liver due to erythrocyte aggregates, resulting in ischemic necrosis. We report on the characteristics of the autoantibodies that led to this severe condition, including literature review, basic and histopathological studies.

## P2-174

**An autopsy case of systemic lupus erythematosus with a fatal course due to fulminant autoimmune hemolytic anemia**

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Conflict of interest: None

[Case Report] A 44-year-old woman was treated with tacrolimus and hydroxychloroquine for systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APS). She was serum immunologically stable for a long time, but had hemosiderinuria, jaundice, and nausea. She was diagnosed as autoimmune hemolytic anemia (AIHA) due to SLE with hypocomplementemia, severe anemia, elevated indirect bilirubin, elevated LDH, and splenomegaly on CT. She was treated with methylprednisolone (1000 mg) with hospitalization, but anemia progressed on hospitalization day2. Red blood cell transfusion, plasma exchange, and intravenous immunoglobulin were administered, and the anemia temporarily improved. However, the progression of anemia, hyperkalemia, and acidosis were observed, and emergency dialysis were performed. She died on hospitalization day3 due to rapid hypotension. During the hypotension, thrombus was observed in the inferior vena cava and radial artery by ultrasound. A pathological autopsy was performed to determine the cause of death. [The autopsy results and discussion] The ischemia in multiple organs suggested multiorgan failure due to marked anemia. No thrombus was found. In addition, a prominent hemophagocytosis was found, which may have contributed to the progression of anemia.

## P2-175

**A case of SLE with pure red cell aplasia**

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Conflict of interest: None

[Case] 34 year old female [Case Presentation] Three months before coming to our hospital, She has been aware of dyspnea on exertion, after contracting the common cold with a one-year-old child. She again common cold and worsening dyspnea. She was admitted for further examination and treatment of his macrocytic hyperchromic anemia with markedly decreased production of Hb 3.4g/dL, MCV 110, MCHC 31.9, and Ret 1%. [Clinical Course] CT and endoscopy showed no bleeding. Although the direct Coombs test was positive, there were no hemolytic findings. Bone marrow examination revealed decreased erythroblast percentage and elevated M/E ratio, and diagnosis of PRCA. Viral was suspected, but parvovirus B19 IgM and PCR tests were negative. No new drugs were used, and no thymoma. She was positive for ANA, antiphospholipid antibodies, low C3c, hypergammaglobulinemia, lymphopenia, and maculopapular hemorrhage suspicious for lupus retinitis, and pleurisy. The patient diagnosis for PRCA with SLE, and immunosuppressive therapy with PSL 0.8 mg/kg and MMF was started. [Clinical Significance] Thymoma, parvovirus B19, drugs, and lymphoid tumors are known as causes of PRCA, but reports of PRCA associated with SLE are rare. We report this case from the viewpoint of diagnosis, pathogenesis, and treatment.

## P2-176

**Imaging studies are useful for diagnosing intracranial hypertension associated with systemic lupus erythematosus**

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Conflict of interest: None

[Background] Intracranial hypertension (IH) is classified as a neuropsychiatric manifestation of systemic lupus erythematosus (SLE) that can cause visual impairment and abducens nerve palsy. IH is diagnosed based on cerebrospinal fluid pressure and fundus findings. However, lumbar puncture is invasive, and accurate assessment of fundus findings is difficult for the rheumatologist. We report three cases in which imaging studies were useful for diagnosing IH associated with SLE. [Case presentations] All patients were newly diagnosed with SLE with different symptoms: lupus nephritis, hemophagocytic syndrome, or lupus enteritis. One patient had headache and blurred vision, while the other patients were asymptomatic. In all cases, head computed tomography (CT) and magnetic resonance imaging (MRI) revealed optic nerve tortuosity, enlarged subarachnoid space around the optic nerve, or flattening or depression of the posterior surface of the eye. All patients had papilledema on fundoscopy and were diagnosed with IH. In the two patients, papilledema improved after the induction therapy with high-dose prednisolone (PSL) and immunosuppressive agents. [Discussion] This report suggests that imaging studies were useful for diagnosing IH associated with SLE.

## P2-177

**A case of systemic lupus erythematosus which flared up during pregnancy without hypocomplementemia or elevated anti-DNA antibodies**

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Conflict of interest: None

[Case] A 29-year-old woman was diagnosed with systemic lupus erythematosus (NPSLE, RPGN, nephrotic syndrome, pleurisy, pericarditis, cytopenia, ANAx2560, anti-DNA antibody). She was treated with high-dose prednisolone and tacrolimus but did not go into remission. Her alopecia, erythema, elevated anti-DNA antibodies, and low complement required re-addition of steroids, hydroxychloroquine, and azathioprine. At age 40, she became pregnant. Early in pregnancy, she had weight loss, anemia, and decreased renal function, but there were no abnormal urinalysis, decrease in complement, or elevation of antibodies. She was given blood transfusions and erythropoietin products. We decreased doses of AZA and TAC and increased doses of prednisolone. She later developed hypertension and proteinuria, and had an emergency C-section at 28 wks 4 days gestation due to non-reassuring fetal status (579g, Apgar Score 3/6, ascites 800 ml). After delivery, her anemia and renal function improved rapidly, but her proteinuria (2 g/gCr) prolonged for 6 months. As renal biopsy showed active lesions (ISN/RPS type IV+V), we increased her dose of prednisolone and switched immunosuppressant drugs. She improved in proteinuria and hypocomplementemia.

## P2-178

**The role of electron microscopic evaluation in repeat kidney biopsy for patients with lupus nephritis**

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Conflict of interest: None

[Object] To identify the significance of electron microscopy evaluation in repeat kidney biopsy (Biopsy 2) for lupus nephritis (LN) [Methods] Twenty-three consecutive LN patients who underwent Biopsy 2 two years after induction therapy were evaluated retrospectively. We defined the following two ideal long-term goals at 5 years: "A," SLEDAI-2K = 0 and prednisolone (PSL) ≦5 mg/day; and "B," proteinuria ≦0.2 g/day with a normal serum Cr level and PSL ≦5 mg/day. Histologically, the electron-dense deposit (EDD) score grades immune deposits based on their intensity, amount, and location. A score of ≦1 was defined as "electron microscopy remission (ER)." [Results] Biopsy 2 were performed at a median of 27 months (interquartile range: 25, 34) from the start of treatment. Only ER could predict the ideal state of A-5y and B-5y at 5 years, with sensitivity (0.83, 0.82), specificity (0.73, 0.67), AUC (0.78, 0.74), and positive likelihood ratio (3.06, 2.46), respectively. EDD scores predicted A-5y, B-5y, and PSL dose at 5 years in proportion to the score. [Conclusions] Although histological activity and prognosis have been estimated using light microscopy, this study showed that electron microscopy evaluation of Biopsy 2 correlates better with long-term outcomes.

## P2-179

**A case of rheumatoid arthritis and limited cutaneous systemic sclerosis who develop systemic lupus erythematosus complicated with refractory thromboticmicroangiopathy**

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Conflict of interest: None

A 78 year-old female patient with rheumatoid arthritis and limited cutaneous systemic sclerosis was sent to our hospital emergently because of fever and consciousness disturbance in August 2020. Physical and laboratorial examinations revealed she had hypertension, thrombocytopenia, schistocytosis and renal disturbance. Thrombotic microangiopathy (TMA) due to malignant hypertension was suspected and antihypertensive agents were initiated. However, her symptoms did not improve. Further examination showed that positive anti-dsDNA antibody, pancytopenia, depletion of complements and elevation of IL-6 concentration in cerebrospinal fluid suggesting she was neuropsychiatric symptoms associated with systemic lupus erythematosus (NPSLE). At that point, she was diagnosed as having NPSLE with secondary TMA and high dose of prednisolone and plasma exchange therapy was initiated. Although fever and pancytopenia were improved, schistocytosis and renal dysfunction were persistent. During the clinical course, she was infected repeatedly and died in January 2021 because of refractory infection. Pathological autopsy revealed TMA in kidney. This case was intractable to treatment because several factors such as hypertension, collagen disease and infection might involve the pathogenesis of TMA.

## P2-180

**A case with Sjogren's syndrome complicated by systemic lupus erythematosus with leukocytoclastic vasculitis and various renal lesions**

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Conflict of interest: None

[Case] A 45-years-old woman with a 25-year history of Sjogren's syndrome (SjS) developed fever, edema, purpura, arthritis, leukopenia, lymphopenia, proteinuria with cellular casts, high IgG 4813 mg/dL, hypocomplementemia, antinuclear antibody x2560 (ho, sp), positive anti-Sm antibody and anti-SS-A antibody. She was diagnosed as having systemic lupus erythematosus (SLE) with SjS. She was referred to our hospital. Anti-DNA antibody was ≧200 IU/mL. A skin biopsy of a purpura revealed leukocytoclastic vasculitis (LV). Lower gastrointestinal endoscopy revealed redness in the colon, which was considered due to vasculitis. On renal biopsy, there was no sclerotic lesion, but mesangial cell proliferation and marked inflammatory cell infiltration in the interstitium. Fluorescent immunostaining revealed IgA and C3 deposition, but no IgG deposition. Lupus nephritis type IIIA coexistence with interstitial nephritis due to SjS were diagnosed. She was successfully treated with glucocorticoid and cyclophosphamide. [Discussion] In this case, the disease activity of SjS, including purpura, LV, and interstitial nephritis, was thought to have appeared with the onset of SLE. We report this case as an interesting and valuable when considering the pathology of SLE and SjS and their relationship.

## P2-181

**A case of antinuclear antibody-negative lupus colitis**

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Conflict of interest: None

[Background] The 2019 EULAR/ACR systemic lupus erythematosus (SLE) classification criteria require at least one positive result of 80-fold or more antinuclear antibody (ANA). This criterion is useful with a sensitivity of 96.1% and a specificity of 93.4%, and ANA-negative SLE is rarely seen. We report a case of ANA-negative lupus colitis with thrombocytopenia. [Case] A 40-year-old woman presented with diarrhea and vomiting. Her platelet count was 0.5 million/μL, and CT scan showed marked intestinal edema in the small and large intestines. Although ANA was 40-fold, anti-dsDNA and anti-Sm antibodies were negative, we diagnosed her as SLE from history of sun sensitivity, sphenoid erythema, target signs in the intestinal tract on CT, bilateral hydronephrosis, and positive anti-cardiolipin IgG antibody. After high-dose intravenous steroid therapy, steroid and hydroxychloroquine, and cyclophosphamide infusion, her platelet count increased, abdominal symptoms disappeared. [Discussion] Although lupus cases with negative ANA have been reported, most of them are diagnosed with nephritis, and cases of lupus colitis with ANA-negative are rare. In the case of colitis with thrombocytopenia, SLE should be considered as the differential diagnosis in the case of ANA-negative.

## P2-182

**A case of systemic lupus erythematosus developing Epstein-Barr virus-positive polymorphic B cell lymphoproliferative disorder, NOS during remission maintenance therapy**

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Conflict of interest: None

A-50-year old female had been diagnosed with SLE with lupus nephritis (ClassIV) 32 years before this admission. For the past several years, she had been in clinical remission with 4 mg/day of PSL, TAC (3 mg/day), and HCQ (200 mg/day). She was admitted because of urticarial erythema, lymphadenopathy (greater than 1 cm in diameter), and splenomegaly, which was refractory to treatment with 30 mg/day of PSL. Serum complement levels were decreased and EBV-DNA copy number in whole blood was 5.57 LogIU/mL. A lymph node biopsy showed altered lymph node architecture and a polymorphic infiltrate. Some lymphocytes were positive for EBER-ISH. Later, she developed purpur and fever. A skin biopsy showed leukocytoclastic vasculitis with EBER-ISH positive lymphocytes. Analysis of blood sample showed most EBV-infected cells were CD20-positive B cells. She was diagnosed with EBV-positive polymorphic B cell lymphoproliferative disorder, NOS and was treated with 60 mg/day of PSL combined with rituximab, which resulted in improvement of her symptoms and disapearance of EBV-infected cells. Given the wide variety of classification and clinical symptoms in EBV-associated lymphoproliferative disorders, it should be considered as a differential diagnosis in patients with atypical and/or refractory SLE.

## P2-183

**A case of SLE with class 5 nephritis and non-cirrhotic portal hypertension (NCPH) during the course of rheumatoid arthritis, which achieved remission with immunosuppressive therapy**

Chiharu Miyamoto, Taisuke Fujita, Ayaka Inoue, Midori Kitayama, Takahisa Onishi, Noriaki Yo, Takashi Yamane
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Conflict of interest: Yes

A 61-year-old male patient with 30-year of RA was treated with iguratimod after long-term MTX therapy. In February X, he developed fever and leg ulcer, and was referred to our hospital. On admission, he had showed hypoxemia, hypocomplementemia, nephritis, interstitial pneumonia and massive ascites effusion. Suspecting a vasculitis, he was treated with glucocorticoid pulse and IVCY, and his respiratory condition rapidly improved. A renal biopsy showed histology consistent with lupus nephritis class V, and he was classified as SLE according to the 2019 criteria. On the other hand, ascites continued to worsen after admission, and we suspected portal hypertension, but there were no findings suggestive of cirrhosis. Hepatic vein catheterization revealed a pressure gradient of 12 mmHg and a diagnosis of non-cirrhotic portal hypertension (NCPH). Liver biopsy showed no fibrosis or disease-specific abnormalities. The ascites decreased gradually with improvement of nephritis and hypocomplementemia by immunosuppressive treatment, and almost disappeared after 5 months of treatment. [Clinical Significance] NCPH often shows a favorable course and therefore, it is important to perform immunosuppressive therapy based on a proper definitive diagnosis, even in complicated conditions.

## P2-184

**A case of a girl with mixed connective tissue disease complicated by recurrent neuromyelitis optica who responded to rituximab**

Sho Mori, Kazuko Yamazaki, Yusei Motonaga, Shotaro Suzuki, Etsushi Toyofuku, Mariko Mouri, Kohei Yoshioka, Seido Ooka, Masaaki Mori, Kimito Kawahata
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Conflict of interest: None

Neuromyelitis optica (NMO) is an autoimmune disease that causes inflammatory demyelination of the optic nerve and spinal cord, resulting in multiple visual loss and sensory abnormalities. Sjögren's syndrome and SLE can be associated with NMO, but mixed connective tissue disease (MCTD) is rare. A 16-year-old girl was diagnosed with NMO four years ago due to left visual loss and anti-AQP4 antibody, and was treated with steroid pulse therapy. Three years ago, she developed refractory stuttering and vomiting, which were diagnosed as relapse of NMO due to dorsal medullary syndrome. Two years ago, she developed fever, Raynaud's symptoms, and positive anti-RNP antibodies, leading to the diagnosis of MCTD. At that time, CSF IL-6 level was elevated at 202 pg/ml and MRI showed left optic neuritis, so she was treated with satralizumab (SAT), an anti-IL-6 receptor monoclonal antibody. However, she had new interstitial pneumonia, recurrent MCTD, and worsening left upper visual field defect. She was treated with RTX, and has remained in remission for 2 months. There are only three previously reported cases of NMO and MCTD combined, and this is the first case in a pediatric patient. To prevent recurrence of NMO, deeper remission should be maintained in cases of collagen disease complications.

## P2-185

**A case with long-lasting pulmonary arterial hypertension associated with mixed connective tissue disease successfully treated with intravenous cyclophosphamide**

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Center for Rheumatic Diseases, Mie University Hospital, Tsu, Japan

Conflict of interest: None

[Case] A 37-year-old woman was diagnosed with mixed tissue connective disease (MCTD) and treated with prednisolone (PSL) in X-16 year. Echocardiography revealed a high tricuspid regurgitation pressure gradient (TRPG) of 88 mmHg, and she was diagnosed as pulmonary arterial hypertension (PAH) and treated with PSL and 1 course of intravenous cyclophosphamide (IVCY). Her TRPG improved to 69 mmHg, subsequently beraprost and sildenafil were administered. In X-9 year, arthritis appeared in her both wrists and was improved with abatacept. In X-3 year, cervical cancer was detected and abatacept was discontinued. After chemotherapy, arthritis flared up and treated with tocilizumab at our department, however mPAP had worsened to 43 mmHg in X-1 year. PSL and 8 courses of IVCY were performed, and mPAP improved to 21 mmHg. [Discussion] For CTD- PAH, immunosuppressive therapy is said to be effective in the early stages or when the disease is active, but if PAH continues for a long time, it is difficult to judge whether it is reversible. This patient had intractable arthritis and was thought to have high MCTD activity, so immunosuppressive therapy was successful. [Significance] This report is significant in that immunosuppressive therapy can be successful even in long-affected MCTD-PAH.

## P2-186

**A case of mixed connective tissue disease (MCTD) complicated by febrile neutropenia (FN) due to autoimmune neutropenia (AIN) requiring multidisciplinary immunosuppressive treatment**

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Conflict of interest: None

[Case] A 39 year-old woman was diagnosed as MCTD in X-1 with puffy fingers, screloderma, arthritis, myositis, reflux esophagitis, and strong positive anti-U1-RNP antibody, and started prednisolone (PSL) and tacrolimus. In X year, she visited with back pain and fever lasting a week, and NEU 120/μL, MONO 630/μL, and CRP 1.20 mg/dL were pointed out. Physical examination revealed no abnormalities without screloderma. Blood tests: Hb 11.1 g/dL, Plt $280\times10^9$/L, no renal or hepatic impairment, elevated myogenic enzymes, or hypocomplementemia. IgG 2708 mg/dL, antineutrophil antibody (+). Bone marrow samples: No abnormalities in morphology, chromosomes, or cell surface markers. Myeloid cell count is increasing. In the absence of new drugs, PSL was increased to 1 mg/kg, but ineffective. Rituximab 375 mg/m2 was terminated due to headache and erythema after 3rd administration. After one additional 2g/kg of intravenous immunoglobulin therapy (IVIG), NEU improved from <100 to >500/μL. After adding immunosupressants, PSL was tapered off 9 months later. [Discussion] There are few adult cases of AIN, and no case with MCTD has been previously reported. IVIG has been suggested to be effective in pediatric cases, and may be option for AIN secondary to MCTD, in addition to immunosuppressive therapy.

## P2-187

**Characteristics of systemic sclerosis (SSc) with overlap syndrome (OS)**

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Conflict of interest: None

[Objective] This study examined systemic sclerosis (SSc) combined with overlapping syndromes (OS). [Methods] The study included 345 SSc patients. [Results] The SSc with OS group consisted of 131 patients (Sjögren's syndrome (SS): 89, rheumatoid arthritis: 18, systemic lupus erythematosus: 12, vasculitis: 6, polymyositis/dermatomyositis: 5). SS was the most common complication (67.9%). There were more women in the SSc with OS group than in the SSc alone group ($p<0.05$), and this trend was more pronounced in the SS combined group ($p<0.01$). In terms of complications, the SSc with OS group had a higher prevalence of pulmonary hypertension and upper gastrointestinal lesions than the SSc alone group ($p<0.05$). Arthritis and renal complications were more common in the SSc with OS group than in the SSc alone group ($p<0.01$). There was no significant difference in mortality or cause of death between the two groups. [Conclusions] The SSc with OS group had the highest prevalence of SS complications, which significantly influenced the clinical presentation of the SSc with OS group. Considering the higher incidence of prognostic pulmonary hypertension in SSc with SS complications, early diagnosis and treatment of pulmonary hypertension should be considered.

## P2-188

**Anti-Ku antibody-positive Polymyositis-Systemic Sclerosis Overlap Syndrome Presenting with Truncal Muscle Involvement: A Case Report**

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Conflict of interest: None

[Case] A 70-year-old man presented with back pain about 10 months ago. Pain in extremities and arthralgia appeared around 4 months ago. In August X, he underwent a blood test, which showed a high CK level of 3835 U/L. Suspected myositis, he was referred to our department for a consultation. Tenderness in paraspinal muscles and camptocormia were observed. Contrast-enhanced MRI showed T2 high-signal areas and enhancement in the erector spinae, latissimus dorsi, and trapezius muscles, and a diagnosis of polymyositis was made. In addition, nailfold bleeding and skin thickening of the fingers and forearms were observed, and a skin biopsy revealed thickening collagenous fibers at the lower dermis, which led to a diagnosis of systemic sclerosis. Later, the patient was found to be positive for anti-Ku antibody. The patient underwent remission induction therapy with high-dose glucocorticoids + rituximab + tacrolimus and his back pain and camptocormia improved. [Clinical Significance] There are few cases in which the truncal muscle is mainly affected like this case, and some may be overlooked. A few similar cases of anti-Ku antibody-positive patients have been reported, and when myositis is suspected, it is necessary to watch for truncal muscle involvement.

## P2-189

**A case of Overlap syndrome (Polymyositis, Systemic sclerosis) presenting with dyspnea on exertion and visual impairment associated with anti-PM/Scl100 antibody**

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Conflict of interest: None

[Case] 83y.o. Female [Complaint] Shortness of breath on exertion, visual loss. [Past History] Uterine Fibroid (49y.o.), Intestinal obstruction (60y.o.), Depressron (77y.o.), Herpes zoster (80y.o.), Glaucoma (81y.o.) [Clinical Course] From March (year X), the patient began to exert dyspnea and palpitations. In April she exerted visual impairment, and was diagnosed with macular edema. 2 days later she exerted a fever and hypertension (>200mmHg sBP) and was started on a depressor, and was admitted to hospital (W). Ground-glass opacity and puffy fingers, periungual erythema was present. We suspected Dermatomyositis with malignant hypertension, or a Scleroderma renal crisis, and performed plasmapheresis, followed by PSL 0.5 mg/kg/day. Rituximab was administered. Data showed normal ADAMTS13 activity and ADAMTS inhibitor not detected, making TTP unlikely. Anti-PM/Scl100 and 75 was positive, suggesting Overlap syndrome of Polymyositis and Scleroderma. After starting MMF, the serum Creatinine level was alleviated. [Clinical Significance] Secondary TMA associated with collagen disease and Scleroderma renal crisis have multiple differential diagonoses. Here we discuss the challenges of treating this condition, in particular with the association of anti-PM/Scl antibodies in previous reports.

## P2-190

**A case of anti-TIF1-gamma antibody-positive polymyositis associated with systemic lupus erythematosus**

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Conflict of interest: None

[Case] A 74-year-old woman with rheumatoid arthritis, Hashimoto's thyroiditis and Sjögren's syndrome presented with leg edema, proteinuria and lymphocytopenia. The patient tested positive for antinuclear antibody (Ab) and anti-dsDNA Ab, while negative for anti-U1 RNP Ab. The renal biopsy showed membranous lesions and full house pattern, and the patient was diagnosed with systemic lupus erythematosus (SLE) and class V lupus nephritis. Then myalgia and muscle weakness developed, and the serum levels of creatine kinase (CK) and C-reactive protein were elevated. A short tau inversion recovery MRI of the arm revealed significant areas with hyperintensity. She had no skin rash suggesting dermatomyositis (DM) and anti-TIF1-γ Ab was positive. The patient was diagnosed with polymyositis without malignancy or interstitial pneumonia. She was treated with high-dose glucocorticoid, intravenous immunoglobulin and tacrolimus. Urine protein and serum CK levels normalized, but muscle weakness persisted. [Clinical Significance] Anti-TIF1-γ Ab positive DM is aassociated with malignant tumors, skin rashes, and dysphagia. Although rare, anti-TIF1-γ Ab positivity may occur in SLE with muscle lesions, and in such cases, it is necessary to search for malignancies and to evaluate swallowing function.

## P2-191

**A case in which rituximab was successful in treating diffuse cutaneous systemic sclerosis accompanied with necrotizing myopathy**

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Conflict of interest: None

A 66-year-old female was referred to our hospital with myalgia and CPK 2,000 U/L. Diffuse cutaneous systemic sclerosis was diagnosed by the findings of progressive scleroderma involving the extremities, mild interstitial pneumonitis, finger pigmentation and synovitis, and positive anti-RNA polymerase III antibody. The pathological findings of muscles were necrotizing myopathy, and progressive myalgia were observed, and CPK increased to 6,900 U/L. The myositis was treated with both glucocor-

ticoid and immunosupressants. The myositis disappeared and no flare was found after tapering to 5 mg/day of prednisone. Rituximab was added for further progression of scleroderma. The mRSS improved from 12 to 8 points at 24 weeks. Clinical Significance: Anti-RNA polymerase III antibody-positive systemic scleroderma is characterized by 1) frequent malignant tumor complications, 2) rapid progressive scleroderma, 3) minimal interstitial pneumonitis, and 4) frequent renal crisis. In this case, high-dose glucocorticoid was given for necrotizing myopathy while paying attention against the renal crisis. The effectiveness of rituximab in treating scleroderma was demonstrated in the DESIRES trial, but the behavior of B cells in scleroderma is still unclear, and it is important to accumulate more cases.

## P2-192

**Takayasu Arteritis diagnosed from Repeated Coronary Artery Stenosis**

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Conflict of interest: None

A 47-year-old female was transported by ambulance to another hospital with chest pain in October of year X-1. Acute anterior wall myocardial infarction was noted. Percutaneous coronary intervention (PCI) was performed for complete occlusion of #6 and #9, and a stent was placed in #6. In April of year X, she began experiencing angina during flat walking, and a coronary artery CT showed a 50% stenosis at both ends of the stent in #6-7, and a stenosis in #9. PCI and stent insertion to #9 was performed. In September of year X, angina reappeared. A coronary artery CT showed a significant stenosis at the entrance of #5 and PCI was reperformed. Repeated coronary artery stenosis and persistent elevation of CRP suggested aortitis syndrome. She was referred to our department for the first time, and based on her chest symptoms and coronary artery stenotic lesions, she was diagnosed as Takayasu arteritis. FDG-PET revealed localized FDG accumulation in the left main coronary artery and adjacent aortic wall. From October of year X, treatment was initiated with prednisolone 45 mg. Takayasu arteritis with sole involvement of the coronary artery is rare. Delay in therapeutic intervention may lead to fatal outcomes, highlighting the significance of early diagnosis from atypical symptoms.

## P2-193

**A case of Takayasu arteritis that had a blood clot in the common carotid artery**

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Conflict of interest: None

A woman in her twenties, she was pointed out for CRP -positive for a long time. In July, she visited a nearby internal medicine. The cervical artery echo diagram revealed that the cervical artery wall was swollen and narrowed. She visited our outpatient clinic in August. The contrast CT recognized the stenosis of the both cervical artery, armor artery, and subclavian artery. In particular, the left total carotid artery seemed to be cut off. In PET-CT tests, the accumulation of FDG-PET in the up and down aorta in addition to the neck artery was found. She was hospitalized and started treatment with steroids and tocilizumab. Four weeks after treatment, the cervical artery echo diagram acknowledged a thrombus filled from the beginning of the left general carotid artery to the branch. MRI Angio was found to have formed a collateral artery from the subclavian artery. The blood flow in the collateral artery was antagonized to the highly stenched total carotidal artery, so the blood flow in the total carotidia may have stagnated and a blood clot was formed.

## P2-194

**A case of Takayasu's arteritis with chronic tonsillitis**

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Conflict of interest: None

[Introduction] Chronic tonsillitis is known as tonsillar focal disease and is highly associated with erythema nodosum (EN), IgA nephropathy (IgAN), and inflammatory bowel disease (IBD). On the other hand, it has recently been reported that Takayasu's arteritis (TA) is complicated with IgAN and IBD. In this case, we report a case in which EN, IgAN, and TA were diagnosed simultaneously in addition to chronic tonsillitis. [Case] A 22-year-old woman presented with fever and muscle pain in both lower legs. Physical examination revealed a fever of 39°C, EN of lower legs, bruit in the left carotid artery, and mild swelling of the tonsils. FDP-PET was positive in the left common carotid artery, brachiocephalic artery, descending aorta, and EN in the legs. Skin biopsy of EN showed infiltration of inflammatory cells with multinucleated giant cells. Thus, a diagnosis of type 2b TA was made, and anti-IL-6 receptor antibody was administered in addition to steroid therapy. A renal biopsy revealed mild IgAN and the tonsillectomy specimen showed chronic tonsillitis with chronic bacterial infection. [Clinical Significance] We experienced a case of TA concomitant with chronic tonsillitis, IgAN, and EN. The possibility of chronic focal infection was considered in the background of TA.

## P2-195

**A case report of a 61-year-old female who is diagnosed with Takayasu arteritis by surgical pathology**

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Conflict of interest: None

[Case Report] A 61-year-old woman had been awake of chest and back pain for 3 months, and was referred for a heart murmur and abnormal ECG wave form. Sinse a transthoracic echocardiogram revealed aortic root dilatation, aortic regurgitation and a flap within her aorta, we diagnosed with aortic dissection of unknown onset. Aortic replacement was performed on the 4$^{th}$ hospital day, and we diagnosed with Takayasu arteritis based on her clinical course and surgical pathology which showed intimal, medial and adventitial fibrous thickening. Her postoperative course was good and she was considered to be in the burned-out stage based on the pathological findings and the negative serum profile of inflammatory reaction, so is followed up without treatment for Takayasu arteritis. [Clinical Significance] Takayasu arteritis and giant cell arteritis share many common clinical characteristics, while there are some differences in epidemiology, complications and so on. Age is especially important for diagnosis and is noted as the absolute requirement in the 2022 ACR/EULAR classification criteria for each disease. However, we have recently encountered and report the case of the-61-year old female who was diagnosed with Takayasu arteritis by surgical pathology.

## P2-196

**A case of Takayasu arteritis with relapse during tocilizumab treatment**

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Conflict of interest: None

[Case Report] A 21-year-old woman was diagnosed with Takayasu arteritis in X-4 years. She was initially treated with prednisolone (PSL) and methotrexate (MTX). In X-2 years, she experienced a relapse of Takayasu arteritis with CRP and symptoms of jaw claudication and headache. Her CRP level normalized after increasing the dose of mPSL to 24 mg. In X-1 years, she was started on tocilizumab in combination with mPSL. In X years, she presented with hypotension in the left arm. Doppler ultrasound revealed thickening and occlusion of the left subclavian artery. She was hospitalized and the dose of mPSL was increased to 32 mg. Tocilizumab was discontinued and infliximab was started. The occlusion of the left subclavian artery did not improve. [Discussion] Tocilizumab is an

effective treatment for Takayasu arteritis. However, CRP levels may normalize during treatment, making it difficult to assess disease activity. In this case, the patient's CRP and ESR were normal, but vascular lesions were progressing. Regular imaging studies, such as Doppler ultrasound, are necessary to monitor disease activity during tocilizumab treatment. [Conclusion] This case report highlights the importance of regular imaging studies in patients with Takayasu arteritis treated with tocilizumab.

## P2-197

**Clinical features of the patients with eosinophilic granulomatosis with polyangiitis**

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Osaka General Medical Center

Conflict of interest: None

[Objective] To investigate the clinical features of eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] We retrospectively studied 34 patients diagnosed with EGPA at our hospital between January 2007 and September 2023. We examined the baseline characteristics at diagnosis, rate of relapse (including asthma exacerbation), and rate of achieving glucocorticoid (GC)-free status, defined as relapse-free and alive for more than one year after discontinuing GC treatment. [Results] Baseline characteristics revealed a mean eosinophil count of 7214/ μL, with 44% of patients testing positive for ANCA. The most common organ involvement at diagnosis was the nervous system. All patients received GC treatment, with 15 patients receiving cyclophosphamide, 18 receiving azathioprine, one receiving methotrexate, and 21 receiving mepolizumab (MPZ). Twenty-nine patients were followed up for one year, while only 17 patients were followed up for five years. The relapse-free survival rates were 92.8% at 1 year and 29.4% at 5 years. Among the 34 patients, three achieved a GC-free status, all of whom were receiving MPZ. [Conclusion] The five relapse-free survival rates at our hospital were low. However, some patients did achieve a GC-free status.

## P2-198

**Three cases of elderly patients with microscopic polyangiitis mainly due to nephritis were treated with prednisolone and avacopan and achieved a reduction in prednisolone dose**

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Conflict of interest: None

Representative case: A 73-year-old man was referred for serum creatinine of 3.04 mg/dL, urinary protein 3+, and occult blood 3+. Based on elevated MPO-ANCA of 92.4 IU/mL, he was clinically diagnosed with ANCA-associated nephritis. Considering his elderliness, we selected oral prednisolone (PSL) 30 mg/day (0.5 mg/kg) as the remission induction therapy. He underwent a renal biopsy on day 21. Out of 9 glomeruli observed, 4 were globally sclerosed and 1 showed fibro-cellular crescent formation. An immunofluorescence study showed a pauci-immune pattern. His serum creatinine remained at 3.08 mg/dL and urinary occult blood persisted. We added avacopan 60 mg/day to PSL 20 mg/day on day 37. After 5 months, the dose of PSL was successfully tapered to 5 mg with improved urinalysis without worsening kidney function. Discussion: In clinical settings for elderly patients, remission induction/maintenance therapy is often performed with glucocorticoid (GC) alone without cyclophosphamide or rituximab, considering their risk of infection and the severity of the disease. The combination of GC and avacopan can be a safe treatment with fewer side effects of GC. We report three cases of ANCA-associated nephritis treated with PSL and avacopan and discuss this therapy.

## P2-199

**Background, clinical course, and outcome of elderly patients with ANCA-associated vasculitis in our hospital**

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Conflict of interest: None

[Objective] The guidelines for ANCA-associated vasculitis (AAV) were revised in 2023, establishing a standard of care for the treatment of AAV, which is undergoing significant change. However, we have experienced many cases in which such patients are troubled by the choice of treatment intensity. Therefore, we have decided to examine the treatment of elderly-onset AAV at our hospital. [Methods] Among patients diagnosed with AAV and treated with new remission induction therapy at our hospital between 2018 and 2022, patients aged 80 years or older were included, and their patient background, treatment, and clinical outcomes. [Results] Of the 42 patients with AAV during the period, 11 patients corresponded to onset at age 80 or older. Age at onset was 83 years; 10 MPA, 1 GPA; 9 patients had some comorbidity; 7 with RPGN, 4 with interstitial pneumonia, BVAS 13, serum albumin 2.7 g/dl, CRP 9.6 mg/dl, Cr 1.61 mg/dl; all had positive MPO-ANCA (149 IU/ml). 2 patients with methylprednisolone pulse therapy, 6 patients with IVCY, 1 patient with rituximab, and 7 patients with azathioprine as remission maintenance therapy. [Conclusions] There is a need to continue to select appropriate treatment for elderly AAV patients with careful consideration of patient background.

## P2-200

**Efficacy of Upadacitinib in Refractory Polyarteritis Nodosa: A Case Report**

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Conflict of interest: None

A 44-year-old male has experienced recurrent painful subcutaneous nodules on both upper arms and lower legs since the age of 20. At 39, he developed polyarticular pain and muscle pain. He was diagnosed polyarteritis nodosa (PAN) based on subcutaneous nodules, polyarticular pain/muscle pain, and a skin biopsy revealing neutrophil infiltration in medium-sized vessels in the deep dermis. Treatment began with 40 mg of prednisolone (PSL), and azathioprine (AZP) was added. Upon referral to our hospital, he was on PSL 10 mg and AZP 25 mg. Attempts to taper PSL to 10 mg resulted in worsened symptoms. Immunosuppressants were changed from mycophenolate mofetil to methotrexate (MTX), tacrolimus, cyclophosphamide, MTX again, tocilizumab (TCZ) every two weeks, and finally TCZ every week, but none proved effective. Adding Upadacitinib (UPA) 15 mg led to rapid symptom improvement. PSL was promptly discontinued, and MTX was tapered from 12 mg to 4 mg. Reports suggest that PAN with elevated IL-6 levels is associated with high disease activity. While TCZ has shown efficacy in refractory PAN in some reports, it was ineffective in this case. There's only one report of tofacitinib, a JAK inhibitor, being effective against PAN. In contrast, UPA was used in this case and demonstrated remarkable efficacy.

## P2-201

**Sudden death during remission induction therapy for microscopic polyangiitis: Pathological autopsy revealed intra-abdominal hemorrhage due to rupture of medium-sized duodenal artery**

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Conflict of interest: None

A 90-year-old man was referred to our clinic with a 3-month history of lower leg pain and a 1-week history of deteriorating leg pain along with fever. Severe grasping pain and motor-sensory disorders were observed in both lower limbs, with no accompanying abdominal symptoms. Laboratory dates showed abnormal urinalysis and elevated levels of CRP (9.55 mg/dL), creatinine (1.31 mg/dL), and MPO-ANCA (182 U/mL). A plain CT scan suggested the presence of interstitial pneumonia, without abdominal abnormalities. The diagnosis of microscopic polyangiitis (MPA) was made, and GC pulse therapy followed by 0.5 mg/kg of prednisolone along with rituximab was performed. The lower leg symptoms exhibited improvement, but on the 11th day of admission, he suddenly developed right hypochondrial pain and passed away within a few hours. The pathological autopsy revealed intra-abdominal hemorrhage caused by the rupture of the medium-sized duodenal artery. Furthermore, necrotizing vasculitis was observed in almost all visceral organs, including the mesentery, kidney, coronary artery, lung, and liver. Clinical significance: It should be noted that patients with MPA rarely develop gastrointestinal lesions due to necrotizing vasculitis affecting medium-sized arteries, which can lead to a high mortality rate.

## P2-202

**A case of microscopic polyangiitis resulting in severe liver injury while receiving avacopan**

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Conflict of interest: None

A 78-year-old woman was diagnosed with microscopic polyangiitis based on renal dysfunction (Cre, 3.62 mg/dL), the presence of ground-glass opacities in both lungs on chest CT, and elevated MPO-ANCA levels. The patient initially responded to high-dose glucocorticoids (GC). However, 10 months later, she developed fever and cough. CT revealed worsening interstitial pneumonia with a CRP level of 12.56 mg/dL. MPA relapse was suspected, and IVCY, high-dose GC, and avacopan therapy were initiated. Forty days after initiating avacopan, the patient reported general malaise, and blood tests indicated severe liver damage with AST and ALT levels at 1532 U/L and 1526 U/L, respectively. Imaging and serological examination revealed no signs of hepatobiliary disease. Drug-induced liver injury was suspected. Avacopan, IVCY, alendronic acid, and atovaquone were considered potential causative agents. Discontinuation of these drugs resulted in a gradual decrease of AST and ALT levels 6 weeks later. Subsequently, atovaquone and alendronic acid were resumed sequentially without any hepatic dysfunction. Liver function was normal eight days after the last IVCY dose, making it an unlikely causative agent. Therefore, the severe liver injury observed in this patient was attributed to avacopan.

## P2-203

**The prognostic impact of remission induction treatment with rituximab or cyclophosphamide in real-world clinical practice for patients with severe antineutrophil cytoplasmic antibody-associated vasculitis**

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Conflict of interest: None

[Objective] To evaluate the prognostic impact of rituximab (RTX) or cyclophosphamide (CY) in microscopic polyangiitis (MPA) and polyangiitis granulomatosa (GPA). [Methods] Using the J-CANVAS registry, we conducted a prospective cohort study of patients with first-diagnosed MPA/GPA with severe organ involvement. Receiving CY or RTX intravenously up to 4 weeks after treatment initiation was defined as exposure. The primary outcome was treatment failure (death, relapse, glucocorticoid escalation, or new RTX/CY introduction), and the secondary outcomes were death, severe infections, and rate of glucocorticoid reduction from 4 to 48 weeks. The adjusted treatment effects were estimated using Cox hazards model and overlap weighting. [Results] A total of 355 patients were included. 80 patients had treatment failure, 16 died, and 46 had severe infections. The hazard ratios of the exposed group were 0.67 (95% confidence interval (CI): 0.41, 1.08) for treatment failure, 1.42 (95%CI: 0.43, 4.66) for death, and 1.91 (95%CI: 0.97, 3.76) for severe infection. Glucocorticoid doses at each time point were similar between the two groups. [Conclusions] In clinical practice, RTX/CY may be effective, but tends to cause severe infections. The rate of glucocorticoid reduction may have influenced our results.

## P2-204

**A case of microscopic polyangiitis with double-positive myeloperoxidase antineutrophil cytoplasmic autoantibody and anti-glomerular basement membrane antibody treated successfully by avacopan**

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Conflict of interest: None

[Case] A 88-year-old female had been suffering from fever for a month. She was examined at a local hospital, but the cause of fever was unknown and so she was referred to our hospital. She had no symptoms except fever, but myeloperoxidase antineutrophil cytoplasmic autoantibody (MPO-ANCA) 1300 IU/mL and anti-glomerular basement membrane (GBM) antibody 68.4 IU/mL were found. A CT scan showed ground-glass opacity at the base of her left lung. We diagnosed her with microscopic polyangiitis (MPA) due to pulmonary involvement and positive MPO-ANCA. We excluded anti-GBM disease because of the absence of alveolar hemorrhage and glomerulonephritis. Since she had no respiratory symptoms and her oxygenation was stable, her lung lesions were not active. She had no organ involvement except lung, and therefore she needed no intense immunosuppressive treatment. We treated her with avacopan and her fever was resolved immediately. We didn't use glucocorticoids or immunosuppressive drugs considering her age, glucose intolerance and osteoporosis. [Clinical Significance] This case report suggests that avacopan may be effective in the treatment of MPA with double-positive MPO-ANCA and anti-GBM antibody. It also suggests that monotherapy with avacopan may be a treatment option in some cases of MPA.

## P2-205

**A case of eosinophilic polyangiitis granulomatosa with marked skin ulceration whole body**

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Conflict of interest: None

Case: 72 years old male Chief complaint: Purpura on extremities and trunk History of Present Illness: The patient had allergic rhinitis for a long time. 1-2 cm in diameter, circular to mottled, black crusted skin ulcerations and necrotic tissue appeared on both lower extremities and spread to the whole body. The skin biopsy showed eosinophil infiltration around microvessels and wall necrosis in part of the arterial wall, and other clinical findings led to the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). On admission, his white blood cell count was 17,000/μL, eosinophils were 34%, CRP was 16.10 mg/dL, and MPO-ANCA was negative. Treatment was started with prednisolone (PSL) 60 mg/day for the initial EGPA and debridement of the necrotic skin tissue. Endoscopy revealed eosinophilic gastroduodenitis. On the fourth day, leukocyte count was 11770/μL, eosinophil count was 0.3%, and CRP was 4.13 mg/dL. The patient was discharged from the hospital on the 47th day with a PSL 30 mg/day. Discussion: The skin of EGPA are often purple patches, erythema, and ulcers of a few millimeters in size on the extremities and other parts of

the body. We report this case because the patient presented with systemic skin lesions.

## P2-206

**Two relapse MPA patients were improved with avacopan**

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Saiseikai Yokohamasinannbu Hospital

Conflict of interest: None

[Objective] Evaluation of effectiveness that relapse MPA patients were used combination avacopan. [Methods] Two relapse MPA patients in reduction PSL were used combination 60 mg/day avacopan. Effectiveness were evaluated with CRP and MPO-ANCA and urine. [Results] Using combination 60 mg/day avacopan improved CRP and MPO-ANCA and urine. [Conclusions] Efficacy of using combination 60 mg/day avacopan was recognized.

## P2-207

**A case of multiple aneurysms associated with polyarteritis nodosa improved by treatment**

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Conflict of interest: None

A 62-year-old man presented to hospital with weight loss of 10 kg/month, weakness and pain of the lower limbs. Laboratory findings included leukocytosis and elevated CRP, with negative tests for ANCA. Although contrast-enhanced CT scan, upper and lower digestive tracts endoscopy, randomized skin biopsy, and bone marrow biopsy were performed, the cause was not determined, and abdominal angiography was performed to distinguish polyarteritis nodosa (PN). It revealed multiple aneurysms and irregular walls in the parenchymal branches of the celiac artery, inferior mesenteric artery, and renal arteries. A diagnosis of PN made. Ten days after initiating treatment with oral corticosteroids and cyclophosphamide, the patient developed abdominal pain with rebound tenderness. A contrast-enhanced CT scan revealed bowel perforation. The patient underwent emergent surgery, and histopathological examination showed neutrophilic infiltration and fibrinoid necrosis of the medium-sized arterial wall. In January X+1, follow-up angiography showed the resolution of the multiple aneurysms. [Discussion] There have been some reports of improvement in aneurysms associated with PN, but it is rare that so many aneurysms have improved. We report here, including a discussion of the literature.

## P2-208

**An enlarging lung cavity during the induction therapy of Granulomatosis with Polyangiitis**

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Conflict of interest: None

[Case] A 57-year-old man was referred to our hospital with weight loss, oral ulcer, conjunctival injection, and abnormal findings in chest X-ray. Laboratory test revealed PR3-ANCA 198U/mL and hematuria. Chest CT showed multiple bilateral nodules including a cavity lesion in the right lower lobe S6. Results of lung biopsy showed no evidence of infection or malignancy, leading to a diagnosis of Granulomatosis with Polyangiitis (GPA). Intravenous methylprednisolone pulse was initiated from day 6 and subsequent oral prednisolone 0.5 mg/kg and rituximab were administered. Chest CT on day 10 revealed a high-density area within the lesion in S6 and the hemoptysis, which he had been experienced from day 4, was suspected to be due to bleeding in the cavity. On day 15, he experienced fever once again and the sputum changed into yellowish. Chest X-ray revealed further enlargement of the lesion in S6 with an air-fluid level in the cavity. Considering the concomitant infection, we initiated treatment with amoxicillin and clavulanate. Follow-up chest CT showed reduction of the lesion in S6 and the fluid within the cavity also disappeared. We report a case of enlarging cavity lesions during the induction therapy in a patient with GPA.

## P2-209

**A case of diffuse large B-cell lymphoma with polyarteritis nodosa-like presentation**

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Conflict of interest: None

[Case] A 77-year-old man was referred for Raynaud phenomenon and a generalized rash lasted for months. He presented with fever, mononeuritis multiplex, digit necrosis, systemic erythema and purpura. Laboratory tests showed eosinophilia, elevated CRP, increased soluble IL-2 receptor, deteriorating renal function, and proteinuria. Test for MPO- and PR3-ANCA were negative, but HBs, HBc antibodies and HBV-DNA were positive. CT imaging showed no lymphadenopathy or vasculitis, but contrast-enhanced MRI of his hands indicated poor blood flow, suggesting vasculitis. A renal biopsy revealed minor glomerular abnormalities. A skin biopsy identified subcutaneous vasculitis accompanied by fibrinoid necrosis, initiating a 50 mg/day prednisolone treatment for suspected polyarteritis nodosa (PAN). Subsequent PET-CT showed increased uptake in lymph nodes throughout his body, and a lymph node biopsy revealed diffuse large B-cell lymphoma (DLBCL). [Conclusions] This case was suspected of tumor-associated vasculitis secondary to DLBCL. Secondary PAN accounts for 28% of systemic PAN, 4% of which is secondary to malignant lymphoma, and it is associated with an increased mortality. When systemic vasculitis is suspected, secondary vasculitis should be carefully ruled out.

## P2-210

**Characters of ANCA-associated vasculitis with severe kidney failure**

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Conflict of interest: None

[Objective] ANCA-associated vasculitis (AAV) complicated by rapidly progressive glomerulonephritis (RPGN) may cause severe renal dysfunction requiring renal replacement therapy. The risk of this disease may have changed with recent advances in therapy, including rituximab, but the risk is not yet known. [Methods] We analyzed clinical information on 29 cases of AAV complicated by RPGN at our hospital, and analyzed renal and non-renal death cases. [Results] 4 of the 29 cases resulted in renal death. Compared with nonrenal deaths, renal deaths were more frequent for patients with severely elevated serum creatinine levels and longer time from onset to initial treatment, and they tended to have difficulty weaning from hemodialysis. [Conclusions] Despite advances in the treatment of AAV, renal death has not been prevented in patients with delayed initial treatment or severe renal dysfunction, which may be an important factor in the treatment of AAV and renal prognosis.

## P2-211

**A case of ANCA-associated vasculitis presenting with lung cavitation during immunosuppressive therapy in rheumatoid arthritis**

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Conflict of interest: Yes

A 78-year-old woman who has been treated with low dose prednisolone, methotrexate (MTX) and tacrolimus (TAC) on rheumatoid arthritis

(RA) for five years. In another hospital, she was detected lung abnormal shadow and elevated CRP in pre-tests for lumbar spinal canal stenosis surgery. She was discontinued MTX and TAC, and then she admitted to our hospital. Laboratory examinations on admission showed that renal dysfunction, microhematuria and myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) high titer (1440 IU/mL). Chest computed tomography (CT) showed bilateral interstitial pneumonia and cavitary lung mass in right lower lobe. The renal biopsy specimens revealed the presence of pauci-immune crescentic glomerulonephritis. She was diagnosed with ANCA-associated vasculitis (AAV) and started treatment with pulse dose steroid and rituximab. Subsequently, her clinical symptoms and renal function resolved, and MPO-ANCA level gradual declined, 248 IU/mL one year later, 26.6 IU/mL two years later. Also, lung cavitary lesion at chest CT seven months later has achieved regression. AAV-associated lung disease is reported various patterns; however, lung cavitation occurs rather infrequently. This report will help future physicians to better diagnose and treat in similar cases.

## P2-212

**A case of granulomatosis with polyangiitis with trismus**

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Conflict of interest: None

A 65-year-old woman had been treated for non-tuberculosis mycobacterial infection at respiratory in our hospital for two and a half years. She had refractory conductive hearing loss with otitis media with effusion nine months ago, and polyarthritis including temporomandibular joint pain and fever two months ago. And then, she was admitted to the respiratory department because of the difficulty in oral intake due to trismus. On admission, her serum CRP level increased to 18 mg/dL. Tazobactam/piperacillin was administered intravenously to the patient for two weeks, but the fever and trismus did not improve. The patient was transferred to our department because MPO-ANCA was found to be positive. After six days, she had some numbness in lower limbs. Peripheral nerve conduction study showed the presence of mononeuritis multiplex. Applying Watts' algorithm, she was diagnosed with granulomatosis with polyangiitis. The patient was treated with prednisolone at a dose of 40 mg/day and with avacopan at a dose of 60 mg/day. The fever and trismus gradually improved, and the levels of serum CRP was decreased. Finally, she was discharged at hospital 44 days after admission. As we believe this case to be quite rare, we describe this case with a literature review.

## P2-213

**A Case of Non-Tuberculous Mycobacterial Infection Complicating granulomatosis with polyangiitis during the Disease Course**

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Conflict of interest: None

<Case Presentation>A woman was diagnosed with ANCA-associated vasculitis and rapidly progressive nephritis syndrome in X-13 years. In May X, she was on treatment with Prednisolone reduced to 3 mg and a chest CT scan revealed multiple pulmonary nodules with cavities and infiltrative shadows. In August, the patient showed elevated inflammatory markers and MPO-ANCA. Subsequently, she was referred to our hospital for further evaluation. Sputum culture revealed M. avium, and the patient was was started on treatment for non-tuberculous mycobacterial (NTM) infection. However, blood sputum was observed and chest CT revealed diffuse ground-glass opacities in both lungs, indicative of pulmonary alveolar hemorrhage secondary to granulomatosis with polyangiitis (GPA). Consequently, the patient received treatment with a combination of steroid pulse therapy, Avacopan, Rituximab, and plasma exchange. Subsequently, she achieved remission. <Consideration>This is a case study of a patient with multiple pulmonary nodules, complicated by NTM infection and GPA. Initially, the cavitary lung lesions were diagnosed as NTM infection. However, the patient also experienced pulmonary alveolar hemorrhage secondary to GPA, posing challenges in treatment management. We report based on our own experience.

## P2-214

**A case of Granulomatosis with polyangiitis (GPA) with the onset at the age of 20**

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Conflict of interest: None

[Case] A 20-year-old female. [Chief complaint] Hemoptysis. [History] One week before admission, she suddenly began to develop bloody sputum repeatedly and visited an emergency room. Her chest CT scan accidentally revealed multiple nodules with cavities in the lungs. Transbronchial lung biopsy showed no infection and necrotizing granulomatous vasculitis of small arteries was found, which resulted in referral to our hospital. Based on physical examination, no systemic manifestation such as fever or weight loss was found and typical organ lesions such as upper respiratory tract, kidney, or peripheral nerves was not detected. Furthermore, PR3-ANCA was positive but very low titer by ELISA. Based on the 2022 American College of Rheumatology GPA classification criteria, she was diagnosed as GPA and started high-dose corticosteroid and rituximab. Hemoptysis and the cavities were quickly disappeared after the treatment. [Discussion] Young onset of GPA is reported to be rare, with an incidence of about 1 in 1 million. We experienced a case of GPA with the onset at the age of 20. The patient had unique clinical features such as lack of systemic symptoms, typical organ involvements, or a low titer of PR3-ANCA. This case will be discussed based on the previous case reports.

## P2-215

**A case of microscopic polyangiitis (MPA) with renal damage from tubulointerstitial nephritis**

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Conflict of interest: None

[A Case] Patient is a 71-year-old woman. Four months ago, she became aware of numbness in the left sole. Three weeks ago, fever, chills and general malaise appeared. When she came to our hospital, her temperature was 38.4°C and there was decreased sensation in the right MTP and plantar area beyond the left heel. Blood tests revealed WBC 11700/μL, Cre 0.52 mg/dL, CRP 18.7 mg/dL, MPO-ANCA 486 IU/mL. Urinary examination revealed urinary protein 1+, urinary occult blood 2+, NAG index 60.1 μg/L and β2-MG 36542 μg/L. After admission, the diagnosis of MPA was made, and the critical organ lesions were determined to be nerves and kidneys, and high-capacity steroids including steroid pulse and RTX were administered. A renal biopsy was performed on the 14th day, which revealed tubulointerstitial nephritis. Thereafter, Cre, protein, and occult blood in urine worsened temporarily, but gradually improved. [Clinical Significance] We have experienced a case of MPA complicated with tubulointerstitial nephritis. Although glomerulonephritis is the main cause of renal damage in MPA, renal damage may develop from tubulointerstitial nephritis. Therefore, we believe that interstitial nephritis markers should be aggressively checked even in the absence of proteinuria or pathological urine sediment.

## P2-216

**ANCA-related vasculitis with aortic wall thickening, hypertrophic meningitis, extraocular myositis, and otitis media: A Case Report**

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Conflict of interest: None

A 75-year-old woman was diagnosed with otitis media with effusion, and at the same time, she presented left-sided temporal pain, left eye pain, and left eye movement disorder. She was diagnosed with idiopathic extraocular myositis and was treated with steroid pulses, which resulted in improvement. However, 2 months later, she presented dysphagia, hoarseness, and fever, and contrast-enhanced chest CT revealed wall thickening of the aortic arch. Head and orbital contrast MRI revealed dural thickening in the right cerebellar tentorium and right frontal region, as well as inflammation in the bilateral medial rectus and left inferior rectus muscles. Since P-ANCA was positive in the blood test, we diagnosed ANCA-associated vasculitis and associated hypertrophic meningitis. Steroid pulse therapy was administered again, and then oral administration of prednisolone 1 mg/kg/day and methotrexate was started, and symptoms improved. Cases of aortic wall thickening caused by inflammation of the aorta and its surroundings due to vegetative vasculitis of large vessels derived from ANCA-associated vasculitis have been reported in the past. Even if aortitis syndrome is suspected by imaging, it is important to assume the possibility of ANCA-related vasculitis based on symptoms.

## P2-217

**Canakinumab for Colchicine and Glucocorticoid-Resistant Protracted Febrile Myalgia Syndrome: A Case Report**

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Conflict of interest: None

Introduction: Protracted Febrile Myalgia Syndrome (PFMS) in Familial Mediterranean Fever (FMF) patients is marked by persistent fever and leg pain, often showing resistance to colchicine. High-dose glucocorticoids, or alternatives like anakinra, have been used with varying success. We report a case where canakinumab proved effective in a patient resistant to both standard therapies. Case Presentation: A man in his 50s had experienced brief, recurrent febrile episodes for years. In Year X-12, he had a severe episode of fever and debilitating leg pain lasting five weeks, followed by regular recurrences. In Year X, he developed intense myalgia, leading to his hospitalization. He exhibited erysipelas-like erythema, and MRI identified muscle inflammation. Genetic testing revealed *MEFV* p. M694I, confirming PFMS. Despite colchicine and prednisolone treatment, his symptoms persisted. From March Year X+1, canakinumab (150 mg subcutaneously) was administered, leading to rapid symptom and inflammation resolution. The patient has maintained remission with ongoing canakinumab therapy. Conclusion: Canakinumab is a potential treatment for colchicine and glucocorticoid-resistant PFMS, underscoring the need for a broader study.

## P2-218

**A case of Familial Mediterranean Fever who later developed Anti-PL-12 Antibody Positive Dermatomyositis**

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Conflict of interest: None

[Introduction] Autoinflammatory and autoimmune diseases are differentiated by the affected organs and clinical phenotypes, but there are some reports of familial Mediterranean fever (FMF) coexisting with connective tissue disease (CTD). [Case] A 36-year-old woman with recurring episodes of fever and stomach pain during menstruation presented with respiratory failure. Gottron's sign, shawl sign, mechanic's hands, proximal muscle weakness and anti-PL-12 antibodies suggested dermatomyositis (DM) with interstitial pneumonia. High-dose corticosteroids, cyclophosphamide and tacrolimus were started and her condition steadily improved. While tapering her steroid dose, menstruation restarted. Subsequently the fever episodes reoccurred, and due to her familial history, she was tested for and diagnosed with FMF. She possessed the heterozygous mutation M694I of Exon 10 on the *MEFV* gene and colchicine alleviated her symptoms. [Clinical Significance] There are no preceding reports of DM coexisting with FMF patients who possess the pathological variant of Exon 10. Our patient was diagnosed with FMF during steroid reduction. Patients with CTD may have coexisting underlying autoinflammatory diseases, and when necessary, it is relevant to re-evaluate for additory information such as family history.

## P2-219

**Two patients under follow-up for rheumatic disease diagnosed as Familial Mediterranean Fever (FMF)**

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Conflict of interest: None

Case 1] A 51-year-old woman suffered myocardial infarction in 2011. In 2016, she came to our hospital with polyarthritis and positive anti-CCP antibody, and was diagnosed as rheumatoid arthritis (RA). She had fever of 39°C several times a year and was hospitalized, but the cause was unknown for 30 years. Case 2] A 50-year-old man was admitted to our hospital for rehabilitation due to cerebral hemorrhage in 2023. On admission, he had a fever of 39°C, polyarthritis, and skin rash. He had fever and arthralgia several times a year for 30 years and was diagnosed as gout. He was treated with NSAID and monitored for progress. Suspecting the possibility of FMF, they were started on colchicine (Co), and no fever was observed thereafter. In both cases, genetic analysis showed no abnormalities in Exon10. Discussion: Both patients were diagnosed and treated for rheumatic diseases, and were followed up for fever of unknown origin. After exclusion of infectious diseases, other fevile diseases, we confirmed that the patients had no fever since the start of Co treatment and made a clinical diagnosis of FMF. After starting colchicine, the patient's quality of life improved. Conclusion: The outpatient clinic for rheumatic diseases should consider a mix of patients with FMF.

## P2-220

**A case of pseudo-VEXAS syndrome revealed by autopsy**

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Conflict of interest: None

An 88-year-old man was diagnosed with myelodysplastic syndrome (MDS) 2 years before visiting our department. Because fever and high inflammation continued for 1 month, PET-CT was performed at our department. He had diffuse bone marrow uptake, but bone marrow examination showed no vacuolar lesions or malignant findings. Considering ANCA-negative vasculitis, we started treatment with PSL 20 mg/day for diagnostic purposes, and the fever relieved and CRP became negative. Five months after starting treatment, systemic erythema appeared, and a skin biopsy led to the diagnosis of Sweet's disease. The patient wasclinicaly diagnosed with VEXAS syndrome, and treatment with Tocilizmab was started, which allowed the dose to be reduced to 10 mg/day of PSL. One year and three months after starting treatment, he died of a bacterial infection. Pathological autopsy revealed tumor cells infiltrating multiple organs, including the myocardium, thyroid, skin, and intestinal tract, leading to the final diagnosis of tumor death due to myelodysplastic/myeloproliferative neoplasm unclassifiable (MDS/MPN-U). Genetic testing of the patient did not identify any abnormalities in the UBA1 gene.

## P2-221

**Presentation of lung involvement, chondritis, large vessel vasculitis, pyoderma gangrenosum, myelodysplastic syndrome, and distinctive cytoplasmic vacuoles in UBA1 gene mutation-negative patient: A case with a clinically resonant phenotype associated with VEXAS syndrome**

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Conflict of interest: None

A 78-year-old man initially diagnosed with myelodysplastic syndrome six months ago due to pancytopenia was subsequently diagnosed with macroangiitis. Further evaluation revealed auricular and tracheal chondritis and pyoderma gangrenosum. Bone marrow examination revealed vacuoles in bone marrow blasts, raising the suspicion of VEXAS syndrome. Somatic mutation analysis targeting exon 3 of the UBA1 gene was performed but revealed no known mutations. The patient was started on prednisolone and colchicine for rash and chondritis. However, disease progression manifested as worsening thrombocytopenia, organizing pneumonia, and rapidly deteriorating renal function. The condition was attributed primarily to the underlying disease. Steroid pulses resulted in temporary improvement, but renal failure persisted, ultimately leading to the patient's death from septic shock. This case highlights the potential influence of unknown somatic mutations beyond exon 3 of the UBA1 gene in the pathogenesis of VEXAS syndrome. As a new disease concept with incomplete understanding of UBA1 gene mutations, the diagnosis of VEXAS syndrome should include a comprehensive consideration of disease pathogenesis beyond UBA1 gene mutations. Based on a literature review, we will report on these findings.

## P2-222

**Long-term case of VEXAS syndrome undergoing combination therapy with azacitidine and baricitinib**

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Conflict of interest: None

The case is a 67-year-old man. In May 20XX, he developed oligoarthritis, chronic urticaria-like symptoms, and fever, and a skin biopsy revealed neutrophil infiltration and was diagnosed with Sweet's disease. He was treated with prednisolone (PSL), and his symptoms improved, however, skin symptoms and arthritis flared repeatedly due to PSL reduction. Baricitinib (bari) was started in February 20XX+5, but the Hb level decreased to around 6 g/dl and the patient was transferred to our hospital. Bone marrow aspiration revealed three lineages of dysplasia, and he was diagnosed as a low-risk group for myelodysplastic syndrome (MDS) with vacuolar degeneration. A peripheral blood UBA1 gene variant search revealed the c. 121A>C: p. Met41Leu mutation, and a definitive diagnosis of VEXAS syndrome was made. The anemia was transfusion dependent, and azacytidine (AZA) was added. He is currently undergoing AZA + Bari combination therapy. [Discussion] The long-term prognosis of VEXAS syndrome is unclear. Steroids, AZA, JAK inhibitors, etc. are used as drug therapy, but the effectiveness of each drug are still unknown. This case is a valuable case because it has been followed for more than 5 years since the onset of chronic inflammation, and AZA and JAK inhibitors have been used together.

## P2-223

**A case of VEXAS syndrome diagnosed during treatment of refractory giant cell arteritis**

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Conflict of interest: None

The patient is a man in his 70s who had been treated with high-dose corticosteroids and methotrexate (MTX) for giant cell arteritis (GCA), but high inflammation persisted and skin rash, macrocytic anemia, new lung shadows appeared in 2 years. Although MTX was discontinued, the anemia progressed and a bone marrow examination led to the diagnosis of MDS. In addition, a Leopard sign was observed on PET-CT examination. Based on these findings, VEXAS syndrome was suspected, and pathological examination and genetic testing were performed. Vacuoles in myelocytes and mutations in the UBA1 gene were identified, so this case was considered to be VEXAS syndrome. After switching from MTX to tocilizumab (TCZ), CRP became negative, but anemia persisted and skin rash and lung shadows still remain. VEXAS syndrome is a disease identified in 2020, and there are no clear diagnostic criteria or treatment guidelines. The clinical symptoms are diverse, and diagnosis and treatment are often difficult. We will share the pathological findings and image findings, and will also include some considerations.

## P2-224

**A case of Schnitzler's syndrome and rheumatoid arthritis treated with methotrexate**

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Rheumatology, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital

Conflict of interest: None

A 78-year-old man presented to our hospital because of a monthly onset of fever, myalgia, and urticaria that had persisted for a week for 5 years. He was diagnosed with Schnitzler's syndrome based on monoclonal IgG gammopathy, chronic urticaria, intermittent fever, arthritis, high inflammatory response, and neutrophil infiltration in the dermis on skin biopsy. He was treated with colchicine but did not improve. One month later, finger and wrist arthritis appeared. Based on high anti-CCP antibody and rheumatoid factor levels, rheumatoid arthritis was also diagnosed. Methotrexate was started and his arthritis and urticaria was improved. Since there have been few previous reports of Schnitzler's syndrome treated with methotrexate, we report this.

## P2-225

**Elevated circulating phospholipase A2 group IV D DNA copies in psoriatic arthritis**

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Conflict of interest: None

[Objective] Phospholipase A2 group IV D (PLA2G4D) is involved in the pathogenesis of psoriasis. We investigated the clinical significance of circulating Phospholipase A2 group IV D (PLA2G4D) DNA levels in psoriasis. [Methods] The measurement of PLA2G4D DNA copies in serum using droplet digital polymerase chain reaction (ddPCR) were performed. [Results] Circulating PLA2G4D DNA copies in patients with psoriasis were significantly higher than those in healthy controls. Circulating PLA2G4D DNA copies were significantly higher in patients with joint involvement than in patients without joint involvement. [Conclusions] Lelevs of circulating PLA2G4D DNA copies may be a useful biomarker for clinical evaluation of psoriatic psoriasis.

## P2-226

**A case of immune-mediated necrotizing myopathy positive for anti-RuvBL1/2 antibodies**

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Fujisawa City Hospital

Conflict of interest: None

[Case] A woman in her 60s developed weakness and finger stiffness in January. Anti-CCP antibody and RF were negative, but CK was 3169 IU/L. Although autoantibodies related to collagen disease were all negative, she visited us in May. MMT decreased to around 4 mainly in the proximal limbs, and pitting edema was observed in both lower legs; CK was 5477 IU/L, ALD 95.1 U/L, and myoglobin 2787 ng/mL. SRP and HMGCR antibodies were negative, and she was considered to have seronegative immune-mediated necrotizing myopathy (IMNM). After a muscle biopsy in June, Three times steroid pulse therapy, oral prednisolone 40 mg/day, and IVIg were performed, but CK remained at around 3000 IU/L. Around this time, the pathological results of IMNM were obtained. This case was positive for anti-RuvBL1/2 antibodies. After she was treated with rituximab (RTX) according to ENMC recommendation, her level of myogenic enzymes improved, and she was discharged. [Clinical Significance] Although this case didn't have skin sclerosis, it was thought to be a rare case of IMNM as positive only for anti-RuvBL1/2 antibodies. Although IMNM is considered to be resistant to treatment, her progress was favorable after RTX treatment based on ENMC recommendation, so we consider it to be clinically useful and report it here.

## P2-227

**A Case of Reactive Vasculitis Following COVID-19 Infection**

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Conflict of interest: None

A 34-year-old male was diagnosed with COVID-19 on day X-14 due to fever, nasal discharge, and cough, which were improved by day X-2. From day X, he experienced bilateral pain in shoulders, hands, knees, and ankles, with fever. Joint swelling emerged on X+1, leading to a consultation at our institution on X+2. He presented with 38.6°C fever, erythema, swelling, and tenderness in multiple joints. No ocular or upper respiratory symptoms were observed. Laboratory findings: WBC 22461/μL, Cre 0.85 mg/dL, CRP 28.8 mg/dL, negative urinary occult blood, proteinuria, antinuclear antibodies, MPO-ANCA, and PR3-ANCA. Pulmonary abnormalities were absent in chest radiography. Symptomatic therapy with NSAIDs was initiated and monitored as outpatient care. While polyarthralgia improved by day X+6, painful erythemas appeared bilaterally on the shins by day X+8. A biopsy on day X+9 revealed septal panniculitis, lymphocytic infiltration, and partial fibrinoid degeneration in small blood vessels. We suspected post-COVID-19 reactive vasculitis and continued NSAIDs. Symptoms and inflammation gradually diminished, normalizing by day X+28. In this report, we describe a case of reactive vasculitis following COVID-19 infection.

## P2-228

**A case of multiple skin eruptions with pathological features of small vessel vasculitis under olaparib treatment for ovarian cancer**

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Conflict of interest: None

A 85-year-old woman who was diagnosed with Stage 4 ovarian cancer. One year ago, she was treated with olaparib after ATH+BSO and achieved complete remission. Seven months ago, she suffered from multiple skin eruption with black crusts on the face and extremities. Skin biopsy revealed small vessel vasculitis and CT scan revealed left subclavian artery, splenic artery, and celiac artery stenosis. Two months ago, she suffered from fever, so diagnosed to polyarteritis nodosa. She was treated with 1 mg/kg prednisolone and methotrexate and her skin eruption was improved. But she was admission due to cellulitis in extremities. A several days later, she was complicated with small intestine perforation and emergency operation was performed. The pathological findings of resected intestine showed multiple ulcers invaded by fungi. After surgery, her general condition did not improve and she died. Autopsy diagnosis suggested that the cause of death was hemorrhage from multiple gastrointestinal ulcers accompanied by fungal infection and respiratory failure from pulmonary aspergillosis. There were two case reports of vasculitis complications due to Olaparib (J Dermatol. 2021, Eur J Dermatol. 2022). Here we report the interesting case of vasculitis complication under olaparib treatment.

## P2-229

**The efficacy and safety of nintedanib in connective tissue disease**

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of nintedanib in interstitial lung disease associated with connective tissue disease [Methods] The patients who treated with nintedanib in our hospital. We compared KL-6 titer for 2 years between pre-use nintedanib patients and post-use nintedanib patients. And we also compared retention rate among the diseases and confirmed reason of discontinuation with nintedanib. [Results] 85 patients were included. Average age was 73 and women were 53. The most major disease was systemic sclerosis (32 cases) followed by inflammatory myopathy (18 cases), rheumatoid arthritis (15 cases), ANCA associated vasculitis (9 cases). Median IL-6 titer decreased in nintedabib group. These were significantly lower at 18 month and 24 month in post-nintedanib group than pre-nintedanib group (18 month; 661.5 vs 954.5, $p=0.03$, 24 month 811 vs 661.5, $P<0.01$). Median retention period was 77 weeks and there was no difference among those of SSc and inflammatory myopathy, RA. 47 patients discontinued nintedanib and most major reason was gastrointestinal symptom (13 cases) followed by transfer (8 cases), worsen ILD (6 cases), death (4 cases). [Conclusions] Nintedanib can be effective for ILD with connective tissue disease and it has possibility to delay the ILD progression.

## P2-230

**A case of Adult-onset Still's disease with different kind of eruption**

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Conflict of interest: None

[Background] Adult-onset Still's disease (AOSD), which presents many non-specific symptoms, such as rash leukocytosis, spiking fever, and sore throat, is a rare auto inflammatory disease. Other clinical features that are frequently observed include lymphadenopathy, arthralgia, serositis, splenomegaly and hepatomegaly. [Case Presentation] The patient was a 74-year-old woman with a high fever (39.8C), sore throat, rashes on face and limbs with pruritus, mainly at the joints (elbow, knee and ankle), with arthralgia. Liver function were abnormal and the ferritin level was above 1500 (normal < 179) ng/L. and was eventually diagnosed with AOSD. She received steroid treatment. After 4 years of diagnosis, she had rash and liver enzyme was elevated, and diagnosed recurrence of AOSD and given the steroid treatment. After 4 years of observation with Tocilizmab, she had rash and edema in left leg. Diagnosed Celluitis, intravenous anti-biotics were effective. [Conclusion] A case of an old-aged woman diagnosed with AOSD is reported, and the possible recurrent AOSD and side effect of Toclilizmab are discussed. This case highlights the importance of early diagnosis and timely treatment of AOSD and different diagnosis of side effects of Tocilizmab.

## P2-231

**A case of elderly-onset familial Mediterranean fever (FMF) in which colchicine was effective**

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Division of Nephrology and Rheumatology, Department of Internal Medicine, Fukui Prefectural Hospital

Conflict of interest: None

Case: A 73-year-old man. He had a fever of 38 degrees that lasted for several days and had joint pain every 2-3 months. At the time of the fever, he showed acute monoarthritis in different areas such as the shoulder, hip, and knee. Every month. The patient was first seen at our hospital due to persistent fever. No chest pain, abdominal pain, or skin rash was observed. Laboratory findings: WBC5500/μL, CRP 0.64 mg/dL, ANA less than 40 times, MPO-ANCA <1.0U/mL, PR- 3ANCA <1.0 U/mL, blood culture was negative, and contrast-enhanced CT did not show any heat source lesions. FMF was suspected, and colchicine was prescribed, and the symptoms disappeared. MEFV genetic testing revealed p. Leu110Pro, p. A mutation in Glu148Gl was confirmed. Mutations other than Exon10 were observed, and there was a response to diagnostic administration of colchicine, which was considered an atypical case of FMF. [Clinical Significance] For FMF that developed in people in their 60s We experienced one case in which colchicine was effective. In Japan, the age of onset is said to be older, but the incidence of onset in people over 50 years old is rare, accounting for approximately 6.0%. When recurrent fever of unknown cause is observed, FMF is recommended. If necessary, genetic testing should be considered.

## P2-232

**A case of spontaneous resolution of eosinophilic fasciitis associated with myositis**

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Conflict of interest: None

A 77-year-old man had generalized myalgia for two weeks without intense physical exertion in June. Ten days before this admission, he had a fever, and edema and thickening of the skin gradually increased all over his body except his hands, toes, and head. He was admitted to our hospital with muscle weakness primarily in proximal muscles. Laboratory examination revealed eosinophilia (3780/μL) and elevated CK level (3219U/L). MRI showed fluid accumulation along the fascia, mainly in the triceps muscle, and high STIR signal within the muscles. Muscle and fascia biopsy showed the inflammatory cell infiltrates composed predominantly of eosinophils within the fascia and muscle bundles. Eventually, a diagnosis of eosinophilic fasciitis with myositis was made. His symptoms spontaneously improved during this admission, and he was discharged after one week. Generalized edema disappeared two weeks later, and CK and eosinophils were normalized two months later. No relapse occurred. Although eosinophilic myositis and eosinophilic fasciitis are defined as separate diseases, some reports show eosinophilic infiltrates within both muscle and fascia, suggesting clinical and pathological overlap. When diagnosing these diseases, both fascia and muscle should be evaluated carefully.

## P2-233

**Multiple fascial calcifications in a patient with polyarthritis and interstitial lung disease**

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Conflict of interest: None

A 79-year-old female, under treatment with 5 mg/day prednisolone for polyarthritis and interstitial lung disease, presented with difficulty moving her muscles and noticed subcutaneous hardening in her limbs. Blood tests revealed high serum ALD levels but normal CK levels. She tested positive for antinuclear antibodies with a 1280-fold speckled pattern, while other specific antibodies, including myositis-specific antibodies, were negative. Ga scintigraphy showed strong accumulation in specific areas of her right upper and lower limbs. CT and MRI scans confirmed fascial calcification, including in the lateral broad muscle and iliopsoas muscle. This is the first to report progressive fascial calcification in an elderly patient. The patient did not meet the EULAR/ACR classification criteria for idiopathic inflammatory myopathies. Given her strong positive antinuclear antibodies and history of interstitial lung disease and arthritis, there's a possibility of an unreported condition, potentially termed "autoimmune ossifying fasciitis," related to her autoimmune abnormalities.

## P2-234

**Florid reactive periostitis of the toe that showed resistance to conservative treatment and required surgical treatment: A case report**

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Conflict of interest: None

[Background] Florid reactive periostitis (FRP) is a rare reactive disease that occurs mainly in the fingers of young adults and characterized by inflammation. We report a case of FRP that required surgery because of resistance to conservative treatment. [Case] A 33-year-old woman presented with a 4-month history of painful hard mass on the left second toe. Although she was received conservative treatment at primary clinic, her symptoms did not improve. On arrival, swelling and tenderness was observed around the hard, subcutaneous mass in the left second toe. Laboratory findings including white blood cell count and C-reactive protein level were normal. X-ray showed osseous lesion attached on the periosteum of the proximal phalange without bone destruction. Since conservative treatment with celecoxib administration did not improve her inflammation, surgery was performed. The pathologic findings led to the diagnosis of FRP, and all symptoms completely resolved 1 week postoperatively. No recurrence was observed 2 years after surgery. [Discussion and Clinical Significance] When treating inflammatory diseases of the hands and feet, FRP should be considered as a differential diagnosis. If the disease shows resistance to conservative treatment, surgical treatment is necessary.

## P2-235

**A case of Nintendinitis requiring differentiation from juvenile idiopathic arthritis**

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Conflict of interest: None

A 12-year-old boy presented with spontaneous pain with heat and swelling in the left index finger for 6 weeks. Blood tests showed that various inflammatory markers were within normal range, and MRI showed subcutaneous soft tissue swelling and bone marrow edema. Detailed history revealed that the patient had changed the controller of a home video game console (Nintendo Switch$^{R}$) from Joy-Con$^{R}$ to Nintendo Switch Pro$^{R}$ four weeks earlier, and had been playing video games for approximately 4 hours a day on weekdays and 12 hours a day on weekends since then. Symptoms of the left index finger became apparent 4 weeks after the controller replacement, but the symptoms improved 2 weeks after the game was discontinued. Nintendinitis is an inflammation of the joints of the upper extremities caused by repeated friction and physical stress due to the use of video game consoles, and was first reported in 1990. The present case was proposed as a Switchitis, because the index finger is used in Nintendo Switch$^{R}$ controllers. This is the first report of Switchitis in the world. When a patient complains of unexplained pain in the digits, this disease should be suspected and the patient's history of game console use should be interviewed.

## P2-236

**The impact of grip strength on upper limb functional improvement after joint replacement surgery in shoulder and elbow of rheumatoid arthritis patients**

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Conflict of interest: None

[Objective] To compare the effects of grip strength on the DASH score in RA patients who underwent arthroplasty for the shoulder (TSA) and elbow joints (TEA). [Methods] RA patients who were able to be evaluated one year before and after TSA and TEA from 2012 to 2022 were included and divided into groups that achieved and did not achieve the MCID of 10.81 in DASH. Then, age, disease duration, CRP, and grip strength were compared between these groups. [Results] In the TSA cases (23 patients, 24 shoulders), significant improvements were observed in DASH and grip strength before surgery (49.4±20.3/120.5±61.2mmHg) and after surgery (40.7±20.1/160.9±62.5mmHg) ($p<0.01$). In the TEA cases (72 patients, 82 elbows), significant improvements were observed in DASH and grip strength before surgery (49.6±20.7/101.8±67.9 mmHg) and after surgery (36.9±21.9/115.8±66.2mmHg) ($p<0.01$). The MCID was achieved in 11/24 TSA cases and 43/82 TEA cases. A significant difference was observed only in the change of grip strength in TEA cases (achievement group 34.9±37.1mmHg/non-achievement group -9.1±39.8mmHg) ($p<0.01$). [Conclusions] In TEA cases, the impact of grip strength on upper limb function was particularly large.

## P2-237

**Walking habits in older rheumatoid arthritis patients improve spine sagittal alignment at 2 years**

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Conflict of interest: None

[Objective] Exercise such as walking is recommended for elderly rheumatoid arthritis (RA) patients who are prone to physical inactivity. The purpose of this study was to prospectively evaluate the effect of walking on spinal sagittal alignment and vertebral fracture (VF) in RA patients at 2 years. [Methods] Of the 87 elderly patients with RA who were able to complete the initial survey, 75 were able to complete the follow-up survey 2 years later (mean age: 71.9 years, follow-up rate: 86.2%). The walking group was twice a week (30 mins or above for each time) for a year. Initial endpoints included age, gender, height, weight, BMI, disease duration, medications, blood samples, disease activity, bone density, and functional disability index. Sagittal vertical axis (SVA) and pelvic tilt (PI)-lumbar lordosis (LL) were investigated for vertebral longitudinal alignment, and grade 1 or higher for VF was defined as fracture. [Results] There were 37 patients (49.3%) in the walking group. Change in SVA (-0.6±16.3 mm/-9.0±14.5 mm) and PI-LL (2.2±10.5°/10.6±11.6°) were significantly different between the walking and control groups. The rate of VF progression was 13.5%/26.3%, not significantly different. [Conclusion] Walking habit in elderly RA patients improves spinal sagittal alignment at 2 years.

## P2-238

**The effectiveness of our original hand exercise program "Hand Exercise for Rheumatoid Arthritis at home; HERA"**

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Hokkaido Medical Center for Rheumatic Disease

Conflict of interest: None

[Objective] Hand exercise for Rheumatoid Arthritis at home (HERA) is a hand function exercise program developed at our hospital, that can be performed with a single towel. In this study, we compared HERA with Strengthening and stretching for rheumatoid arthritis of the hand (SARAH), which has been already established as an effective rehabilitation program for RA patients. [Methods] Thrity-seven RA admitted patients were included. Hand function assessment (grip strength, pinch strength, hand pain VAS, Quick DASH) and RA disease activity assessment (DAS28-ESR, HAQ-DI, musculoskeletal ultrasound) were performed before and after one-month intervention. The results were analyzed retrospectively. [Results] Ten patients in the control group, 13 in the HERA group, and 14 in the SARAH group were evaluated. Grip strength improved in the HERA and SARAH groups (control vs HERA: right grip $p=0.019$, left grip $p=0.009$, control vs SARAH: right grip $p=0.001$, left grip $p=0.003$, and HERA vs SARAH: right grip $p=0.954$, left grip $p=0.999$). [Conclusion] The HERA group showed an significant improvement in grip strength comparable to that of the SARAH group. HERA was as effective as SARAH in strengthening hand function.

## P2-239

**Exercise Habits of RA Patients**

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Conflict of interest: None

Exercise is recommended in RA patients, but may cause joint pain. In this study, we investigated the actual exercise habits of RA patients and examined appropriate exercise. A questionnaire was sent to RA patients, and 147 (37 males and 110 females, mean age 54 years, mean disease duration about 4 years) responded to the survey. 22.4% had an exercise habit before the onset of the RA and 16.3% after the onset of the RA. Forty respondents cited "lack of time," 25 cited "aching joints," 27 cited "worry about aching joints," and 13 cited "don't like to exercise" as reasons for not having an exercise routine. In Japan, 33.4% of men and 25.1% of women have an exercise habit, and the percentage among RA patients surveyed in this study was small in comparison. In a similar survey conducted in a non-RA group, 48% of the respondents answered "lack of time," suggesting a common reason. This was considered a common reason. Exercise is effective in preventing muscle weakness and maintaining joint function and bone density, and group exercise is also considered more effective than individual exercise. It was thought that selecting exercise according to disease status and suggesting exercise that does not place a heavy burden on joints may lead to the development of exercise habits.

## P2-240

**Mediation effect of nutritional status on physical activity and skeletal muscle mass in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Physical inactivity in patients with rheumatoid arthritis (RA) is one of the risk factors for loss of skeletal muscle mass (SM). However, it was not clear whether the physical activity (PA) is directly related to SM or whether it is mediated by other factors. In this study, we hypothesized that the nutritional status acts as a mediating factor, and examined whether there is a relationship between PA and SM. [Methods] Thirty-nine RA outpatients (mean age: 70.3 years, mean SDAI: 7.4) were enrolled. PA was measured using an accelerometer. All patients were classified into Geriatric Nutritional Risk Index (GNRI) less than 98 (malnutrition group) and 98 or more (normal group), and their PA were compared. Mediation analysis was performed with the SM index as the dependent variable, PA as the explanatory variable, and GNRI as the mediating variable. [Results] The malnutrition group had significantly lower SM index, longer sedentary behavior (SB), and shorter low-intensity activity ($p<0.05$). There was

no direct effect of SB and light-intensity activity on SM; however, there was an indirect effect mediated by nutritional status ($\beta$=0.38-0.48, p<0.05). [Conclusions] Replacing SB with PA, combined with nutritional therapy, may increase SM in patients with RA.

## P2-241

**Effects of SARAH Exercise on Anxiety and Depression in Patients with RA**

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Conflict of interest: None

[Objective] Anxiety and depression in patients with rheumatoid arthritis (RA) are more prevalent than in healthy subjects, and they induced a decrease in quality of life. Recently, an effective treatment program for upper limb function in patients with RA (SARAH exercise) has been developed and spread. SARAH exercise has been reported to be effective in a clinical course for RA. There have been no previous reports on the psychological changes related to SARAH exercises in addressing anxiety and depression. This study aimed to investigate the efficacy of these exercises. [Methods] Seven hospitalized patients with RA (1 male, 6 female, mean age 71.4±8.1 years) after orthopedic surgery (lower limb) from April to September 2023 underwent SARAH exercises to improve upper limb function. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety (HADS-A) and depression (HADS-D) before and after the hospitalization. [Results] Mean score of HADS-A decreased from 8.1±4.8 before starting SARAH exercises to 5.8±3.8 at the last observation. 6 of 7 cases (85%) showed improvement. On the other hand, the HADS-D increased from 6.5±2.9 to 8.0±4.1, respectively. Only 2 of 7 cases (28%) showed improvement. [Conclusions] SARAH exercises may reduce anxiety in RA patients.

## P2-242

**Characteristics of rheumatoid arthritis patients for whom home-visit treatment was introduced and their use of rehabilitation**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients are also aging, and there are constant requests for the introduction of homecare treatment. In this study, we investigated the utilization rate of rehabilitation services for RA patients. [Methods] We investigated the characteristics, level of independence in daily living, and reasons for the introduction of homecare treatment in RA patients who were referred to our hospital between April 2021 and August 2023. The background of patients who did not use rehabilitation services was also examined. [Results] The RA patients had a mean age of 82.3±9.3 years, mean duration of disease of 17.6±12.6 years, and DAS28 (CRP) of 3.0±1.4. The most common reasons for the introduction of home-visit treatment were debility due to aging (54.3%). However, despite this background, the utilization rate of rehabilitation services was 48.6%. The most common reason given was “the patient’s own wish” (55%). The reasons for this may include a lack of understanding of the patient’s disease and the need for rehabilitation, as well as differences in the ability of the person in charge to make proposals to the patient. [Conclusions] The utilization rate of rehabilitation is low among RA patients, and it is necessary to provide patient guidance and ongoing suggestions.

## P2-243

**Trial of Laughter Yoga Experience in Rheumatoid Arthritis Patients**

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Conflict of interest: None

[Objective] Laughter Yoga is a simple health practice combining laughter and yoga breathing exercises, and everyone can easily participate in. We experienced Laughter Yoga, conducted a questionnaire survey, also studied changes in salivary cortisol levels one of the stress hormones in RA patients [Methods] Subjects were patients, their friends and family. The main content of this experience was laughing aloud and taking deep breaths. The survey items on the questionnaire included the purpose of participation, degree of laughter during this session and face scale. Saliva samples were also collected from RA patients before and after the experience. [Results] Responses were obtained from all 17 participants. The main purposes of participation were interest, to want to laugh and to relieve stress. Regarding the degree to which they laughed during the trial, 14 respondents laughed a lot, 2 respondents were caught up in the surroundings and 1 respondent somewhat. The average of the face scale was decreased after the experience. The cortisol secretion in saliva after the trial decreased in 5 out of 7 RA patients. [Conclusions] Laughter Yoga can be expected to improve the mood of people by giving them a chance to laugh a lot. It also has the potential to reduce stress in RA patients.

## P2-244

**Effects and Challenges of SARAH Exercises for Hospitalized Rheumatoid Arthritis Patients**

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the effectiveness of strengthening and stretching for rheumatoid arthritis of the hand (SARAH) modification program for hospitalized patients with RA. [Methods] Eight patients with RA who were admitted to our hospital for orthopedic surgery of the lower extremity between 2021 and 2022 and were available for follow-up data after SARAH-modified ExP were selected. The mean DAS28CRP4 was 3.2. The duration of intervention for each patient was 4-6 weeks, and the frequency of intervention was 5 times per week. Assessment items were grip strength and interphalangeal distance with estimation of ADLs and IADLs. [Results] Grip strength and interphalangeal distance improved in 7 of 8 patients (88%). Three patients became able to open and close a plastic bottle by themselves, two patients to squeeze, and one to use a knife better. A male patient in his 70s with past histories of depression, neurosis, poor motivation, and comprehension could not improve after the intervention of SARAH-modified ExP. [Conclusions] SARAH-modified ExP for hospitalized patients with RA showed short-term efficacy in 88% of these cases. Methods of continuation back to home and evaluation of long-term efficacy are considered future issues.

## P2-245

**Use of tacrolimus (TAC) in rheumatoid arthritis (RA) patients who want pregnancy or with flare up during pregnancy**

Satoshi Ito[1], Masanori Sudo[1,2], Sayuri Takamura[1,2], Daisuke Kobayashi[2], Nariaki Hao[1], Asami Abe[1], Hiroshi Otani[1], Kiyoshi Nakazono[1], Akira Murasawa[1], Ichiei Narita[2], Hajime Ishikwa.[1]
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Conflict of interest: Yes

[Objective] To clarify the progress of RA patients who used TAC when trying to become pregnant or during pregnancy. [Methods] We analyzed patients with TAC (2.7±0.54 mg/day) in 13 patients who want pregnancy and 1 patient with flare-up. [Results] The mean age was 34.6±4.1 y.o. and the mean disease duration was 57.9±134.8 mos. 5 patients used MTX and discontinued it. PSL was used in 8 patients (2.0±2.0 mg/day) and SASP in 6. DAS28-CRP in 12 patients excluding 2 patients with bDMARDs introduction, decreased 2.3±0.89 to 1.9±0.90 (not significant). 12 patients including 6 with infertility treatments gave birth and 1 patient was pregnant. 5 patients underwent Caesarean sections due to fetal growth restriction and other conditions. There were no abnormalities in infants ex-

cept for hyperbilirubinemia and low birth weight. It took 7.3 ± 9.5 and 5.9 ± 9.4 mos. from the start of TAC and the pregnancy approval to the pregnancy, respectively. [Conclusions] TAC reduces Th1/Th2 ratio and cellular immunity. TAC was approved for infertility as the advanced medical care B by MiHLW. Pregnancies were achieved early in RA patients, including those undergoing infertility treatment, and TAC appeared to be effective when trying to become pregnant or during flare-ups during pregnancy.

## P2-246

**A case of acute lymphoblastic leukemia developed in a 5-year-old child who was born to a mother with RA and was exposed to etanercept in utero**

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Conflict of interest: None

[Background] Administration of etanercept to pregnant patients with rheumatoid arthritis (RA) is safe in terms of teratogenicity. However, long-term effects of etanercept on fetuses exposed *in utero* is difficult to track. Child acute lymphoblastic leukemia (ALL) develops through a 1st hit during the embryonic period, when preleukemic clones appear, and a 2nd hit after birth, when a part of preleukemic clone acquires genetic changes and become leukemic cells. [Case Presentation] The mother with RA was in remission with etanercept and prednisolone. She stopped taking etanercept at 3 weeks and 6 days of gestation. Because RA relapsed, administration of etanercept was restarted and the dose of prednisolone was increased at 12 weeks and 3 days of gestation. She gave birth normally at 38 weeks and 1 day of gestation. When the patient was 5 years old, he developed petechiae and cervical lymphadenopathy, as well as multiple intracranial hemorrhages and right vitreous hemorrhage due to leukostasis. The patient was diagnosed with T lymphocytic ALL. The patient is currently in remission with maintenance therapy. [Clinical Significance] Considering that the 1st hit on ALL occurs during the fetal period, it is noteworthy that the patient who was exposed to etanercept *in utero* developed ALL.

## P2-247

**A Study of Cases of Confirmed Pregnancy During Rheumatoid Arthritis Treatment**

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Conflict of interest: None

[Objective] In this study, we examined cases in which pregnancy was confirmed during RA treatment. [Methods] We selected patients with RA who had become pregnant in the past 10 years during outpatient treatment, and investigated the drugs used, pregnancy, and delivery status. [Results] The age at the time of the 18 confirmed pregnancies ranged from 23 to 37 years, with a mean age of 32.9 years. The breakdown was 9 first pregnancies, 7 second pregnancies, and 2 third pregnancies. Pregnancy was confirmed during treatment with BIO or csDMARD on 12 occasions. In the 18 pregnancies, 16 women delivered without complications (16 normal delivery, 2 cesarean sections), and 2 miscarriages occurred. The miscarriages included one each of golimumab (GLM) with methotrexate (MTX) and etanercept (ETA) alone. After delivery, RA symptoms worsened and drug therapy was resumed 10 times, including 4 times with tocilizumab (TCZ), 3 times with ETA, 2 times with infliximab (IFX), and 1 time with GLM. [Discussion] After 18 successful pregnancies, 16 of them resulted in successful delivery. Recently, the number of pregnancies during BIO treatment has been increasing, but miscarriages have been observed in pregnancies treated with MTX and GLM, and pregnancy during MTX treatment is contraindicated.

## P2-248

**The pregnancy and childbirth of rheumatoid arthritis patients at our hospital**

Maiko Yoshimura[1], Yanakawee Siripongvutikorn[1], Atsuko Tsujii[1], Kurumi Yamamoto[1], Akira Nishigaichi[1], Akihiko Nakabayashi[1], Hyota Takamatsu[1,2], Shiro Ohshima[1,2]
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Conflict of interest: None

[Objective] To know the pregnancy delivery of patients with rheumatoid arthritis in our hospital. [Methods] I extracted patients with RA of the woman of 18-40 years old that visited a hospital for treatment in our hospital rheumatology department for from April, 2019 to April, 2023. I recorded the delivery within this period. [Results] There were 24 patients (delivery number was 27). The delivery average age was 32.2±8.2 years old. Anti SS-A antibody (52KDa) was positive 1, negative 16, unknown 7. The obstetrics complications were 2 premature birth, 1 blood transfusion due to the bleeding, and 1 chorion amnionitis. The treatment at the time of the pregnancy, biologics use were 12 patients (ETN 6, CZP 6), csDMARDs use 3 (SASP 2, TAC1), PSL only 4, no-drug 7. The activity at the time of the pregnancy were remission 21, low disease activity 2. [Conclusions] There were relatively many patients who used biologics at the time of the pregnancy in the RA patients of our hospital. (11/24) all cases were controlled by remission or low disease activity, and the report of the unplanned pregnancy was not almost found. I know the fact of the pregnancy delivery of the RA patient of our hospital and want to keep it alive for future medical care.

## P2-249

**Drugs for treatment of WoCBA generation patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry**

Nozomi Kaga[1], Toshiaki Aizawa[1], Takeshi Kashiwagura[2], Moto Kobayashi[3], Tsutomu Sakuraba[3], Hiroshi Aonuma[4], Yusuke Sugimura[5], Naohisa Miyakoshi[6]
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Conflict of interest: None

[Objective] This time, we investigated therapeutic drugs for WoCBA generation patients registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry. [Methods] Among 1917 RA patients treated at 25 hospitals in Akita Prefecture registered in the 2021 AORA registry, we investigated therapeutic agents for 76 patients of the WoCBA generation (18-45 years old). [Results] The breakdown of therapeutic drugs for WoCBA generation patients was methotrexate (MTX) in 59 patients, biological agents in 28 patients, salazosulfapyridine in 17 patients, iguratimod in 14 patients, prednisolone in 12 patients, and bucillamine in 8 patients (some overlaps).). Among biologics, etanercept was the most common (13 patients), golimumab (6 patients), adalimumab (4 patients), tocilizumab (3 patients), certolizumab pegol (1 patient), and abatacept (1 patient). [Conclusions] We reported on therapeutic drugs for WoCBA generation patients registered in the AORA registry. Not all WoCBA generation patients want to become pregnant, and even if they do want to become pregnant, some patients do not have good RA control and are aiming for remission first, which is why MTX use is thought to be increasing. It was done.

## P2-250

**Registry for Japanese rheumatoid arthritis patients of childbearing Age (PRAISE-H)**

Chinatsu Takai[1], Izumi Fujioka[1], Mikako Goto[1], Nobuyuki Yajima[2,3,4], Sakiko Isojima[2], Tatsuya Atsumi[5], Akira Sagawa[6], Akira Furusaki[6], Izumi Yasuda[6,7], Yujiro Kon[8], Katsunori Ohnishi[9], Koji Taneichi[10], Masaru Yoshimura[11], Kazuaki Katsumata[12], Yuichiro Fujieda[5], Kensaku Okamoto[13], Kitaru Tanaka[13], Tsuyoshi Takeda[14], Hideki Kasahara[15], Yuhei Shibata[16], Atsuko Murashima[1]

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Conflict of interest: None

[Objective] We have established the Pregnancy and Rheumatoid Arthritis in Hokkaido Registry (PRAISE-H) to investigate the fertility and pregnancy outcomes in RA patients, long and short-term prognosis of RA, the impact of RA on quality of life, employment and economic burden. [Methods] This study is a multicenter prospective cohort study. Men and women aged 20 to 40 years within 3 years of diagnosis of RA are included. Surveys are conducted every 6 months during the non-pregnant period, at pregnancy diagnosis, at 12, 22, and 32 weeks gestation, and at 1, 3, 6, and 12 months postpartum using REDCap. VAS and MDHAQ, SF36v2, economic toxicity index; COST questionnaire, labor productivity index; WPAI, pregnancy outcomes and complications are collected from patients, and disease activity, laboratory data and treatment are collected from attending physicians. [Results] 79 patients (71 women and 8 men) were enrolled from 13 hospitals. Median age at enrollment was 33.5 years, 65% used MTX, 26% used bDMARDs, and CZP was the most commonly used with 35%. Twelve pregnancies have been reported, 10 were live births, 1 was spontaneous abortion, and 1 pregnancy is ongoing. [Conclusions] This study is expected to identify issues specific to the younger age and lead to proper clinical care.

## P3-001

**Medical information seeking behavior in patients with Systemic lupus erythematosus: The TRUMP2-SLE Study**

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Conflict of interest: None

[Objective] We aimed to clarify patterns of access to health information among patients with SLE. [Methods] In this cross-sectional study conducted at five academic centers, 516 patients with SLE were analyzed. We described the first health information source which patients preferred to access and actually accessed, and type of online health information source if they chose an online source. In addition, we described the age distribution of users by online health information source. [Results] The median age of the patients was 46 years and 88.2% were women. The health information source they preferred to access first was their physician, followed by a website/blog. On the other hand, the most common sources of health information actually accessed were the website/blog. The medical institution's website was the most common online information sources, while other patient's websites and blogs were often used. Proportion of access to SNS was less than 10% regardless of the online information sources, and more than half of the users were in their 20-30 age group. [Conclusions] Patients frequently access online health information sources. We need to take into account the fact that patients are seeking online health information sources not generated by health care providers.

## P3-002

**Investigating trust in health information sources and its correlates among patients with systemic lupus erythematosus: The TRUMP2-SLE study**

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Conflict of interest: None

[Objective] We aimed to clarify the levels of trust in health information sources and its correlates among patients with SLE. [Methods] In this cross-sectional study conducted at five academic centers, 516 patients with SLE were analyzed. We described the levels of patients' trust (4-point Likert scale) in 12 sources of health information. The relative risk of factors associated with trust in health information sources was estimated using modified Poisson regression adjusted for age, gender, education, household income, marital status, duration of illness, health literacy (HL), time spent on the Internet, and disease activity. [Results] Many patients trusted healthcare providers as information sources, while relatively few trusted homepages (HP)/blogs and SNS. However, regular internet use was a factor that increased the likelihood of having trust in both HP/blogs and SNS. Higher functional HL also increased the likelihood of having trust in physicians, while decreased the likelihood of having trust in both HP/blogs and SNS. [Conclusion] The proportion of patients who trust in the Internet and SNS is much lower than that who trust in their physicians. However, they are more likely to trust in online media if they use the Internet regularly or have poor functional HL.

## P3-003

**Risk weight calculation of fragility fractures in patients with rheumatic diseases (1)**

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Conflict of interest: None

Objective: To introduce ingenuities for more accurate prediction of fragility fractures (FF) in patients with rheumatic diseases (RDs). Methods: RD patients who were followed up for at least 2 years were picked up.

The primary endpoint was to set the incidence of the first FF (inc-FF). Clinical parameters were calculated in βvalue using a univariate model multiplied by the logarithm of the p-value using a multivariate model (factor-specific risk weight; FSRW). FSRWs were summed for each case (total risk weight; TRW), and the inc-FF cut-off index (COI) was determined. Sensitivity and specificity (S&S) were determined regarding FF+/- for the dividing COI (exCOI/unCOI) (proc-1). Patients were divided by risk factors with the FSRW exceeding the COI (S/N), and the S&S was calculated as a control. Also, S was excluded, and the same procedure as proc-1 was performed on the N. Patients with exCOI or S and unCOI were determined S&S (proc-2). Results: A total of 1,228 patients in them, the inc-FF developed in 179 (14.6%). The factor with FSRW that exceeded the COI was only prevalent FF. The S&S were 30.1% and 95.3% in proc-1, whereas 31.2% and 94.9% in proc-2 (31.4% and 94.7% in the control). Conclusions: Accuracy improves only slightly under conditions with prominent risk factors.

## P3-004

**Risk weight calculation of fragility fractures in patients with rheumatic diseases (2)**

Ichiro Yoshii
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Conflict of interest: None

Objective: To introduce ingenuities for more accurate prediction of fragility fractures (FF) in patients with rheumatic diseases (RDs). Methods: RD patients who were followed up for at least 2 years were picked up. The primary endpoint was to set the incidence of the first FF (inc-FF). Risk ratio (RR) of the significant factors using a univariate model was multiplied by every factor for each patient, and the calculated value as a total risk weight (TRW). From the TRW, the cut-off index (COI) was determined. Sensitivity and specificity (S&S) were determined regarding FF+/- for the dividing COI (exCOI/unCOI) (proc-1). Patients were divided by risk factors with the RR exceeding the COI (S/N), and the S&S was calculated as a control. Also, S was excluded, and the same procedure as proc-1 was performed on the N. Patients with exCO and S, and unCOI were determined S&S (proc-2). Results: Of 1,228 patients in them, the inc-FF developed in 179 (14.6%). The factor that exceeded the COI was only prevalent FF. The S&S were 33.5% and 92.5% in proc-1, whereas 24.1% and 97.3% in proc-2 (31.4% and 94.7% in the control). Conclusions: Specificity infers, but sensitivity is superior in proc-1 compared to the control, whereas accuracy of specificity improves, but sensitivity is reduced in proc-2.

## P3-005

**Relationship between laughter and locomotive syndrome in rheumatoid arthritis patients: T-FLAG study**

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Conflict of interest: None

[Objective] Rheumatoid arthritis (RA) patients have a higher incidence of depression than the general population. And, RA is a causative disease of locomotive syndrome (LS). This study investigated the relationship between laughter and LS in RA patients. [Methods] Among 696 patients visited in 2023 (T-FLAG study), 667 RA patients were available for investigating patient backgrounds. A score of 16 or higher in the 25-question Geriatric Locomotive Function Scale was defined as LS. The odds ratio (OR) of laughter related to LS was calculated using multivariable logistic regression analysis. [Results] 290 (43.5%) were RA patients with LS. Age (LS group/non-LS group) was 72.4±12.1/65.6±13.8 years, and CDAI was 9.8±9.1/3.6±4.9. The laughter frequency ("every day, 1-5 times a week"/"1-3 times a month, almost never") was 74.5%/25.5% in LS group and 90.7%/9.3% in non-LS group. CDAI (OR 1.16, 95% confidence interval 1.13-1.20) and "laughter" (OR 0.30, 95% confidence interval 0.18-0.50) were identified as significantly associated factors with LS. [Conclusions] In this study, "laughter" was significantly associated with LS. In addition to suppressing disease activity in RA patients, the engagement of medical professionals in laughter can be a beneficial intervention for LS in RA patients.

## P3-006

**Serum soluble PD-1 levels associate with the development of rheumatoid arthritis in anti-CCP-positive subjects at-risk for rheumatoid arthritis**

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Conflict of interest: None

[Objective] We aimed to investigate the association between initial serum soluble PD-1 (sPD-1) levels and RA development, and the changes in serum sPD-1 levels before and after the onset of RA in our prospective anti-CCP-positive cohort at-risk for RA. [Methods] Thirty-four anti-CCP-positive subjects visiting our clinic for joint stiffness/pain without clinical arthritis and three anti-CCP-positive asymptomatic subjects identified at health check-ups were enrolled. Serum sPD-1 levels were measured at baseline and the development of clinical arthritis fulfilling 2010 ACR/EULAR criteria for RA was monitored. Serum sPD-1 levels were measured at the onset of RA as well. [Results] Of the 37 subjects, 84% was female, median age was 58 years-old, and median follow-up was 350 days. RA developed in 12 subjects during follow-up. The serum sPD-1 levels at baseline were significantly higher in the progressors to RA than those in the non-progressors (in median, 247 pg/mL vs. 129 pg/mL; $p < 0.05$). In the progressors, there were no significant changes in serum sPD-1 levels at baseline and the onset of RA (in median, 247 pg/mL vs. 308 pg/mL; $p = 0.52$). [Conclusion] Our study suggests that high levels of serum sPD-1 at baseline predict the future development of RA in anti-CCP-positive subjects.

## P3-007

**Enhanced expression of mRNA for interferon signature genes in CD34+ cells of the bone marrow in rheumatoid arthritis**

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Conflict of interest: None

[Objective] Interferon-stimulated genes (ISGs) have been shown to be upregulated in peripheral blood (PB) in rheumatoid arthritis (RA), including MX1, IFI44L, PARP9 and DTX3L. We examined mRNA expression of these ISGs in RA bone marrow (BM) CD34+ cells. [Methods] BM samples were obtained from 49 RA patients and 34 OA patients, who gave informed consent, during joint operations via aspiration from iliac crest. CD34+ cells were purified from BM mononuclear cells using magnetic beads. The expression of mRNA for ISGs was examined by quantitative RT-PCR. [Results] Expression of mRNA for IFI44L, PARP9 and DTX3L in BM CD34+ cells was significantly higher in RA than in OA. The mRNA expression of these ISGs was not correlated with serum CRP or with the use of MTX or steroid. The mRNA expression of the respective ISGs was closely correlated with each other, while the correlation between PARP9 and DTX3L was the closest (r=0.949). Notably, mRNA expression of PARP9 and DTX3L was significantly correlated with NFkB1 mRNA expression in RA. [Conclusions] The results indicate that mRNA expression of ISGs was enhanced in RA BM CD34+ cells. The data also suggest that the enhanced mRNA expression of PARP9 and DTX3L might result in abnormal responses of BM CD34+ cells to TNFα through enhancing NFkB1 mRNA.

## P3-008

**CD14+ dendritic-shaped cells in rheumatoid arthritis synovial tissue are involved in chronic inflammation as dendritic cells**

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Conflict of interest: None

[Objective] CD14+ dendritic-shaped cells are monocyte-derived immune response cells that express CD90 in RA synovial tissues and play a key role in RA pathogenesis. In this study, we investigated the possibility of dendritic cell differentiation of $CD14^{high}CD90^{int}$ cells. [Methods] After in vitro culture of RA synovial tissue, $CD14^{high}CD90^{int}$ cells were harvested and used in this study. After the culture in dendritic cell differentiation induction, cell morphology, IL-6 and TNF-α levels in the culture supernatant, and CD83 and HLA-DR expression levels in the cells were measured. Furthermore, $CD14^{high}CD90^{int}$ cells were co-cultured with lymphocytes, and the cell activation was examined by the expression levels of inflammatory cytokines. [Results] $CD14^{high}CD90^{int}$ cells showed increased expression of inflammatory cytokines in the culture supernatant and intracellular CD83 and HLA-DR after induction of dendritic cell. In co-culture experiments with lymphocytes, $CD14^{high}CD90^{int}$ cells after induction of dendritic cells showed higher cell number and higher expression of inflammatory cytokines in the supernatant than $CD14^{high}CD90^{int}$ cells. [Conclusions] CD14+ dendritic-shaped cells are considered to differentiate into HLA-DR+ dendritic cells by contact with lymphocytes in RA synovial tissues.

## P3-009

**Examination of vascular endothelial cadherin expression in local rheumatoid arthritis synovium**

Shinichiro Nishimi, Takeo Isozaki, Eriko Ishidaka, Kunika Shimizu, Kazutaka Kawamori, Noriko Konishi, Airi Nishimi, Sho Ishii, Kuninobu Wakabayashi
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Conflict of interest: None

[Objective] VE-cadherin is a protein involved in adhesion formation of vascular endothelial cells. The investigation of VE-cadherin in local joints has not been sufficient. Here, we investigated the expression of VE-cadherin in local joints in RA. [Methods] We examined the expression of VE-cadherin in the synovial tissue of RA and OA patients using immunostaining. In addition, the concentration of VE-cadherin in the synovial fluid of patients with RA and OA was measured by ELISA. Finally, to analyze the function of VE-cadherin in RA synovial fluid, we used immunoprecipitation to examine the differences in lumen formation of vascular endothelial cells between synovial fluid from which VE-cadherin was removed and control fluid. [Results] We found that VE-cadherin in RA synovial tissue. There was no significant difference in the concentration of VE-cadherin in the synovial fluid of RA patients compared to that in OA. In RA synovial fluid from which VE-cadherin was removed, there was a significant decrease in the number of lumen formation by vascular endothelial cells using Matrigel compared to synovial fluid using control IgG. [Conclusions] VE-cadherin was present in RA joint tissue and joint fluid. It was suggested that VE-cadherin in RA joint fluid may be involved in angiogenesis.

## P3-010

**Cytokine expression in synovial fluid-derived fibroblasts of rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate the cytokines expression on RA synovial fluid-derived fibroblasts (SF-dF) and whether the difference of subsets proportion of SF-dF affect the treatment. [Methods] $PDPN^{+}$SF-dF subsets ($CD34^{-}TH1^{-}$, $CD34\text{-}THY1^{+}$, $CD34^{+}THY1^{+}$) were analyzed using flow cytometry. SF-dF were stimulated with TNFα or SF and mRNA expression and protein expression of cytokines (IL6, IL8, MMP3, VEGF and GM-CSF) were evaluated using qPCR and ELISA. We statistically analyzed the relationship between the differential proportion of subsets and cytokines expression and treatment. [Results] The mRNA expression of IL6, IL8, MCP1, MMP3, and VEGF, and the protein expression in the culture medium of IL6, IL8, MCP1, MMP3, VEGF, and GM-CSF were increased by TNFα. The mRNA expression of PDGF, GM-CSF, RANKL, and VEGF decreased by SF stimulation. Positive correlation was observed between the concentrations of MMP3 and RANKL in the unstimulated culture medium and the proportion of the $PDPN^{+}CD34^{-}THY1^{-}$ subset. Patients with the high proportion of $PDPN^{+}$SF-dF, especially the $CD34^{-}THY1^{+}$ subset, at the primary culture were more likely be treated with Bio-DMARDs/JAKi after one year. [Conclusions] The differential proportion of SF-dF subsets may be involved in cytokines expression and the response of treatment.

## P3-011

**Impact of Clinical Arthritis and Arthritic Changes on Hand-Related Physical Function in Elderly Rheumatoid Arthritis Patients**

Hiroto Nishimura[1], Ryota Hara[1], Yusuke Ozaki[1], Kensuke Okamura[1], Nobushiro Nishimura[2], Hiromasa Kawashima[2], Hidetoshi Matsuoka[2], Emiko Tatsumi[2], Shiro Ono[2], Kenichi Samejima[3], Naoki Shimmyo[2], Yasuhiro Akai[4], Kenji Nishio[4], Kiyomi Yoshimoto[2], Yasuhito Tanaka[1]
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Conflict of interest: None

Objective: The aim was to investigate the impact of clinical arthritis in hand joint OA on hand-related physical functional impairment in elderly RA patients. Methods: We studied 65 RA patients aged 70 or above between April 2017 and November 2021. We categorized patients with Larsen grade 3 or higher as the RA change group (19 cases), with a KL median 2 or higher as the severe OA group (10 cases), and less than 2 as the mild OA group (36 cases). Clinical arthritis was defined as joint swelling, and the number as SJC Hands. Within HAQ-DI, we defined Dressing, Eating, and Grip as hand joint function-related (Hands-HAQ). We analyzed adjusting for gender, CCP, and CRP using an ordinal logistic regression model. Subgroup analysis was also performed for late elderly patients. Results: The ordinal logistic regression analysis (95%CI, p-value) showed that the severe OA group (vs. mild OA group) had aOR of 1.58 (0.5-5.13, p=0.44), the RA change group 4.92 (1.46-17.6, p=0.012), and SJC Hands aOR of 1.47 (1.26-1.75, $p \leqq 0.001$). In the subgroup analysis, the aORs were 4.42 (1.06-20, p=0.05), 8.85 (1.6-57.6, p=0.016), and 1.56 (1.26-2.03, $p \leqq 0.001$). Conclusion: Eelderly RA patients with radiographic evidence of OA or RA-related changes may be affected by physical functional impairment.

## P3-012

**Interrelationship between sarcopenia and frailty in patients with rheumatoid arthritis analyzed from the multicenter prospective observational study (PRESENT Study)**

Masahiro Tada[1], Yoshinari Matsumoto[2], Tatsuya Koike[3], Kenji Mamoto[4], Tomoyuki Nakamura[5], Shohei Anno[6], Takahiro Iida[7], Hitoshi Goto[5], Noriaki Hidaka[1]
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Conflict of interest: None

[Object] RA have higher rates of sarcopenia (SAR) and frailty (FRA). The relation between those is not clear. We investigated the characteristics of those to clarify the interrelationship. [Methods] Data from the multicenter prospective observational study (PRESENT Study) were used. AGWS 2019 criteria were used for SAR and severe SAR, and J-CHS criteria for FRA and pre FRA. 200 RA were divided with or without SAR and FRA, and disease activity, treatment, body composition, and muscle function were compared. [Results] The incidence of SAR and severe SAR was 20% and 10%. SAR was significantly older, had longer disease duration, advanced Stage and Class, higher RF positivity, higher CRP, higher MTX use, lower muscle and fat mass, and lower grip strength. The incidence of FRA and pre FRA were 40% and 54%. FRA was significantly older, advanced Stage and Class, higher DAS28-ESR, higher mHAQ, higher CRP, higher glucocorticoid usage rate, lower muscle mass, and lower grip strength and walking speed. SAR and FRA were combined in 10% (50% of SAR and 25% of FRA). A significant positive correlation was found between severe SAR and FRA (CC: 0.31, $p<0.001$). [Conclusions] The incidence of SAR and FRA was 20% and 40%. Both were in 10%. FRA had high disease activity and decline in muscle function.

## P3-013

**Positive Rheumatoid Arthritis-Related Autoantibody Rates in Patients with previous and current Smoking Habits**

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Conflict of interest: None

[Objective] We investigated changes in autoantibody positivity rates (dSP) associated with changes in the smoking status and in autoantibody induction rates in patients (pts) with a history of smoking. [Methods] The study included 852 pts with RA between 2012 and 2021. We retrospectively investigated dSP and smoking status in all pts, and dSP rates were compared based on chronological age group of disease onset in all pts and in those with a history of smoking. [Results] The dSP rates among pts with RA decreased over the periods as follows: 77%, 54%, and 42%, respectively. The percentage of pts aged ≧65 y.o. at the time of disease onset increased to 17%, 47%, and 70%, respectively over the aforementioned time periods. The dSP rate among those with a history of smoking decreased to 82%, 61%, and 47%, respectively for each age group at disease onset. [Conclusions] The prevalence of smoking has decreased across Japan in recent years owing to intensive social efforts to prevent passive smoking. It is suggested that population ageing with onset RA, greater focus on social environmental activities to promote smoking cessation, and the widespread use of fluoride-containing toothpaste are important contributors to the decrease in autoantibody induction rates among patients with RA.

## P3-014

**Analysis of bone structure in the proximal femur of rheumatoid arthritis patients using 3D-SHAPER - Comparison by anti-CCP antibody levels -**

Ikuko Tanaka[1], Takashi Kato[2], Takashi Kida[3], Takuya Yanagida[3], Motokazu Kai[4], Kunikazu Ogawa[4], Yusuke Suzuki[1], Hidenao Imada[1], Hitomi Nagasaka[1], Yutaka Kawahito[3], Hisaji Oshima[5], Shigenori Tamaki[1]
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Conflict of interest: None

[Objective] In this study, we compared the structural strength of the proximal femur of ACPA-positive female RA patients using 3D-SHAPER (3DS). [Method] Subjects were 240 ACPA-negative non-RA cases (control group), 36 RA cases with ACPA value less than 50 U/mL (Low group), 37 RA cases with ACPA value 50 U/mL or more and less than 200 U/mL (Middle group), 36 RA cases with ACPA value more than 200 U/mL (High group). Using DXA data of the proximal femur, quantitative CT-like three-dimensional bone structure analysis was performed using 3DS. [Results] Bone mineral density of the proximal femur was significantly lower in the Middle group (-4.8%, $p<0.01$) and High group (-4.2%, $p<0.05$) than in the control group. Cortical volumetric BMD was significantly lower in the High group (-2.9%, $p<0.01$) than in the control group. Cortical bone surface density, which indicates bone strength, was significantly lower in the Middle group (-5.7%, $p<0.05$) and High group (-5.8%, $p<0.01$) compared to the control group. Cortical bone thickness was significantly lower in the Middle group (-3.4%, $p<0.05$) and High group (-3.2%, $p<0.05$) than in the control group. [Conclusion] In ACPA-positive RA patients, the cortical bone parameters were lower in the ACPA Middle and High groups than in the control group.

## P3-015

**Analysis for markers of immunological remission in molecular targeted therapy for rheumatoid arthritis**

Shiro Ohshima[1,2], Hyota Takamatsu[1,2], Akihiko Nakabayashi[2], Maiko Yoshimura[2], Akira Nishigaichi[2], Kurumi Yamamoto[2], Atsuko Tsujii[2], Yanakawee Siripongvutikorn[2], Jun Hashimoto[2], Atsushi Ihata[4], Koichiro Takahi[5], Yoshiro Horai[6], Shigeru Yoshizawa[7], Masataka Torigoe[8], Masao Katayama[9], Satoshi Ito[10], Yuichi Maeda[11], Hirokazu Takaoka[12], Toshihiro Matsui[3], Kentaro Isoda[1,2]
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Conflict of interest: None

[Objective] To investigate the usefulness of immunoglobulin sugar chain abnormalities as a marker of immunological remission in molecular targeted therapy for rheumatoid arthritis. [Method] In RA patients who achieved clinical remission with molecular target therapy and were able to decide to discontinue the drug, G0 (proportion of galactose deficiency) and S0 (proportion of sialic acid deficiency) were determined in IgG by immunoglobulin sugar chain analysis at the time of discontinuation. The ratio will be measured using liquid chromatography and mass spectrometry to examine whether it can be used as a marker for predicting remission maintenance for one year after discontinuation. [Results] Both G0 and S0 ratio were markedly increased in RA cases. Furthermore, it was also revealed that these abnormalities were reduced in cases in which clinical remission was achieved, and were significantly lower in the group in which remission was maintained 1 year after discontinuing the drug. [Discussion] IgG glycan abnormalities may be useful as a marker for diagnosis, activity, and remission of RA. Furthermore, it was suggested that abnormalities in IgG sugar chains (increased G0 S0 ratio) in RA are important in elucidating the etiology and pathology.

## P3-016

**Difficulty in diagnosing the cause of synovitis after arthroscopic rotator cuff repair: A case report**

Terufumi Shibata[1], Teruaki Izaki[2], Akira Maeyama[1], Tomonobu Hagio[1], Yutaro Yamasaki[1], Yuki Sugino[1], Naoko Himuro[3], Katsuhisa Miyake[3], Takuaki Yamamoto[1]
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Conflict of interest: None

A 66-year-old male presented with right shoulder pain during work. An initial assessment at a local hospital indicated a rotator cuff tear. One month post-symptom onset, he was referred to our hospital for a comprehensive evaluation and treatment. His medical history revealed a 30-year habit of smoking 20 cigarettes daily. Laboratory tests including WBC and CRP were within normal limits. Despite conservative treatment, his pain persisted. Arthroscopic rotator cuff repair was performed, revealing no specific synovitis. Although his symptom was improved postoperatively, right shoulder joint pain recurred 1 year and 9 months after the surgery. X-ray showed bone erosion on the humeral head adjacent to the capsule attachment. MRI confirmed an intact rotator cuff and significant synovial hypertrophy in the glenohumeral joint. Examination also revealed tenderness and swelling in multiple extremity joints, in addition to the shoulder. Laboratory tests showed that both RF and CCP antibodies were positive and elevated CRP (3.9 mg/dl) was confirmed. Consequently he was diagnosed with elderly-onset rheumatoid arthritis. Introduction of DMARDs led to relief of his symptoms. Rheumatoid arthritis should be considered in the differential diagnosis for synovitis that develops postoperatively.

## P3-017

**Cytokine kinetics in rheumatoid arthritis patients with dupilumab against eosinophilic sinusitis**

Hiroshi Ishida
Department of Rheumatology, Ishida RA Clinic

Conflict of interest: None

[Objective] 2rheumatoid arthritis (RA) patients were well controlled by MTX and TNF inhibitor, however they have also allergic diseases such as bronchial asthma (BA) and eosinophilic sinusitis (ES). Pulmonologist added dupilumab (DMB) that is an inhibitor against IL-4/IL-13alpha receptor to improve BA and ES. Indeed, BA and ES were dramatically improved, but RA was drastically worsened. [Methods] To explore what happen in these RA patients with DMB treatment, we have titrated cytokine levels such as IL-4, IL-6, IL-10, IL-13, TNF-alpha levels in sera by sandwich-ELISA methods. Also, these levels were compared with clinical markers in RA patients. [Results] IL-6 and TNF were increased, but IL-10 and IL-13 were decreased with DMB addition. IL-6 and CRP were of course good positive correlation, IL-10 and ESR were negative correlation. TNF and MMP-3 were also good positive correlation. [Conclusions] Biological reagents are useful for many various diseases not only rheumatic diseases but also allergic diseases. We should consider cytokine network in wide variety of viewpoints. RA is constituted by mainly Th1 immune response. so Th2 inhibitor biologics might be worsen RA. We must carefully choose biologics.

## P3-018

**High-Dimensional Analysis of Seropositive and Seronegative Rheumatoid Arthritis Patients' T-cell Phenotypes: An Integrated Approach with Mass Cytometry and Machine Learning**

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Conflict of interest: None

[Objective] Explore T-cell phenotype differences between seropositive rheumatoid arthritis (SP-RA) and seronegative rheumatoid arthritis (SN-RA) patients. [Methods] T-cells from 16 untreated SP-RA (Anti-CCP antibody+ and Rheumatoid factor+) and 17 SN-RA patients were analyzed for 25 T-cell markers using mass cytometry. Using the Flow-SOM (Self-Organizing Maps), 44 T-cell clusters (TCL 00~43) were identified. Background variables between the two groups were adjusted with IPTW, and Discriminative TCLs (D-TCLs) were identified using the Adaptive LASSO (Least Absolute Shrinkage and Selection Operator). The performance of D-TCLs was evaluated using the Support Vector Machine (SVM) with Bootstrap (n=1000). [Results] Six TCLs were identified as D-TCLs. Among them, TCL21 belonged to the activated Th1 type Tph category, TCL02 was characterized by Central memory CD4+ T-cell markers (CXCR3+CD28+CD38+CCR7+ICOS+PD-1+), and two TCLs, TCL31 and TCL35, were identified as CD4 CD8 Double Negative T-cells with markers CD161+ and HLA-DR+CD38+TIM-3+, respectively. SVM validation indicated an accuracy of 86.2% and an AUC-ROC of 0.915, underscoring their high discriminative ability. [Conclusions] Identifying T-cell phenotype differences between SP-RA and SN-RA offers key insights into RA pathophysiology.

## P3-019

**Role of Alternative Splicing of RTKN2 gene in the Pathogenic Mechanism of Rheumatoid Arthritis**

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Conflict of interest: Yes

[Objective] RTKN2 gene is specifically expressed in regulatory T cells. Our Immune Isoform Atlas (IIA) highlighted that a splicing QTL signal for RTKN2 gene colocalizes with GWAS signals for rheumatoid arthritis (RA). This study aims to clarify the role of RTKN2 gene in RA pathogenesis. [Methods] We analyzed the correlation between the expression ratio of RTKN2 isoforms as annotated in IIA and the genotype of the RA GWAS risk variant using RNA-seq data from 104 $CD4^+$ T cell samples from healthy individuals. Amino acid sequences of RTKN2 isoforms were compared using MAFFT. Furthermore, we performed long-read capture RNA-seq for RTKN2 gene using either PMA/Ionomycin-stimulated or unstimulated Jurkat cells and evaluated the alterations in expression levels and isoform expression patterns upon stimulation with IsoQuant. [Results] The GWAS risk allele influenced the expression ratio of RTKN2 isoforms, altering in their last exons in $CD4^+$ T cells. These isoforms exhibited variations in the amino acid sequence of their PH domain. Stimulation with PMA/Ionomycin led to a 10.7-fold increase in RTKN2 expression, and two additional isoforms were expressed. [Conclusions] The alternative splicing of RTKN2 gene, leading to structural modifications in the PH domain, is implicated in RA pathogenesis.

## P3-020

**Oropharyngeal microbiota in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The lower respiratory tract (LRT) microbiota has been suggested to contribute to the pathogenesis of rheumatoid arthritis (RA). We examined the oropharyngeal microbiota, which has similarity to the LRT microbiota, in patients with RA to explore its relationship with the disease. [Methods] Oropharyngeal lavage collected from 48 patients with newly diagnosed and untreated RA and 47 age- and sex-matched healthy controls (HC) were subjected to shotgun metagenomic analysis. β-diversity was calculated with UniFrac. The association of the relative abundance of individual species with the disease and other clinical features were examined using R-package MaAsLin2. [Results] Significant differences in β-diversity were found at both genus and species levels. Fifteen species and 36 were significantly enriched and depleted in patients compared to HC, respectively. Twelve of 15 species and 30 of 36 species remained enriched and depleted in RA after adjusted by smoking history, which RA patients had with higher rate. Species differentially altered in RA were not associated with either disease activity or a titer of anti-citrullinated peptide antibody. [Conclusions] The oropharyngeal microbiota in RA significantly differ from that in HC and may be associated with disease development.

## P3-021

**CXCL13 as a possible immunological surrogate marker of dermatomyositis**

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Conflict of interest: None

[Objective] CXCL13 is a chemokine involved in the pathophysiology of connective tissue diseases by contributing to ectopic lymphoid follicle formation. [Methods] We evaluated 59 patients (2018-2023) with new-onset dermatomyositis (DM) (n = 42) / polymyositis (PM) (n = 17) to evaluate clinical and pathophysiological significance of CXCL13 in DM and PM. Plasma CXCL13 levels were measured by ELISA, and their correlation with clinical characteristics and treatment was analyzed. [Results] Plasma CXCL13 levels were higher in patients with DM than those with PM ($P = 0.016$) and could differentiate these subsets with a cut-off value of 81.1 U/L (area under curve = 0.8). In patients positive for anti-aminoacyl-tRNA synthetase antibodies, those with DM had significantly higher plasma CXCL13 levels than those with PM ($P = 0.001$). Plasma CXCL13 levels correlated with serum levels of creatine kinase ($P = 0.007$), but not with KL-6 ($P = 0.288$) in patients with DM. Following treatment, plasma CXCL13 levels significantly decreased in patients with DM ($P = 0.008$). [Conclusions] Plasma CXCL13 levels were high, especially in patients with DM. CXCL13 can be an important chemokine implicated in the pathophysiology of DM, which serves as a novel immunological marker of disease activity in patients with DM.

## P3-022

**A case of anti-TIF-1gamma antibody positive dermatomyositis with severe dysphagia that developed during follow-up of rheumatoid arthritis**

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Conflict of interest: None

A 71-year-old man had been followed up for rheumatoid arthritis. He was admitted to the hospital for malaise, bilateral leg myalgia, and systemic skin rash appeared 3 weeks ago. He had undergone lobectomy and chemotherapy for lung cancer 12 years ago. Physical examination revealed facial erythema, Gottron's sign, Gottron's papules, shawl sign, proximal weakness. Blood tests showed elevated CK and positive anti-TIF-1γ antibody. CT showed a mass in the left lobe of the liver. A liver biopsy made a diagnosis of recurrent lung cancer. Steroid pulse and intravenous immunoglobulin therapy improved the skin rash and CK level, but severe dysphagia appeared and aspiration pneumonia developed. The patient's general condition deteriorated, and he died after 3 months of hospitalization. Anti-TIF-1γ antibody is one of the myositis specific antibodies, which is associated with a high rate of complication of malignancies. It is also reported that anti-TIF-1γ antibody and complication of malignancies are related to dysphagia. In general, remission of dysphagia occurs with the remissions of dermatomyositis but sometimes it may be prolonged. It should be noted that anti-TIF-1γ antibody positive dermatomyositis, like this case, may cause difficulty in management of patients due to dysphagia.

## P3-023

**A case of dermatomyositis associated with TIF1-gamma antibody positive esophageal cancer that was successfully treated with preoperative chemotherapy and curative resection of the tumor, avoiding long-term oral steroid therapy**

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Conflict of interest: None

[Case] 74 years old male. On X-39, proximal muscle weakness of extremities, fatigue, hoarseness, facial edema, dysphagia, periorbital edematous erythema, and desquamative erythema on the extensor surfaces of the hands appeared. CPK 6494 IU/L, aldolase 6.6 IU/L, myoglobin 439.1 ng/mL, CRP 0.31 mg/dl, blood sediment 25 mm/hour, TIF1-γantibody was positive. Gastrointestinal endoscopy to the anterior wall of the thoracic region and lower esophagus, diagnosed histologically as early-stage thoracic esophageal cancer. On X-4, he started DCF therapy along with steroid pulse therapy, high-dose intravenous immunoglobulin, and rituximab. After this therapy, On X+94, a sub-total esophagectomy was performed, and the patient underwent a successful curative resection. [Abstract] In myositis complicated by malignant tumors, curative resection of the tumor has a favorable effect on the course of myositis, but it is difficult to achieve an ideal therapeutic effect due to the adverse effects of immunosuppressive therapy, deterioration of the general condition caused by muscle weakness, and local and systemic effects of the tumor. In the present case, by avoiding long-term oral steroid therapy, preoperative chemotherapy was introduced at an early stage, and curative resection of the tumor was achieved.

## P3-024

**A case of overlap syndrome of anti-Mi-2 antibody-positive dermatomyositis and systemic lupus erythematosus**

Eri Matsuki[1], Shinya Abe[1], Tomohiro Takehara[1], Takaya Suzuki[1], Takaaki Nawano[1], Masahiro Miyata[1], Soichiro Kon[1], Yukino Yokokawa[1], Sayumi Watanabe[1], Keita Kamei[1], Natsuko Suzuki[2], Kazunobu Ichikawa[1], Masafumi Watanabe[1]

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Conflict of interest: None

[Case] 49-year-old female. [Chief complaint] Myalgia, skin rash. [History] Approximately 1 year ago, she had developed a skin rash on the upper eyelids and forehead. 4 months ago, she had developed skin rash on fingers. 3 months ago, she had developed muscle pain in the extremities and fever. She was referred to our hospital because her CK level was extremely high (2737 U/L). She was admitted to our hospital with suspicion of dermatomyositis (DM). [Course] She had DM-specific skin findings such as heliotrope rash and Gottron's rash, and met the diagnostic criteria for DM. She also tested positive for anti-cardiolipin antibody and was comprehensively diagnosed with systemic lupus erythematosus (SLE), and was diagnosed with overlap syndrome. Myositis-specific autoantibodies were strongly positive for anti-Mi-2 antibody. She was treated on steroids (PSL 1 mg/kg/day), combined with tacrolimus, hydroxychloroquine. One month after starting treatment, she received immunoglobulin therapy. Serum CK level decreased to the 300 U/L. [Discussion] The frequency of overlap of SLE and DM in overlap syndrome is low, and reports in Japan are limited. This case mainly consisted of DM findings, and was treated according to the standard treatment for both diseases, resulting in a favorable course.

## P3-025

**Rescuing a Patient with Anti-Mi-2 Antibody-Positive Dermatomyositis Complicated by Hemophagocytic Syndrome**

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Conflict of interest: None

[Case] A 69-year-old male presented with dermatomyositis (DM)

symptoms, including rash, muscle pain, and weakness. Laboratory results showed elevated creatine kinase at 6911 U/L and positive anti-Mi-2 antibodies (Abs). Muscle biopsy confirmed inflammatory myositis. The patient received a diagnosis of anti-Mi-2 Ab-positive DM and was treated with prednisolone (1 mg/kg) and methotrexate. Unfortunately, there was limited improvement in muscle weakness and fatigue. During treatment, ferritin levels increased, thrombocytopenia and hypofibrinogenemia developed, and a bone marrow aspirate confirmed hemophagocytosis, leading to a hemophagocytic syndrome diagnosis. The patient received methylprednisolone pulses, high-dose intravenous immunoglobulin therapy, and cyclophosphamide pulses. Subsequently, he exhibited significant improvement in muscle strength, resolution of fatigue, and hematological recovery. [Clinical Significance] Reportedly, anti-Mi-2 Ab-positive DM typically responds well to glucocorticoids. However, this case presented a severe complication - hemophagocytic syndrome, which has been previously associated with fatal outcomes. This case implies the importance of early intervention with a combination of therapeutic immunosuppressive agents to save lives of such patients.

## P3-026

**Autopsy case of severe and refractory anti-NXP-2 antibody-positive inflammatory myositis presenting as edematous myositis**

Yuki Terashima, Hiroto Tomoda, Nanae Okimoto, Keisuke Hirobe, Kei Karakida, Sayuri Mizumoto, Issei Takahashi, Tomoko Sano, Tomohiro Kato, Takaaki Ito, Akane Ito, Yoshitaka Ueda, Nanase Honda, Eisuke Takamasu, Kae Onishi, Yuji Miyoshi, Masako Utsunomiya, Yoshiki Nagai, Naoto Yokogawa, Kota Shimada
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Conflict of interest: None

[Case] An 82-year-old female was admitted to the previous doctor due to swelling in both upper limbs, muscle weakness, and elevated CK levels. She had no rash, dysphagia also progressed rapidly, and she was started on prednisolone for polymyositis. She was transferred to our hospital due to a poor response to treatment. Her muscle strength was significantly decreased. CT scans did not show interstitial pneumonia or malignancies. The electromyography suggested myositis. Anti-NXP2 antibody was positive. Muscle biopsy showed variations in muscle fiber diameter, necrotic and regenerating fibers, and microinfarctions. We added tacrolimus and IVIG therapy, but there was no improvement. And she repeatedly experienced aspiration pneumonia. On the 27th day of hospitalization, she died of acute respiratory failure. Autopsy showed findings consistent with myositis, but no MxA was observed. [Discussion] Edema of the limbs is uncommon in idiopathic inflammatory myositis and may be associated with a severe and refractory clinical course. In a previous report, 25% of edematous myositis was anti-NXP2 antibody positive. As seen in our case, anti-NXP-2 antibodies should be tested in severe and refractory edematous myositis.

## P3-027

**A case of gastrostomy for dysphagia associated with anti-NXP-2 antibody-positive dermatomyositis, and improved swallowing function after intermittent administration of IVIg**

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Conflict of interest: None

[Case Presentation] A man in his 60s presented to the emergency department with fever and dysphagia. He hospitalized with a diagnosis of aspiration pneumonia. The pneumonia improved with antimicrobials, but the cause of dysphagia was not identified. He was tubal feeding with nasogastric tube. After admission, Gottron's sign was observed and suspected dermatomyositis. Blood tests were positive for anti-NXP-2 antibodies. The diagnosis of dermatomyositis was made on the basis of skin and muscle symptoms, blood tests and muscle biopsy. He was treated with steroid pulse therapy, oral PSL (60 mg), MZB (150 mg), IVIg (400 mg/kg). 3 weeks later, skin and muscle symptoms and blood tests showed improvement. However, his dysphagia did not improve and he was forced to undergo gastrostomy. After treatment with intermittent IVIg was continued, his dysphagia improved. After the third dose of IVIg, gastrostomy removal was possible. Currently, he still spends without any exacerbation of respiratory symptoms. [Discussion] Gastrostomy for dysphagia associated with dermatomyositis with positive anti-NXP-2 antibodies; we experienced a case in which intermittent administration of IVIg resulted in improvement of swallowing function. The case is reported with a literature review.

## P3-028

**A Case of Anti-Nuclear Matrix Protein (NXP) -2 Antibody-positive Dermatomyositis Successfully Treated with Rituximab**

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Conflict of interest: None

A 31-year-old woman noticed erythema on her eyelids in August 20XX, and experienced muscle pain in her thighs one month after. Based on her worse symptoms, she was referred to dermatologists first. Blood examination revealed elevation of creatine kinase (CK: 3373 IU/L). Interestingly, the auto-antibody specific for NXP-2 was only positive, but others reactive for ARS, MDA-5, Mi-2, and TIF1-γ were negative. As the results, she was diagnosed with dermatomyositis with dysphagia, followed by the treatment with prednisolone 40 mg/day (1 mg/kg/day) together with high dose of intravenous immunoglobulin and cyclosporine. Unfortunately, these immunosuppressive therapies were ineffective for her, therefore she was consulted to our hospital. After hospitalization, she was treated again with both high dose of corticosteroids and intravenous cyclophosphamide; however, her symptoms were not changed. Finally, administration of Rituximab every week (total of 4 times) had dramatically improved her CK value and muscle weakness. So far, severe disease status of dermatomyositis with anti NXP-2 antibody has been reported even though its frequency is rare. Here, we have reported our valuable case who had been successfully treated with Rituximab.

## P3-029

**Nuclear matrix protein 2 antibody-positive dermatomyositis associated with hepatocellular carcinoma**

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Conflict of interest: None

Dermatomyositis (DM) is a systemic, idiopathic, inflammatory myopathy, and multiple autoantibodies associated with it have already been identified. While its exact cause is unknown, DM is frequently associated with malignancies. Reports of dermatomyositis associated with hepatocellular carcinoma (HCC) are rare, and to the best of our knowledge, there are no reports of anti-NXP-2 antibody-positive dermatomyositis associated with HCC. In the present report, he had a large HCC lesion, and surgical treatment and proton beam therapy could not be performed because of the patient's poor liver function. He had weakness in his upper limbs and couldn't open the PET bottle. Some therapeutic response was observed through immunosuppressive therapy, and he was able to be discharged.

## P3-030

**Two cases of NXP-2 antibody-positive polymyositis/dermatomyositis complicated by refractory cutaneous calcinosis**

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Conflict of interest: None

[Case 1] 44-year-old female. In 2018, she developed fever, myalgia in the proximal limbs, muscle weakness, and increased CK. She was diagnosed with polymyositis and started treatment with prednisolone (PSL). The skin calcinosis caused much pain. The patient was transferred to our hospital in 2015 because of the difficulty in her daily life. she is being treated with a JAK inhibitor. [Case 2] A 51-year-old female. Diagnosed with dermatomyositis in 2016 due to skin rash, myalgia, and dysphagia. She was treated with PSL and TAC. She developed calcinosis cutis in 2009. The patient first visited our department in 2010. Subcutaneous induration appeared and was accompanied by pain, so lime was removed twice. In 2010, the skin eruption worsened, and the patient was changed to azathioprine (AZA), which improved the skin eruption. [Conclusions] Cutaneous calcinosis is observed in less than 20% of cases of dermatomyositis, and is an intractable pathological condition that accompanies young-onset dermatomyositis. Among myositis-related specific antibodies, many cases are positive for anti-NXP-2 antibodies. The two cases of polymyositis and dermatomyositis that we experienced were complicated by cutaneous calcinosis, making treatment difficult. Let us consider these cases.

## P3-031

**Successful treatment with IVIg for anti-NXP2 antibody-positive dermatomiositis. A case rerort**

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Conflict of interest: None

[Background] Currently, disease-related antibodies can be comprehensively detected using an indirect immunofluorescence antibody assay in dermatomyositis. We present a case of dermatomyositis with anti-NXP2 antibody positivity who responded well to intravenous immunoglobulin therapy (IVIg). [Case] A 30-year-old female suffered muscle pain in both upper and lower limbs starting the previous month. Due to elevated CK levels, she was referred to our hospital. She presented heliotrope rash, muscle tenderness and weakness, and markedly elevated CK levels at 4550 U/l. Muscle electromyography showed myogenic changes, and contrast-enhanced MRI revealed myositis. Autoantibodies were all negative, and muscle biopsy did not show inflammatory cell infiltration or degenerative necrosis. She started to treat with prednisolone (PSL) 50 mg (1 mg/kg) and tacrolimus (TAC). When the steroids were tapered, her symptoms got worse. Comprehensive antibody testing using A-Cube® revealed positive anti-NXP2 antibodies. IVIg was performed, which resulted in normalization of CK levels and improvement in muscle strength. [Clinical Significance] In this case, the diagnosis of dermatomyositis became more certain using A-Cube®.

## P3-032

**A patient with immune-mediated necrotizing myopathy refractory to triple therapy with PSL, TAC, and MMF and positive for antiMDA5, anti-Ro-52, and anti-SRP antibodies was treated with rituximab**

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Conflict of interest: None

A male patient aged 48 came to our hospital on May 11, with redness of the left eyelid, discomfort in knees and ankles, and painful skin rash on both hands. The dermatologist suspected the skin rash to be Sweet's disease and conducted a skin biopsy. On 16, he began taking PSL 30 mg. The CT scan revealed infiltrates in both lungs, and the biopsy results suggested DM as there were no findings of neutrophilic infiltration. The high anti-MDA5 antibody level led to a diagnosis of DM. On 26, MMF 1500 mg and TAC were added to the treatment. However, myalgia developed and CK level increased, despite an increase in dosage to 60 mg of PSL and 3000 mg of MMF. He experienced an improvement in skin rash, arthritis, and IP, but CK didn't improve. He was also found to be positive for anti-SRP antibodies, which led to a diagnosis of immune-mediated necrotizing myopathy (IMNM). He was prescribed RTX, resulting in his CK to the normal range. Discussion: In regards to IIM, antibodies play a vital role in determining diagnosis, prognosis, and treatment options. Our report focuses on a patient who tested positive for three antibodies: MDA5, Ro-52, and SRP. Although IP was in remission with a combination of PSL, MMF, and TAC, IMNM was unresponsive to treatment until remission was achieved with RTX.

## P3-033

**The case series study of anti-SRP antibody myopathy patients**

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Conflict of interest: None

[Objective] The aim of this study is to evaluate the clinical characteristics of patients with anti-signal recognition particle antibody (SRP)-myopathy. [Methods] Eight cases were diagnosed as SRP-myopathy in our department from April 2012 to September 2023. Based on medical records, the physical findings and laboratory findings were collected. [Results] Seven patients were female. The median age was 57 years old at the onset of SRP-myopathy. All patients showed proximal muscle weakness, especially neck muscle, and severely elevated the levels of creatine phosphokinase (CPK). Two patients showed dysphagia and four patients showed interstitial lung disease. Four patients had anti-Ro-52 antibody and one patient had anti-PM-Scl70 antibody, besides SRP antibody. Prednisolone was used in all patients as initial treatment. Three and two patients were administered tacrolimus and azathioprine, respectively. Intravenous high-dose immunoglobulin therapy was used in two patients who showed treatment-resistant for immunosuppressive (IS) therapies. Patients with high CPK values at diagnosis tended to be continue muscle weakness even though CPK values improved. [Conclusions] In this case-series, patients with high CPK values at diagnosis may be resistant to IS treatments.

## P3-034

**A case of anti-HMGCR antibody-positive immune-mediated necrotizing myopathy, successfully treated with high-dose intravenous immunoglobulin**

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Conflict of interest: None

**Case**: A 66-year-old man visited to orthopedic surgeon because of weakness of proximal muscles with no findings of spinal canal stenosis. And then he was introduced to neurology, pointed out prominent muscle weakness, atrophy in the proximal muscles of the extremities and a high CK level of 5717 U/L. And finally introduced to our department. MRI showed high intensity of T2-weighted images in the shoulder, iliopsoas, dorsal, buttocks and thighs muscles. A muscle biopsy was performed on the right deltoid muscle, showing consistent with necrotizing myositis. Anti-HMGCR antibody was also positive, indicating immune-mediated necrotizing myositis. After steroid pulse therapy and post prednisolone treatment with tacrolimus, Levels of CK and aldolase were improved, but muscle strength was weak without walking. After two courses of high-dose intravenous immunoglobulin (IVIG) infusion at dose of 400 mg/kg for 5 days, his muscle strength increased and he was able to walk. **Discussion**: We have experienced a case of muscle weakness due to immune-maediated necrotizing myopathy, successfully treated with IVIG therapy. Significant recovery of muscle strength in patients with necrotizing myopathy treated with IVIG in addition to standard steroid and immunosuppressant therapy was observed.

## P3-035

**A case of anti-SAE antibody-positive dermatomyositis with marked response to high-dose immunoglobulin therapy for dysphagia and dysarthria that appeared after initiation of steroid therapy**

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Conflict of interest: None

A 70-year-old man noticed redness on the dorsum of both hands and eyelids. He also developed dyspnea and visited his local doctor. He was diagnosed with bacterial pneumonia and was given antibiotics. His condition did not improve, and he was referred to our Respiratory Department. He was suspected to have an autoimmune disease and referred to our department. His myositis symptoms were mild. His skin symptoms and skin biopsy results suggested dermatomyositis. CT showed interstitial pneumonia, but his oxygenation was good. Although the diagnostic criteria for dermatomyositis were met, typical myositis-specific autoantibodies (MSAs) were negative. Treatment was started with prednisolone 1 mg/kg/day, and skin symptoms improved, but dysphagia and dysarthria progressed rapidly. Despite steroid pulse therapy was administered, the dysphagia continued to worsen. Later, he was found to be positive for anti-SAE antibodies and he was treated with high-dose immunoglobulin therapy. His swallowing function improved markedly, and he was discharged home. Each MSA has a characteristic clinical presentation, which is useful in determining the diagnosis and treatment strategy. The present case is positive for the rare anti-SAE antibodies and is reported here with some discussion of the literature.

## P3-036

**Two cases of anti-Ku antibody-positive polymyositis complicated by myocarditis**

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Conflict of interest: None

Case 1: An 81-year-old woman was referred to our hospital because of persistently elevated levels of creatine kinase (hyperCKemia) 18 months ago. She was asymptomatic under observation, and was examined closely due to elevating CK and positive cardiac enzymes, which showed CK 2110 U/L, troponin T (TnT) 0.404 ng/mg, and anti-Ku antibody 3+. UCG and ECG had no abnormalities. Chest CT showed mild reticular shadows. Thigh MRI showed myositis and EMG showed myogenic changes. Myocardial and rectus femoris biopsy revealed inflammatory cell infiltrate. She was diagnosed with polymyositis (PM) complicated by myocarditis and interstitial pneumonia. Case 2: A 36-year-old woman was referred to our hospital because she had hyperCKemia at the time of delivery 1 month ago. She was asymptomatic and under observation, and was examined closely due to palpitations, which showed CK 3159 U/L, TnT qualitative +, anti-Ku antibody +. UCG had mild hypokinesia. Thigh MRI showed myositis, and EMG showed myogenic changes. Myocardial and rectus femoris biopsy revealed inflammatory cell infiltrate. She was diagnosed with PM complicated by myocarditis. Discussion: The characteristics of myocarditis in anti-Ku antibody-positive PM has not been clarified. We report the cases with some literature review.

## P3-037

**A case of anti-Ku antibody-positive polymyositis complicated by myocarditis**

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Conflict of interest: None

[Case] A 73-year-old woman presented with dyspnea. Blood tests showed elevated myocardial deviation enzymes. She was admitted to our hospital with suspected ischemic heart disease. Coronary angiography revealed no stenosis, and she was followed up with a diagnosis of myocardial damage of unknown cause. After discharge, her dyspnea slowly worsened. Blood tests revealed further elevations in creatine kinase (CK) and myocardial desensitization enzymes. Suspecting idiopathic inflammatory muscle disease, the patient was referred to our department. Thigh MRI showed high intensity areas on STIR mainly in the semimembranosus muscle. Muscle biopsy from the left semimembranosus muscle revealed an inflammatory cell infiltrate in the intramuscular sheath. Blood tests on admission revealed positive anti-Ku antibodies. Cardiac contrast-enhanced MRI showed myocardial edema and delayed contrast at the same site. We diagnosed anti-Ku antibody-positive polymyositis complicated by myocarditis. We started treatment with glucocorticoids, mycophenolate mofetil and intravenous immunoglobulin. After the treatment, her dyspnea and CK levels improved. Although several cases of anti-Ku antibody-positive idiopathic inflammatory myopathy have been reported, this is a rare case of myocarditis.

## P3-038

**A case of anti-Ku antibody-positive polymyositis with immune-mediated necrotizing myopathy (IMNM)-like findings on muscle biopsy pathology**

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Division of Immunology&Rheumatology Department of Internal Medicine, Sumitomo Hospital, Osaka, Japan

Conflict of interest: None

[Case] A 55-year-old woman had bilateral hearing loss and involuntary movements for 5 years and dysarthria for 4 years. She was referred to our department because of muscle weakness and skin hardening. Myogenic enzymes were found to be elevated, with CK 1935 U/L and aldolase 54.2 U/L, as well as muscle weakness. Electromyography showed myogenic changes, and anti-Ku antibodies were positive. A diagnosis of anti-Ku antibody-positive polymyositis was made. PSL 20 mg/day was started, and myogenic enzymes decreased rapidly thereafter. On the other hand, a muscle biopsy showed findings of immune-mediated necrotizing myopathy (IMNM). However, both anti-SRP and anti-HMGCR antibodies were negative, and the clinical course was not typical for IMNM. [Discussion] The anti-Ku antibody is known as an autoantibody related to overlap syndrome, along with anti-U1-RNP and anti-PM/Scl antibodies. IMNM-like findings on muscle biopsy in this case was incompatible with the clinical course; IMNM-like findings with overlap syndrome-related autoantibodies are atypical and have not been reported with anti-Ku antibodies in particular, compared to other antibodies. Here we report a case of anti-Ku antibody-positive myositis with IMNM-like histological findings, including a review of the literature.

## P3-039

**Anti-mitochondrial M2 antibody-positive myositis complicated by CO2 narcosis and successfully treated with rituximab**

Kenta Horie[1], Jun Ishizaki[1], Erika Horimoto[1], Daisuke Hiraoka[1], Hitoshi Yamasaki[2], Takuya Matsumoto[1], Koichiro Suemori[1], Katsuto Takenaka[1]
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Conflict of interest: None

[Case] A 69-year-old man with a history of multiple myeloma, which had achieved remission through chemotherapy, presented with dysphagia, dyspnea, and elevated levels of CK. While myositis-specific autoantibodies were all negative, anti-mitochondrial M2 antibody (AMA-M2) was positive. He was diagnosed with AMA-M2 positive myositis and moderate-dose prednisolone (PSL) was initiated. However, elevated CK levels persisted, leading to hospitalization for therapeutic escalation. After admission, PSL was increased to high-dose (1 mg/kg/day), and intravenous immunoglobulin (IVIG) was also started. Nevertheless, he developed CO2 narcosis and required non-invasive positive pressure ventilation one week

after admission. Therefore, rituximab (RTX) was added. Thereafter, his symptoms improved and CK levels decreased. PSL was tapered down to 15 mg without relapse, and he was transferred to the rehabilitation hospital on the 65th day of hospitalization. [Discussion] AMA-M2 positive myositis may present not only with muscle symptoms but also with cardiac and respiratory muscle complications. Although remission was not achieved with glucocorticoids and IVIG, the addition of RTX might be effective.

## P3-040

**A case of inflammatory myopathy associated with anti-mitochondrial antibody (AMA) complicating dysphagia and cardiomyopathy**

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Conflict of interest: None

[History of Present Illness] The patient is a healthy 59-year-old man. He had lost weight by 10 kilograms over a year. Seven months prior, he began to experience progressive muscle weakness in the legs. He contracted coronavirus 2019 two months ago, which marked the onset of dysphagia. Due to elevated creatine kinase levels, neuromuscular disease was suspected. Blood tests and whole trunk computed tomography revealed hypoalbuminemia, elevated liver and biliary enzymes, and lymphadenopathy. These findings led to the suspicion of AMA-positive myopathy coexisting with Primary Biliary Cirrhosis (PBC) and Sjögren's Syndrome. The diagnosis was confirmed based on positive serum antibodies. He also had dysphagia, arrhythmia, and abnormalities in cardiac wall motion. Prompt treatment with steroids was initiated. [Discussion] AMA-positive myopathy often presents with a chronic disease course, muscle atrophy, and cardiopulmonary involvement, which is distinguishable from other idiopathic inflammatory myopathies. AMA-positive myopathy can lead to organ impairments that have a significant impact on the patient's prognosis; however, its treatment is yet to be well-established. Through this case, we can gain insights into the management of AMA-positive myopathy with severe organ involvement.

## P3-041

**Successful treatment with combination of metronidazole, elemental diet, and digestive enzyme formula for frequently recurrent pneumatosis cytoides intestinalis (PCI) complicated with clinically amyopathic dermatomyositis (CADM)**

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Conflict of interest: None

A 62-year-old woman was referred to our hospital because of Gottron's sign and interstitial pneumonia (IP) on chest CT in September X. As MDA5 antibody was positive and skin biopsy showed inflammatory cell infiltration without muscle enzyme elevation, a diagnosis of CADM was made. She began having respiratory distress by worsening of IP, PSL 55 mg, IVCY and TAC were started in November X. Thereafter, decrement of ferritin and MDA5 antibody titer was noted and IP was improved and never flared up. However, PCI occurred repeatedly 6 times. After administration of cefmetazole, she felt better and no relapse occurred until January X+2, when she had abdominal distension with free air on abdominal CT while taking PSL 7 mg. In addition to fasting and oxygen administration, combination therapy with metronidazole, elemental diet, and a digestive enzyme formula were started. The patient quickly recovered and two years have passed since then, neither IP nor PCI have recurred. Clinical Significance: Repeated relapses of PCI under low disease activity with low dose steroid are rare and intractable. The combination therapy was very effective and might be useful for such patients. The effectiveness of regimens containing antibacterial agents implies that intestinal bacteria play a role in PCI.

## P3-042

**Clinical characteristics of pneumatosis cystoides intestinalis in patients with dermatomyositis**

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Conflict of interest: None

[Objective] Pneumatosis cystoides intestinalis (PCI) is a rare disease characterized by presence of multilocular cysts in the gastrointestinal wall. In this study, we investigated the clinical characteristics of PCI in patients with dermatomyositis (DM). [Methods] We retrospectively investigated the clinical records of 75 patients with DM diagnosed in our department from April 2015 to September 2023, to determine the presence of PCI, clinical features and treatment. [Results] Five patients (2 males and 3 females) had PCI. The mean age at DM diagnosis was 62.2±8.4 years. Anti-MDA5 antibodies were positive in 3 cases, and anti-EJ antibody in one case. Interstitial pneumonia was complicated in 5 cases and mediastinal emphysema in one case. Symptoms at PCI diagnosis were constipation in 2 cases and asymptomatic in 3 cases. The duration from DM onset to PCI was 822.2±686.4 days, and PSL at PCI diagnosis was 16.0±8.1 mg/day. All patients were improved on imaging by fasting. [Conclusions] We thought PCI is not a rare complication of DM including asymptomatic cases. Most patients improve with conservative treatment, but some reports showed patients with serious outcomes. Therefore, long-term and careful follow-up is required.

## P3-043

**A Case of Scurvy Presenting with Suspected Pediatric Rheumatic Diseases**

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Conflict of interest: None

[Introduction] Scurvy, a result of vitamin C deficiency, often leads to delayed diagnoses due to its rarity in developed countries and diverse clinical symptoms, necessitating unnecessary invasive tests. [Case Report] A 10-year-old girl presented with year-long lower limb pain, recent low-grade fever, 10% weight loss. Severe anemia, elevated IgG levels, and increased antinuclear antibodies raised suspicion of pediatric rheumatic diseases. Examination revealed bleeding gums and lower limb petechiae but no joint swelling. Prolonged selective eating primarily white rice, natto, tofu resulted in very low vitamin C level, confirming scurvy. Invasive tests were avoided due to child's developmental diversity. Treatment with intravenous and subcutaneous vitamin C and iron rapidly improved symptoms, enabling walking within six days. A month post-discharge, no recurrent symptoms were observed, and blood vitamin C levels normalized. The patient remained antinuclear antibody positive with persistently elevated IgG levels. [Clinical Significance] Meticulous clinical examination and detailed patient history are essential for prompt diagnosis and treatment of scurvy, reducing unnecessary tests. This case highlights the unique presence of antinuclear antibody positivity and elevated IgG levels.

## P3-044

**A case of mixed histiocytosis difficult to diagnose and treat, presenting IgG4-related disease-like lesion distribution**

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Conflict of interest: None

[Case] A 71-year-old man had skin rash on his trunk for seven years. Two months before, he was aware of both leg edema. On day X, he was

referred to our hospital. Eyelid xanthomas, and small brown spots on the trunk were observed. IgG4 37 mg/dL. CT scan showed bilateral intra-orbit lesions, pericardial effusion, wall thickening of ascending aorta, pancreatic enlargement, and soft-tissue shadow around bilateral kidneys. Bone scintigraphy showed abnormal accumulation at the distal end of long bones. Histopathologically, small brown spots on his trunk showed proliferation of CD1a and CD207 (Langerin)-positive, CD163-negative cells, suggesting Langerhans cell histiocytosis (LCH). On the other hand, eyelid xanthoma and bone lesions showed CD163-positive, CD1a- and CD207 (Langerin)-negative cells, consistent with Erdheim-Chester disease (ECD). BRAF V600E mutations were detected in all the specimens, and diagnosis of mixed histiocytosis was made. He received chemotherapy with vinblastine, but the disease progressed, and he died on day X+65. [Discussion] ECD is a type of non-Langerhans cell histiocytosis, and BRAF V600E mutation is frequent in patients with ECD and LCH. ECD is similar to IgG4-related disease in lesion distribution, and should be kept in mind as differential diagnosis.

## P3-045

**Two cases of angioimmunoblastic T-cell lymphoma (AITL) requiring differentiation from systemic lupus erythematosus (SLE)**

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Conflict of interest: None

Case 1 A 77-year-old woman was diagnosed with AITL in August X-12. The patient went into remission after chemotherapy. In September X-1, enlargement of the lymph nodes in the cervical region was detected, but a biopsy didn't showed lymphoma. SLE was suspected with stomatitis, lymphopenia, anti-dsDNA antibody positivity and antinuclear antibody positivity. The patient treated with hydroxychloroquine. Enlargement of a groin lymph node was detected in January X and was diagnosed with AITL after a biopsy. The patient received chemotherapy for AITL, but became refractory and died in August X+1. Case 2 A 76-year-old man with erythema and fever was referred to our hospital in March X. SLE was suspected with stomatitis, kidney damage, thrombocytopenia, and antiphospholipid antibody positivity. His condition temporarily improved with the introduction of steroids, then quickly worsened. The patient was diagnosed with AITL based on an axillary lymph node biopsy. Remisson was achieved after the administration of chemotherapy for AITL. Conclusion AITL is often accompanied by autoimmune abnormalities, such as the appearance of autoantibodies. Therefore, it may sometimes be necessary to differentiate it from an autoimmune disease. Lymph node biopsies should be actively performed.

## P3-046

**A case of childbirth-like pain after receiving the COVID-19 vaccine**

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Conflict of interest: None

Female in her 60s. Current medical history: she received the corona vaccine on June 22, From June 29th, the patient developed a general feeling of malaise and a strong feeling of heaviness in both lower legs. On July 2, she started having frequent twitching in her back. Her family members were worried and visited the emergency department. She was able to have a conversation, but the chronology of her symptoms was vague. There were no abnormalities in cervicothoracic spine MRI, lumbar spine MRI, nerve conduction test, and cerebrospinal fluid test. ANAx40 nuclear membrane type were positive. Cortisol was 18.9 and ferritin was 73, which were slightly high. After that, she started complaining that her whole lower back hurt, like when she was giving birth. Acetaminophen and pregabalin had some effect but the low-grade fever persisted. Based on the clinical course, it was diagnosed as a side effect of the coronavirus vaccine, and administration of dexamethasone 6 mg/day was started on the 6th day of illness, and her symptoms improved dramatically. Conclusion: We experienced a case in which fatigue, twitching, and slight fever appeared one week after receiving the coronavirus vaccine, followed by pain. We discuss the possibility of vaccine-related intracerebral inflammation.

## P3-047

**Multiple Cerebral Infarctions in a 25-Year-Old Ulcerative Colitis Patient: A Case of Löffler Endocarditis due to Idiopathic Hypereosinophilic Syndrome**

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Conflict of interest: None

[Case Summary] A 25-year-old female with ulcerative colitis well-controlled using vedolizumab and mesalazine sought medical attention due to dizziness. As an MRI showed multiple cerebral infarctions, she was referred to our neurosurgery department. Concerns of a cardiac issue led to a cardiology consultation, revealing thickening of the left ventricular posterior wall (LVPW) and mitral regurgitation on echocardiography. Considering the elevated eosinophil count, suspicions regarding the association of eosinophilia with her condition arose. After ruling out other causes, idiopathic hypereosinophilic syndrome was determined through genetic testing and bone marrow examination. The echocardiographic thickening of the LVPW confirmed Löffler endocarditis. Treatment commenced with anticoagulants and prednisolone (PSL), which significantly reduced eosinophil counts but subsequently flared during PSL tapering. This led to the introduction of mepolizumab therapy, allowing PSL discontinuation and gradual improvement in the LVPW thickening. [Clinical Significance] This case underscores the importance of accurate differential diagnosis in eosinophilia cases, particularly when addressing cardiac complications.

## P3-048

**Postoperative clinical results in TKA for RA valgus knee at our hospital**

Keiichiro Yamamoto
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Conflict of interest: None

[Objective] To compare the postoperative clinical outcomes of TKA performed on RA valgus knee at our hospital with TKA for the RA varus knee. [Methods] 67 patients on primary TKA for RA knees between February 2010 and December 2020, were follow-up for at least 2 years after surgery, and had confirmed ROM, KOOS, KSS, and FJS-12. The FTA measured in the preoperative standing Xp was defined as 170° or less for the valgus knee group and 171°or more for the normal alignment or varus knee (the varus knee group), and postoperative clinical outcomes were compared. [Results] The mean age at surgery was 67.6 years. The valgus knee were 16 knees and varus knees were 51 knees. The mean preoperative FTA of the valgus knee was 166.2°, the varus knee was 182.1°, and the mean postoperative FTA of the valgus knee was 177.1°, the varus knee was 175.7°. The only Knee Functional score was significantly lower than varus knees in the valgus knees (P=0.001). [Discussion] Clinical outcome of TKA in valgus knee are often reported to be lower than the valgus knee because of the difficulty in soft tissue balance. Similarly, Knee Functional Score was significantly lower in the varus knee in this study. [Conclusions] The Knee Functional score was significantly lower for valgus knees than the varus knees.

## P3-049

**Clinical results of navigated cruciate-substitute total knee arthroplasty for the patients with rheumatoid arthritis**

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Department of Orthopedic Surgery, Komaki City Hospital, Japan

Conflict of interest: None

[Objective] The purpose of this study was to investigate the clinical results of navigated cruciate-substitute (CS) total knee arthroplasty (TKA) for the patients with RA. [Methods] Ten knees (1 male, 9 female, mean age 58.8 years, mean disease duration 9.7 years) who underwent navigated CS TKA for RA at our institution were included in the study. PSL in 5 cases,

MTX in 6 cases, and biologics or JAK inhibitors in 4 cases were used to control RA disease activity. Preoperative disease activity averaged 3.2 for DAS28-CRP in the 6 patients for whom data were available. The mean preoperative ROM (extension/flexion) was -4/132°, FTA averaged 181°, and MRI showed residual PCL in all patients. Triathlon CS (Stryker) were used for all patients and the patella was replaced in all cases. Clinical outcomes, complications, and revision rate at the last follow-up were investigated. [Results] At a mean follow-up of 3.6 years, knee ROM (extension/flexion) was average -1/130°, JOA score was average 87.5. Complications included intraoperative tibial fracture in one case, but there was no infection, no revision cases. [Conclusions] The short-term results were relatively good. CS TKA for the patients with RA could be an option with an appropriate indication.

## P3-050

**Over 7-year Postoperative Results of Cementless Total Knee Arthroplasty in Rheumatoid Arthritis**

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Department of Orthopedic Surgery, Nagano Matsushiro General Hospital, Nagano, Japan

Conflict of interest: None

[Objective] We performed cementless TKA for RA in our department, and investigated the mid- to long-term clinical results after surgery for more than 7 years. [Methods] TKA for RA was performed in our department from January 2008 to December 2012 on 35 patients and 51 knees, of which 17 patients and 22 knees could be followed up for more than 7 years. There were 16 women and 1 man, and the average age at the time of surgery was 68.3±13.6 years old (31-80 years old). The average follow-up period was 8.8 ± 2.0 years (7 to 14 years), and the TKA models were Stryker's NRG® in 20 knees, Zimmer's NexGen® in 2 knees, and cementless CR type TKA in all knees. clinical evaluation were changes in joint range of motion (ROM) before and after surgery, loosening of the implant on X-rays, and presence or absence of complications. [Results] Good ROM was maintained postoperatively. There were no cases in which implant loosening was observed on X-rays, and there were no complications such as infection or revision, but fractures around the implants due to trauma were observed in two knees. [Conclusions] In this study, good mid- to long-term results were obtained even with cementless TKA.

## P3-051

**Analysis of Long-term clinical outcomes in Cemented Posterior Stabilized Total Knee Arthroplasty for patients with Rheumatoid Arthritis by comparing patellar resurfacing and patellar nonresurfacing**

Mitsuhiro Hariu[1], Yuta Imamura[1], Rintaro Nakanishi[1], Ryosuke Momma[1], Yasushi Naganuma[1], Kiyoshi Iwazaki[1], Michiaki Takagi[2]
[1]Department of Orthopaedic Surgery, Nihonkai General Hospital, [2]Department of Orthopaedic Surgery, Faculty of Medicine, Yamagata University

Conflict of interest: None

[Objective] To investigate long-term clinical outcomes in cemented PS- TKA by comparing patellar resurfacing (PR) and patellar nonresurfacing (PNR) for patients with RA. [Methods] We investigated 40knees of a follow-up of more than 10 years among patients with RA who have undergone a cemented PS- TKA at our hospital. They were divided to two groups (PR: 12 cases 16 knees, PNR: 21 cases 24 knees) and were examined clinical outcomes, radiological evaluation, complication and revision surgery. [Results] Cemented PS-TKA showed statistically significant improvement of ROM and JOA score in both groups compared to those before surgery. While no significant difference was found in the rate of AKP and cane-free walking between the two groups. Narrowing of PFJ space was seen 79.2% in PNR and the radiolucent line detected was 50% in PR and 25% in PNR radiologically. There was no revision TKA in the two groups. [Conclusions] Although narrowing of PFJ space was found in about 80% of patients in PNR, they had no AKP. A significant difference was also found in clinical results compared with those preoperatively in the two groups. These results suggested to keep better clinical outcomes longitudinally in cemented PS TKA for patients with RA in spite of patellar resurfacing or patellar nonresurfacing.

## P3-052

**The evaluation of cementless total knee arthroplasty using patient-based score in patients with rheumatoid arthritis**

Rie Kodama, Yoshio Uchida, Yusuke Sugimori, Kenichi Shimane, Takuji Nishikawa
Department of Rheumatology, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan

Conflict of interest: None

[Objective] The purpose of this study was to evaluate the usefulness of cementless total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA) using patient-based scores. [Methods] 15 knees of 14 RA patients who underwent TKA from September 2021 to February 2023 were included in this study. The cementless TKA group (L group) included 7 knees and the cement TKA group (C group) included 8 knees. Preoperative and at 6 months postoperative clinical evaluations and X-ray were assessed. For patients-based clinical evaluations, the Knee Society Score (KSS) and KOOS were collected. [Results] The mean age of the patients was 68.9 years old, and 5 patients were males. Preoperative FTA was 176.6° in L group and 175° in C group ($p=0.78$). The mean range of motion in the knee joint improved 115° to 107.9° in L group, and 99.6° to 111.8° in C group ($p=0.13$). As for KSS scores, symptom, patient satisfaction and functional activity score were significantly improved in both groups ($p<0.05$). There were no significant differences in postoperative KSS or KOOS between the two groups. [Conclusions] This study demonstrated good short-term results of cementless TKA in patients with RA. Although long-term follow-up is required, cementless TKA can be an effective method for treating RA patients.

## P3-053

**Improvement of Disease Activity in Rheumatoid Arthritis through Total Knee Arthroplasty**

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Department of Orthopaedic Surgery, Saitama Medical University, Saitama, Japan

Conflict of interest: None

[Objective] This study aimed to assess the impact of total knee arthroplasty (TKA) on disease activity in rheumatoid arthritis (RA) patients at our institution. [Methods] From Oct 2021 to Mar 2023, 24 RA patients underwent primary TKA. Fourteen patients (15 knees) with continuous RA management and no non-RA-related hospitalizations were included. Synovectomy was performed when possible. Disease activity, measured using DAS28-CRP, was compared preoperatively and six months postoperatively with paired t-tests ($\alpha=0.05$). [Results] The study included 6 males and 9 females (10 knees) with an average age of 69.5±8.0 years. Preoperative DAS28 was 3.27±0.83. Postoperatively, DAS28 significantly decreased to 2.02±0.51 ($p<0.0001$). Post-TKA, 11 patients achieved remission, 2 had low disease activity, and 2 had moderate disease activity. CRP levels decreased from preoperative 1.05±1.67 mg/dL to postoperative 0.43±0.49 mg/dL ($p=0.056$). In patients with moderate or higher preoperative disease activity, DAS28 significantly decreased from 3.53±0.70 to 2.09±0.54 ($p<0.0001$), and CRP levels decreased from 1.28±1.80 mg/dL to 0.46±0.54 mg/dL ($p=0.045$). [Conclusions] TKA in RA patients significantly reduces disease activity, indicating its effectiveness in improving patients' conditions 6 months post-surgery.

## P3-054

**Short term results of the Asian specific knee prosthesis**

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Conflict of interest: Yes

(Background) In this study, we have reported a short term results of the Asian specific knee prosthesis. (Patients and Methods) Thirteen knees

were assessed in this study. Nine patients were osteoarthritis and three patients were rheumatoid arthritis. Mean age was 72.6 years old. We operated these patients using the Asian specific knee prosthesis, Future Knee based on Asian knee morphology developed by Teijin Nakashima. We evaluated pre and postoperative range of motion, FTA, and the in vivo kinematics of two knees assessed by fluoroscopic analysis. (Results) Mean preoperative minimum flexion angle was 18.1 degree and maximum flexion angle was 108.5 degree. Postoperative minimum flexion was 3.8 degree and maximum flexion was 111.5 degree. Mean preoperative FTA was 187.5 and postoperative FTA was 175.3. All patients improved range of motion and FTA postoperatively. In vivo kinematics of the femoral component relative to the tibial component gradually rotated externally during deep knee flexion in evaluated two knees. (Discussion) Short term results of the Asian specific knee prosthesis, Future Knee were good.

## P3-055

**Incidence of Venous Thromboembolism after Total Knee Arthroplasty in Patients with Rheumatoid Arthritis and Osteoarthritis: A Propensity Score Matching Analysis**

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Conflict of interest: None

[Objective] To compare the incidence of venous thromboembolism (VTE) after total knee arthroplasty (TKA) between patients with rheumatoid arthritis (RA) and those with osteoarthritis (OA). [Methods] The subjects comprised 104 knees with RA and 810 knees with OA. Doppler ultrasonography was routinely performed preoperatively and on postoperative day 2, 14 for diagnosis a deep vein thrombosis (DVT). A propensity score was determined for each patient based on the following criteria: age, sex, body mass index, anesthesia, surgical time, blood transfusion, anticoagulant use, nonsteroidal anti-inflammatory drugs (NSAIDs) use, VTE history, cancer, hypertension, diabetes, hyperlipidemia, smoking status. Primary outcome was the incidence of DVT after TKA. [Results] A total of 97 matched pairs were included in the study. The incidence of DVT was 19.6% in the RA group and 40.2% in the OA group, indicating a much lower incidence of postoperative DVT in RA group [OR 0.36, 95%CI 0.19-0.69]. The incidence of proximal DVT was 2.1% in the RA group and 0% in the OA group, showing no significant difference. Symptomatic pulmonary embolism (PE) was not found in all patients. [Conclusions] The incidence of DVT after TKA was significantly lower in RA than in OA patients.

## P3-056

**The Relationship Between Biologic Agents and JAK Inhibitors Usage and D-Dimer Levels in Rheumatoid Arthritis Patients After Total Knee Arthroplasty**

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Conflict of interest: None

[Objective] This study aims to investigate the association between the use of b/ts DMARDs in RA patients who have undergone TKA and the levels of D-dimer, as well as the incidence of VTE. [Methods] We retrospectively investigated the medical record of 55 TKA (48 cases) with RA between 2017 and 2022. The study involved an investigation of D-dimer and CRP levels, preoperative DAS28-CRP scores, and the occurrence of postoperative VTE. Comparative analyses were performed between the b/ts DMARDs user group (Group B) and the non-user group (Group N). [Results] Significant differences were observed in preoperative DAS28-CRP values (Group B: 2.8±1.0 vs. Group N: 3.5±0.9). Nevertheless, there were no significant differences between the two groups in preoperative and postoperative CRP levels, as well as preoperative and postoperative D-dimer levels. The incidence of VTE was 37% in Group B and 21% in Group N, without any statistically significant difference. A weak positive correlation was detected between CRP and D-dimer only in the preoperative Group N ($r=0.45$, $p=0.04$). [Conclusions] There is no correlation between CRP and D-dimer in the patients using b/ts DMARDs. In addition, there was no significant difference in the incidence of VTE between patients with and without b/ts DMARDs.

## P3-057

**A case of pseudoaneurysm occurring after TKA for rheumatic severe flexion contracture knee**

Tetsuya Tamaru[1], Masanari Ota[2], Kazuhiro Kai[1], Atsushi Kimura[1], Masamitsu Hara[1], Hirofumi Bekki[1], Koji Sakuraba[1], Junichi Fukushi[1]
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Conflict of interest: None

[Purpose] We reported a case of one-stage total knee arthroplasty (TKA) for a severely contracted knee due to rheumatoid arthritis (RA), and a pseudoaneurysm occurred more than 2 months after TKA. [Case] A 59-year-old woman was diagnosed with RA 10 years ago and started taking MTX, but she developed liver and kidney damage and defaulted clinic appointments. She was in Steinbrocker Stage IV Class IV, DAS28-ESR 5.36 at her first visit. The ROM of both her knee joints was -50° to 95°. We underwent closed mobilization, additional osteotomies in the femur and tibia, and a posterior joint capsule resection. We used a stemmed implant, and her postoperative ROM improved to 0-130°. Left TKA was performed 3 months after right TKA. She had elevated D-dimer levels 1 week postoperatively. We investigated and found a pseudoaneurysm of her right popliteal artery. She underwent right popliteal artery-posterior tibial artery bypass surgery by vascular surgeons. According to herself, she developed a strain-like symptom in her right lower leg during rehabilitation around 2 months after surgery, and since then she has been aware of a pulsatile mass. [Conclusion] TKA for RA severe flexion contracture knees is challenging, and complications including vascular damage must also be considered.

## P3-058

**Two-staged total knee arthroplasty for monoarthritic knee with sever contraction that required differentiation from pyogenic arthritis**

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Conflict of interest: None

We report a case of two-staged total knee arthroplasty for monoarthritic knee with sever contraction that required differentiation from pyogenic arthritis. [Case] A 56-year-old man had left knee pain for 2 years. Radiographs showed that the femorotibial and the patellofemoral joint spaces had disappeared, and the joint surfaces appeared to be destroyed. Inflammatory response was elevated, although anti-CCP antibodies were negative. Arthroscopic biopsy was performed. All tissue culture was negative, and pathological examination revealed synovial invasion into the bone tissue. After rheumatoid arthritis was diagnosed, TKA with osteotomy of the tibial tuberosity was performed. One year after the surgery, the gait is stable, and the range of motion has improved. [discission] Chronic monoarthritis with increased inflammatory response should be differentiated from rheumatoid arthritis and infectious arthritis caused by Mycobacterium tuberculosis or non-tuberculous Mycobacterium tuberculosis. In this case, pyogenic arthritis could not be ruled out based on local and imaging findings. Arthroscopic biopsy was considered necessary prior to TKA. We believe it is important to perform two-staged TKA for atypical arthritis.

## P3-059

**Unicompartmental knee arthroplasty (UKA) for rheumaoid arthritis: Report of 3 cases**

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Conflict of interest: None

[Objective] In general, UKA is not indicated for inflammatrory diseases such as rheumatoid arthritis. In the present study, we report 3 cases of medial UKAs condected for well controlled rheumatoid patients. [Case] Case 1. An 80-year-old female with knee osteonecrosis (ON) underwent medial UKA 2 year after diagnosed as RA. Preoperatively, the range of knee motion was 0-125 and JOA score was 45. 6 month postoperatively, the range and score were 0-140 and 85, respectively. Case 2. An 75-year-old female with osteoarthritis underwent medial UKA 5 year after diagnosed as RA. Preoperatively, the range of knee motion was 0-120 and JOA score was 40. 13 month postoperatively, the range and score were 0-135 and 85, respectively. Case 3. An 75-year-old female with knee ON underwent medial UKA 5 year after diagnosed as RA. Preoperatively, the range of knee motion was 0-140 and JOA score was 40. 13 month postoperatively. the range and score were 0-125 and 80, respectively. All surgeries were performed with consistent techniques, using the same prosthesis design (Zimmer PPK) and findings of flare of artiritis and loosening of the implant were not confirmed postoperatively. [Conclusions] UKA could be offered as an option for well controlled rheumatoid patient who fits the selection criteria for UKA.

## P3-060

**Association between renal dysfunction and periodontopathic bacterial infection in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] The present study aimed to assess the association of renal dysfunction with periodontitis and periodontopathic bacterial infection in patients with rheumatoid arthritis (RA). [Methods] We conducted a retrospective cohort study that collected clinical and laboratory data from 127 patients with RA whose informed consent was obtained in Niigata Rheumatic Center. Renal dysfunction was evaluated by an estimated glomerular filtration rate (eGFR) value that was calculated using the serum creatinine level. [Results] The number of patients with RA in each eGFR stage was 49 in G1, 58 in G2, and 20 in G3, respectively. The G3 group showed significantly higher levels in mean age (p=0.002), % of female (p=0.01), % of sites with probing depth and clinical attachment level ≧4 mm (p=0.03 and p=0.02), and anti-*Porphyromonas gingivalis* immunoglobulin G (anti-*P. gingivalis* IgG) (p=0.04) than the G1 plus G2 group. Bivariate and multivariate analyses after adjusting for the age, gender, smoking, and drug revealed a significant association between eGFR value and anti-*P. gingivalis* IgG level (p<0.001 for both) in 127 patients with RA. [Conclusions] Renal dysfunction is associated with periodontopathic bacterial infection in patients with RA.

## P3-061

**Actual clinical practice of cytomegalovirus infection in our department: verification of its detection method and risk factors of infection**

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Conflict of interest: None

[Objective] To evaluate the clinical usefulness of cytomegalovirus (CMV) antigenemia assay (HRP-C7) and blood CMV DNA polymerase chain reaction (PCR) in patients with collagen tissue disease (CTD), and to assess the incidence of CMV infection in our patients. [Methods] Medical records of the hospitalized patients who were treated in our department from February 2021 to July 2023 were reviewed retrospectively. Among the patients, those who received the blood tests of HRP-C7 and CMV DNA PCR were enrolled. The results and the related clinical data were analyzed. [Results] A total of 601 patients are enrolled in this study. The median age was 65 years and the male-female ratio was 1: 2.4. The results of the HRP-C7 were highly correlated with that of the PCR. In cases requiring treatment, the PCR showed positive followed by the HRP-C7. After the treatment, when the HRP-C7 was confirmed negative twice, the result of the PCR also tended to turn negative. Impairment of activities of daily living was considered as a risk factor for requiring treatment. [Conclusions] In clinical practice of CTD, the PCR may be useful for early detection, and the HRP-C7 may be useful for assessing therapeutic effects in CMV infection. Further analysis is required, including which cases should be actively screened.

## P3-062

**Continuous local antibiotics perfusion for bone and joint infections in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To report on the safety and efficacy of continuous local antibiotics perfusion (CLAP) for bone and joint infections in ten rheumatoid arthritis (RA) patients. [Methods] Ten RA patients with bone and joint infections between 2020 and 2023 were included in this study. Infections comprised periprosthetic knee joint infections (4 cases), polyarticular septic arthritis (4 cases), periprosthetic infection after ankle joint fusion (1 case), and fracture-related infection (1 case). Variables included patient characteristics, infection history, infection treatment, efficacy assessment (remission, recurrence, times of surgeries), and safety assessment (renal function, gentamicin levels, other complications). [Results] CLAP involved an average of 106 mg/day of gentamicin (range: 60-180 mg/day) for 15 days (range: 7-39 days). All cases achieved remission of infection with an average of 1.3 surgeries. Although one periprosthetic joint infection case recurred, the implants were retained in all cases. Two cases had renal dysfunction, improving in three weeks. No other adverse events were observed. [Conclusions] CLAP effectively controlled infections in all cases, offering a minimally invasive treatment for bone and joint infections in RA patients.

## P3-063

**Examination of preventing hepatitis B virus reactivation in patients with rheumatoid arthritis: A cross-sectional study using the AORA registry**

Rena Wakabayashi[1,12], Yusuke Sugimura[2,12], Yoichi Kataoka[3,12], Masaaki Ogino[1,12], Kazuhiro Shoji[4,12], Natsuo Konishi[5,12], Hidetoshi Watanabe[6,12], Takeshi Kashiwagura[7,12], Tsutomu Sakuraba[8,12], Toshiaki Aizawa[9,12], Hiroshi Aonuma[10,12], Nozomi Kaga[9,12], Moto Kobayashi[8,12], Naohisa Miyakoshi[11,12]
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Conflict of interest: Yes

[Objective] Reactivation of hepatitis B virus (HBV) is at risk from immunosuppressive drugs for rheumatoid arthritis (RA) and should be carefully prevented. We aim to investigate preventive measures for HBV

reactivation in RA patients in the AORA registry. [Methods] 1914 patients with RA were recruited in AORA 2021, and the number of patients with occult HBV infection (OBI) and their backgrounds was investigated. [Results] OBI patients were 193 (10.1%), of which 151 (78.2%) were female, the mean age was 71.1 years, and the mean disease duration was 14.5 years. The types of antirheumatic drugs were: PSL in 50 (mean dose 3.1 mg), MTX in 193 (mean dose 6.9 mg/week), other conventional synthetic disease-modifying antirheumatic drugs (DMARDs) in 107, biologic DMARDs in 52, and Janus kinase inhibitors in 2. HBV-DNA testing was performed in 159 (82.3%) and HBV-DNA was detected in 5 (3.3%). Two patients were regularly followed by a gastroenterologist, but none of them received nucleoside analog or suffered liver damage because their HBV-DNA levels were higher than the criteria. [Conclusion] Recently, it has been described the introduction of a screening system and interprofessional work for hepatitis are necessary. It is important to strengthen the prevention of HBV reactivation.

## P3-064

**Comparison of the cytomegalovirus antigenemia test and cytomegalovirus DNA quantitative polymerase chain reaction results in connective tissue disease**

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Conflict of interest: None

[Objective] Diagnostic utility of cytomegalovirus (CMV) DNA quantitative polymerase chain reaction (qPCR) in connective tissue disease (CTD) has not been established. In this study, CMV pp65 antigenemia test (CMV-Ag) results were compared with plasma CMV-DNA levels in CTD patients. [Methods] Ninety samples collected from 42 patients (29 male, 61 female, mean age: 59.2 ± 19.3 years) were evaluated in the study. EZR was used for statistical analysis. [Results] Mean values of CMV-Ag and CMV-DNA tests were 3.4 positive cells/50000 WBC and 1480.6 IU/ml, respectively. There was a significant correlation between CMV-Ag and CMV-DNA results ($r= 0.78$, $p<0.01$). ROC curve analysis showed that CMV-DNA of 270 U/mL in plasma corresponds to ≧1 positive cells/50000 WBC (sensitivity: 89.7%, specificity: 100%). CMV-Ag and CMV-DNA were both negative in 48 samples, while both were positive in 18 samples. In 30 samples CMV-Ag were negative and CMV-DNA were positive, while there were no samples with CMV-Ag positive and CMV-DNA negative. ROC analysis showed that any sample with CMV-DNA result less than 270 IU/ml, could be accepted as CMV-Ag negative. [Conclusions] There was a significant correlation between CMV-Ag and CMV-DNA results and CMV-DNA test was igher analytical sensitivity.

## P3-065

**Clinical study of Aspergillus antigen measurement in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] Aspergillus galactomannan (GM) antigen in serum is useful in blood diseases, but there are few reports on its clinical significance of in rheumatoid arthritis (RA) patients. We retrospectively investigated the clinical course of RA patients who tested positive for GM antigen. [Methods] GM antigen was measured in all 144 RA patients who visited our department in 2012, and 29 patients (twice, cut-off value ≧ 0.5) were included. The development of aspergillosis was examined during the clinical course using medical records. [Results] Twenty-nine patients (men/female 10/19, average age 71 years, average disease duration 10 years) were included with a mean follow-up of 71 months. In 2012, CT scans showed findings suspicious for fungus balls in 2 cases. During the follow-up period, steroids were used in 76% of cases, csDMARDs in 90%, bDMARDs in 14%, and tsDMARDs in 7% of cases for RA. Two patients were treated for pulmonary aspergillosis, and as of 2012, the patients had fungal balls. [Conclusions] Approximately 20% of patients with rheumatoid arthritis tested positive for GM antigen, but only less than 10% of them developed pulmonary aspergillosis. If there were no obvious signs of aspergillosis in the images, the risk of developing the disease was considered to be low.

## P3-066

**Recent Pneumocystis jirovecii pneumonia cases with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To clarify the characteristic of recent Pneumocystis jirovecii pneumonia (PJP) cases with RA by a single -center analysis. [Methods] Patients with rheumatoid arthritis (RA) who were admitted to our hospital between April 2013 and March 2023 because of PJP were analyzed. Clinica parameters including clinical information and treatment were retrospectively collected and predictors for death caused by PJP were also analyzed. [Results] Ten PJP patients were included. Nine were treated with MTX (7.0 mg/week), 7 with PSL (6.0 mg/day), no patients with biologics. Three were deceased. When patients were stratified by the outcome and compared, no difference was observed in gender, age, or background disease. Serum CRP level at PJP diagnosis was higher in the deceased cases (24 mg/dL vs. 12 mg/dL, $P=0.01$). No difference was observed in other serum biomarkers such as beta-D-glucan, LDH, pro-fibrotic markers (KL-6, SP-D) or treatment including MTX or glucocorticoid. [Conclusions] Surprisingly, in recent PJP cases with RA, patients with low-dose glucocorticoids or MTX alone were also found to have PJP. In recent deceased cases, only serum CRP was higher but background or treatment did not seem to be affected at the onset of PJP.

## P3-067

**Study on the occurrence of adverse events in glucocorticoid (GC) treatment of PMR (polymyalgia rheumatica) patients**

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Conflict of interest: None

[Objective] To investigate the adverse events (AEs) of glucocorticoid (GC) in patients with polymyalgia rheumatica (PMR). [Methods] Target patients were PMR registered at our hospital. AEs included pneumonia, other infections, vertebral and proximal femoral fractures, cerebrovascular events, hyperglycemia/electrolyte abnormalities, and death. Regarding the occurrence of first AEs, COX regression analysis was performed using GC withdrawal, age at the start of treatment, gender, eGFR, and RDCI (rheumatic disease comorbidity index) as explanatory variables. [Results] There were a total of 91 patients (40 males), mean age at diagnosis was 77.0 years, mean observation period was 1623 (131-6137) days, and mean RDCI was 1.8. After 2772 days (7.6 years), 50.1% had not withdrawn from GC, and AEs occurred 106 times in 42 patients (46.1%), the shortest time was 57 days, and 16 patients (17.6%) died. A positive correlation was observed between the number of days of GC administration, total dose, and number of AEs ($R^2=0.920$, $R^2=0.257$). Additionally, multivariate COX regression analysis revealed that the risk factors for the occurrence of the first AE were GC withdrawal and RDCI (coefficients 0.32 and 1.70, $p=0.0059$, $p<0.001$, respectively). [Conclusions] GC treatment for PMR patients is high risk.

## P3-068

**A case of BK virus infection diagnosed from unknown fever that appeared during the course of rheumatoid arthritis complicated systemic lupus erythematosus**

Takanori Nakagaki[1], Yoshihiro Sho[2], Mahiro Yamamoto[2], Kota Imaizumi[2], Aya Sakamoto[2], Takayasu Suzuka[2], Yumiko Wada[2], Takeshi Shoda[2], Takuya Kotani[2], Tohru Takeuchi[2]
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Conflict of interest: None

[Patient] A 71-year-old woman [Course] The patient developed rheumatoid arthritis in X-21, was diagnosed with systemic lupus erythematosus in X-6, was in remission, and had been maintained in remission with prednisone (PSL) 5 mg/day + tacrolimus 2 mg/day + hydroxychloroquine 300 mg/day + methotrexate 8 mg/week+abatacept 125 mg/week since X-1. He was admitted to the hospital in December because of herpes zoster which had been persistent since September, X. At the time of admission, his renal function had worsened. All immunosuppressive drugs except for PSL were discontinued. Her symptoms improved after about two weeks, but she continued to have a fever of 37 to 38 degrees Celsius. PCR was performed, and 41 million copies of BK virus were detected in urine and 350,000 copies of BK virus in blood, and the patient was judged to have BK virus infection. The patient's fever improved after the PSL dose was reduced [Disccusion] BK virus is known to be reactivated by immunosuppressive therapy in the transplantation field, and is a cause of nephropathy. In the field of collagen disease, BK virus infection may also occur as a result of highly immunosuppressive therapy, and it is necessary to distinguish between renal function decline and fever.

## P3-069

**A case of cat scratch disease with organ involvement that developed during treatment for rheumatoid arthritis**

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Conflict of interest: None

Case: A 79-year-old woman who had been treated with abatacept and tacrolimus for rheumatoid arthritis presented with a two-month history of fever and enlarged painful lymph nodes in the right axilla. PET-CT scan showed intense FDG uptake in multiple organs, including the right axillary lymph nodes, liver, and spleen. Based on the animal exposure history of several cats and bite marks on her right hand, azithromycin was initiated on the assumption of cat-scratch disease (CSD). The symptoms persisted despite this treatment, so a right axillary lymph node biopsy was performed for further investigation. The axillary lymph node tested positive for *Bartonella henselae* DNA in PCR assay and serological evaluation showed a significant increase in *B. henselae* IgG titer in the convalescent period, confirming the diagnosis of CSD. The symptoms gradually improved with four weeks of antibiotic combination therapy of azithromycin and rifampicin. Discussion: In addition to typical lymphadenopathy, CSD may present with extranodal involvement including liver, spleen, and bones, which may cause fever of unknown origin. Since CSD is often difficult to diagnose, it is essential to pursue histological and microbiological examination in addition to a detailed history and physical examination.

## P3-070

**A case of multiple subcutaneous abscesses resembling nodular lymphangitis caused by Candida albicans**

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Conflict of interest: None

[Case] A 70-year-old woman with a history of microscopic polyangiitis and diabetes developed edema and small papules on her right lower leg. She was admitted with suspected stasis dermatitis, but multiple subcutaneous nodular lesions were palpable from the right lower leg to the right inguinal region. MRI showed multiple subcutaneous nodules with low signal on T2 and high signal on diffusion-weighted imaging in the subcutaneous fat from the thigh to the lower leg. A nodule on the thigh was aspirated and cultured, revealing C. albicans as the sole cause of the multiple subcutaneous abscesses. She was treated with oral fluconazole and the nodules shrank. She did not have candidemia. [Discussion] Nodular lymphangitis is an infection in which microorganisms spread through the lymphatic vessels and form nodules or abscesses. The most common pathogens are Sporothrix spp., Nocardia spp., and Mycobacterium spp. Candida-induced nodular lymphangitis is rare, but has been reported in a few cases. We suggest that prompt puncture and culture are useful for diagnosis when multiple subcutaneous nodules occur in immunosuppressed patients.

## P3-071

**A case of bladder cryptococcosis associated with anti-TIF1-gamma antibody-positive dermatomyositis**

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Conflict of interest: None

<Case> 64-year-old man <Chief complaint> pain during urination <Current medical history> Treatment was initiated with PSL 70 mg for an anti-TIF1-γ antibody-positive dermatomyositis with onset in 2019. As the patient had concomitant breast cancer, chemotherapy and hormonal therapy were also given concurrently. The patient was refractory to treatment and was treated with PSL 26 mg and tacrolimus 4 mg in June 2021. In September, a CT scan showed a subcutaneous mass in the abdomen, which was biopsied and identified as Cryptococcus neoformans. After surgical resection, the patient was treated with fluconazole for more than one year and the cutaneous cryptococcosis was cured; in September 2023, the patient was referred to a urologist again because of pain during urination, bladder wall thickening on CT and positive anti-TIF1-γ antibody, which suggested bladder cancer. A biopsy confirmed the diagnosis of bladder cryptococcosis. <Clinical significance> Anti-TIF1-γ antibody-positive dermatomyositis is widely known to be frequently complicated by malignancy. If the malignancy cannot be resected, the disease is often refractory to treatment, requiring intense immunosuppressive therapy. Anti-TIF1-γ antibody-positive dermatomyositis requires careful attention to infection as well as malignancy.

## P3-072

**A case: Latent cryptococcal infection in the lung of a Sjogren patient disseminated to CNS**

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Conflict of interest: None

[Clinical Case] 87 years old female with Sjogren syndrome had been observed for lung nodules since 2 years ago. She admitted our hospital because she has been having falls lately and felt muscle weakness. On physical examination, consciousness alert, no neurologic deficit. On laboratory data, slight inflammation is detected. On MRI and CT, no significant findings are detected. She was hospitalized for observation. On 3rd day, she got fever, on 5th day her consciousness was depressed. MRI DWI revealed diffuse high signal of the cerebral cortex and On CT scan, lung nodules become greater and spread. By CSF analysis, infectious inflammatory response (cell count↑, protein↑, glucose↓) and yeast-like fungus stained with Indian ink is revealed. we diagnosed her with cryptococcal meningoencephalitis and pneumoniae, then treated with two weeks of amphotericin B and flucytosine, then six weeks of fluconazole. [Clinical Significance] Recently, it was discovered that Cryptococcus establishes an asymptomatic latent infection in the lung of immunocompetent hosts and this latent infection can disseminate to other tissues on immunosuppressed

patients such as our patient. We suggest that lung lesions suspected of cryptococcal infection should be examined if a patient have symptoms or not.

## P3-073

**A case of adult-onset Still disease (AOSD) exacerbated by disseminated cryptococcosis**

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Research Center for Allergy and Clinical Immunology, Asahi General Hospital, Chiba, Japan

Conflict of interest: None

[Case] 74-year-old male [Chief complaint] headache [Present illness] One year before admission, he was diagnosed with AOSD. He was in remission with high-dose steroids, TCZ and MTX, and was treated with PSL 12.5 mg/day, MTX and TCZ as an outpatient. One week before admission, he presented to the hospital with headache and anorexia. Suspecting a relapse of AOSD, the dose was increased to PSL 30 mg/day, but a head CT scan showed a mass lesion, and C. neoformans was identified in blood and CSF cultures. Disseminated cryptococcosis was diagnosed and induction therapy with L-AMB + 5-FC was started. However, low platelet count, decreased fibrinogen, elevated liver enzymes, and elevated serum ferritin and IL-18 levels persisted. Bone marrow examination was unremarkable, and he was treated with plasma exchange therapy, suspecting a relapse of AOSD due to disseminated cryptococcosis. After plasma exchange therapy, laboratory findings showed a trend toward improvement and antifungal drugs were continued. [Clinical Significance] The findings suggesting a relapse of AOSD may be due to increased production of inflammatory cytokines such as IL-6 and IL1β in C. neoformans infection. Plasma exchange may be an effective therapy for the coexistence of AOSD flares and opportunistic infections.

## P3-074

**Comparison of different lung ultrasound evaluation methods in interstitial lung disease (ILD) associated with idiopathic inflammatory myopathy (IIM)**

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Nippon Medical School

Conflict of interest: None

[Objective] Lung ultrasound (LUS) is becoming a popular imaging tool for assessing interstitial lung disease (ILD), but utility of LUS in ILD associated with IIM (IIM-ILD) is still under debate. In this study, two LUS evaluations methods, i.e., B-line scores mainly reflecting fibrosis and edema in the interstitium and ARDS-LUS score encompassing consolidations, were compared for their correlation with ILD parameters of IIM-ILD. [Methods] Eighteen consecutive patients with untreated IIM-ILD were selected from our LUS registry. Simple regression analysis was conducted to examine correlations of B-line scores at 14 and 58 (B-line-14 and 58) and ARDS-LUS score with semi-quantitative high-resolution CT (HRCT) scoring and parameters reflecting ILD severity and prognosis. [Results] ARDS-LUS, B-line-14 and B-line-58 scores were all correlated with the HRCT score (r = 0.79, 0.77, 0.73, respectively). There was correlation of ARDS-LUS or B-line-14 with KL-6 (r = 0.52, 0.56) or predicted forced vital capacity (r = -0.76, -0.78). The ARDS-LUS was the only parameter correlated significantly with P/F ratio (r = -0.48). [Conclusions] Both ARDS-LUS and B-line scores were useful tools for assessing IIM-ILD, while ARDS-LUS might have an advantage over B-line scores in the severity assessment.

## P3-075

**The Study on Evaluation of Finger Extensor Tendons Using Joint Ultrasound in Patients with Early Rheumatoid Arthritis**

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Conflict of interest: None

[Objective] In early rheumatoid arthritis (RA), tenosynovitis is a characteristic finding on joint ultrasound (US), often preceding synovitis. Recent studies reported the presence of synovial sheaths in the dorsal extensor tendons of the metacarpophalangeal (MCP) joints. To explore this, we evaluated finger extensor tendons using US in early RA patients. [Methods] Between October 2021 and March 2023, 49 patients (35 females, 14 males, mean age 68) with primary joint pain were newly diagnosed with early RA. We assessed dorsal extensor tendons of both hands' MCP joints, palmar flexor tendons, and extensor carpi ulnaris tendon using ultrasound. Positive periarticular inflammation was detected with tendon enlargement or PD signal. [Results] Periarticular inflammation around the dorsal extensor tendons of MCP joints was observed in 18 cases (37%) of the patients. Palmar flexor tendons of the MCP joints showed tenosynovitis in 25 cases (51%), and the extensor carpi ulnaris tendon exhibited tenosynovitis in 16 cases (33%) of the patients. [Conclusion] Periarticular inflammation around MCP joint extensor tendons in early RA, like flexor tendons and extensor carpi ulnaris, supports synovium presence, indicating finger extensor tendon evaluation aids early RA detection.

## P3-076

**Nonspecific findings at the Achilles tendon enthesis in patients with suspected spondyloarthritis**

Yuko Yoshida[1], Tadashi Okano[2], Shingo Washida[1], Yuka Domae[1], Asami Yagami[1], Kenji Mamoto[3], Yutaro Yamada[3], Takahito Kojima[3], Hiroaki Nakamura[3]
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Conflict of interest: None

[Clinical Significance] Achilles enthesitis occurs frequently in spondyloarthritis (SpA), but lesions may be seen in areas other than the Achilles tendon enthesis. Thickening of the Achilles tendon is an important finding in the diagnosis of familial hypercholesterolemia. It may be difficult to differentiate by clinical examination. It is important to perform ultrasound examinations and to understand each pathological finding. [Case 1] A 55-year-old woman. She suspected spondyloarthritis due to swelling in her MCP joint of right middle finger and Achilles tendon. Achilles tendon swelling and power Doppler signal was observed by ultrasound examination at proximal part, not the enthesis. T-Chol and LDL-C level was higere. [Case 2] 64-year-old male. He was already diagnosed with plaque psoriasis. He had joint pain, and PsA was suspected. The Achilles tendon showed thickening and inflammation proximal to the enthesis by ultrsound. Blood tests showed normal level of T-Cho and LDL-C, but he has already taking statins. Because, his both parents had died of myocardial infarction and he already diagnosed familial hypercholesterolemia. Despite treatment statins, he had active Achilles tendonitis. Further int.

## P3-077

**Comparison of intra-articular ultrasonographic synovial findings in RF-positive and -negative spondyloarthritis patients**

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Conflict of interest: None

[Objective] Patients with spondyloarthritis are usually negative for rheumatoid factor (RF). However, there are some spondyloarthritis patients who are RF positive. We compared the ultrasound findings of patients with RF-positive and -negative spondyloarthritis patients. [Methods] 551 consecutive cases of spondyloarthritis who underwent ultrasound

examination were included. Ultrasound examination was performed on the MCP, PIP, and DIP joints of the fingers and wrist joints. [Results] There were 435 (89.0%) RF negative patients and 54 (11.0%) positive patients. Regarding ultrasound findings, there were no significant differences in gray scale (GS) and power Doppler (PD) scores of the fingers and wrists depending on whether RF was positive or negative. In addition, 434 cases (95.6%) were negative for anti-CCP antibodies, and 20 cases (4.4%) were positive. Regarding ultrasound findings, there were no differences in the GS and PD scores of the fingers and wrists depending on whether anti-CCP antibodies were positive or negative. [Conclusions] There was no difference in echo field synovitis findings depending on whether RF was positive or negative in patients with spondyloarthritis.

## P3-078

**Imaging evaluation and implication of dura mater lesions for clinical findings in immune-mediated hypertrophic pachymeningitis**

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Conflict of interest: None

[Objective] To evaluate the volume and localization of the thickened dura mater, and their impact on clinical findings in immune-mediated hypertrophic pachymeningitis (HP). [Methods] The volume of the contrast-enhanced dura mater on brain MRI was evaluated in 19 patients with HP (HP-patients), including ANCA-related, IgG4-related, and idiopathic HP, and 10 patients with multiple sclerosis as controls. The impacts of HP volume on neurological symptoms and cerebrospinal fluid (CSF) markers, along with the cut-off volumes, were analyzed. [Results] Significantly higher volumes of the contrast-enhanced dura mater were observed in HP-patients than in controls. In HP-patients, those with cranial nerve (CN) VIII neuropathy had a significantly higher volume of the thickened dura mater in the cranial fossa than those without CN VIII neuropathy. The cut-off volume in the cranial fossa was more frequently exceeded in patients with CN VIII neuropathy than in those without CN VIII neuropathy. A positive correlation between the volume of the thickened dura mater in the tentorium cerebelli and CSF protein levels was significantly observed in HP-patients. [Conclusions] The quantification of HP lesion is useful for elucidating the relationship with the clinical findings in immune-mediated HP.

## P3-079

**The hand MRI bone marrow edema could potentially be a risk factor for rapid radiographic progression in patients with rheumatoid arthritis treated with conventional synthetic DMARDs**

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Conflict of interest: None

[Objective] To examined whether MRI bone marrow edema (BE), an independent prognostic factor for joint destruction, could be a prognostic factor for RRP in RA treated with csDMARDs. [Methods] The study involved 155 csDMARD treated RA patients who were examined for joint destruction one year before and after the analysis using X-ray (mTSS method) (PLOS ONE 2018, Trial Registration Number: UMIN000012200). As a post-hoc analysis, the MRI bone marrow edema (BE) score at the time of analysis was evaluated for all subjects using the OMERACT method, and the following three points were examined. [Results] Background factors of the Non-RRP group (108 cases) and the CRRP group (clinically related X-ray progression: mTSS> 3, 47 cases, including 33 cases of RRP) were compared. Significant differences were observed in the disease duration (shorter), MRI BE (more frequent), DAS28-ESR, CRP, and mTSS (higher values). Patient data was divided into 5 groups according to the ΔmTSS/year ratio and in the RRP group, the MRI BE score was significantly higher than in the other groups. A significant correlation was observed between the MRI BE score and ΔmTSS/y (Pearson Correlation Coefficient R=0.57, P<0.001). [Conclusions] In RA treated with csDMARDs, hand BE could potentially be a predictor for RRP.

## P3-080

**Bone changes in the shoulder joint associated with rotator cuff tears-A Study using of X-Ray and MRI-**

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Conflict of interest: None

[Objective] We investigated the influence of rotator cuff tear on bony changes in the shoulder joint. [Methods] The subjects were 40 RA patients (20 with rotator cuff tears (RA tear group) and 20 without rotator cuff tears (non-RA tear group)) who had shoulder pain and underwent X-rays and MRIs, and 20 patients with rotator cuff tears who did not have RA (control group). The study included age, duration of disease, and fatty degeneration of rotator cuff tears. Bone changes included Larsen classification to evaluate glenohumeral joint destruction (GHD), glenohumeral tuberosity destruction (GTD), and bone cyst (BC) of the greater tuberosity bare area. [Results] The mean age of the RA tear group/non-RA tear group/control groups was 71/69/75 years. The mean duration of disease was 113/88/38 months. The RA tear and control groups; GHD was significantly higher in the RA tear group (50%) and non-RA tear group (10%); GTD was significantly higher in the RA tear group (60/15/0%); and BC of the bare area was significantly higher in the RA tear group (70/45/30%). [Conclusions] The RA rupture group showed more bone destruction of the glenohumeral joint and greater tuberosity and bone cyst in the greater tuberosity bare area than the non-RA rupture group and the general rotator cuff rupture group.

## P3-081

**Whole spine MRI in axial Psoriatic arthritis**

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Conflict of interest: None

Purpose: Psoriatic arthritis (PsA) is known to have multiple domain symtoms, one of which is the axial lesion. The ASAS classification criteria for axial spondyloarthritis include confirmation of sacroiliitis on x-ray or MRI, but there is no definition or specific imaging studies that have been determined for axial psoriatic arthritis (axPsA). This study aimed to investigate the usefulness of whole spine MRI including all spines and sacroiliac joints in patients with axPsA. METHODS: We retrospectively analyzed the medical records of PsA patients who were underwent whole spine MRI and diagnosed that had axial lesions. We analyzed patients' characteristics and MRI findings. RESULTS: The mean age of the 43 patients was 47.47 (±12.7) years, and 26 (60.5%) were male. 24 (55.8%) patients had sacroiliac joint involvement and 39 (90.7%) patients had spinal involvement. 15 (34.9%), 25 (58.1%), and 28 (65.1%) had cervical, thoracic, and lumbar spine, respectively. CONCLUSION: In this study, about half of the patients had no MRI findings of the sacroiliac joint. On the other hand, spinal lesions were more common. This study showed that whole spine MRI imaging was considered useful to avoid overlooking spinal lesions which is important for axPsA.

## P3-082

**The usefulness of Diffusion-weighted Whole-body Imaging with Background body signal suppression in the diagnosis of polymyalgia rheumatica**

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Conflict of interest: None

[Objective] Polymyalgia rheumatica (PMR) is sometimes difficult to differentiate from rheumatoid arthritis. Many reports suggest that it is a useful tool of ultrasound examinations (US) and FDG·PET/CT. However, the detection sensitivity of the US depends on the skill and FDG · PET/CT is not applicable in Japan, the radiation exposure is high. Diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) is non-contrast whole-body imaging so that is widely useful for detecting inflammation. Hence we examined the usefulness of DWIBS in the diagnosis of PMR. [Methods] We retrospectively evaluated clinical findings, blood tests, and image findings of PMR patients that underwent DWIBS at the time of diagnosis. [Results] A total of 11 patients (male 45.5%), average age 76.8 years. The group that could be detected by DWIBS (groupI) and the group that could not be detected (groupII). GroupI /groupII is 10.8±4.97/6.53±4.60 in CRP (mg/dL), 84.6±9.20/81.8±18.3 in ESR (mm/h), 360±216.7/249.6±217.1 in MMP-3 (ng/dL), 95±23.94/77.66 ±16.87 in ALP (U/L) and 653±142.4/704.6±230 in fibrinogen (mg/dL). Although no significant difference was observed, CRP tended to be higher in groupI. [Conclusions] DWIBS may be useful in diagnosing PMR in cases with high CRP.

## P3-083

**Cervical spine radiography was useful in the diagnosis of rheumatoid polymyalgia to rheumatoid arthritis: a case report**

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Conflict of interest: None

[Object] Elderly-onset rheumatoid arthritis (EORA) is often difficult to distinguish from polymyalgia rheumatica (PMR), it is not uncommon for the diagnosis to change to EORA during the course of PMR treatment. We report a case in which cervical spine X-rays were helpful in making the diagnosis of RA from PMR. [Case] A 76-year-old woman was referred to our general medicine from another clinic 4 years before first visit because of fever, bilateral shoulder and buttock pain, and an increased inflammatory response that lasted about 4 months. She was diagnosed with PMR and treated with steroids for 3 years. 8 months after the completion of treatment, her symptoms flared up and she was referred to our department. Physical examination revealed no obvious joint swelling or tenderness, and blood tests showed elevated CRP 2.29 mg/dl, but RF and anti-CCP antibodies were negative. On X-ray, the only change in the small joints was a suspicious erosion in the left MTP joint and no abnormalities in shourder joints, but there was an atolantoaxial subluxation in the cervical spine. RA was diagnosed and MTX was initiated. She was in remission at 1 year of treatment. [Clinical Signification] When performing X-rays in RA practice, cervical spine imaging (especially dynamic imaging) should be performed.

## P3-084

**Evaluation of bone fragility in RA knee using Dual Energy CT**

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Conflict of interest: None

[Objective] Dual-Energy Computed Tomography (DECT) can discriminate between two arbitrary reference materials based on the X-ray absorption. The purpose of this study was to evaluate bone mineral density based on the Hydroxyapatite (HAP) and water component separated by the DECT in patients with RA and OA knees before TKA. [Methods] Bone density (femur, lumbar vertebrae), blood Ca concentration, CRP, and ESR were measured in 15 RA and OA patients, respectively. DECT emphasizes the water component, and sets regions of interest (ROI) for the distal femur, the proximal tibia, the patella, and the tibial shaft. Each parameter was statistically compared between the RA group and the OA group. [Results] There was a negative correlation between the bone density of the femoral neck and lumbar vertebrae and the Water/HAP density of the proximal tibia and tibial shaft, but no correlation was found for the femur. Between the two groups of RA and OA, only Water/HAP in the proximal tibia was significantly higher in RA. No significant difference was observed in bone density. [Conclusions] Since the water density of the RA tibia was significantly higher than that of OA, DECT may be a useful tool for understanding local bone fragility at the surgical site.

## P3-085

**The Utility of Non-Contrast 3-Dimensional Maximum Intensity Projection Images in Rheumatoid Synovial Assessment**

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Conflict of interest: None

[Objective] MRI images in patients with rheumatoid arthritis often exhibit reduced expression of inflammatory lesions due to coil specificity and imaging conditions. In contrast, dynamic contrast-enhanced MRI has proven effective in detecting inflammatory lesions. This study aims to analyze the effectiveness of non-contrast 3-dimensional maximum intensity projection (3D-MIP) in diagnosing rheumatoid lesions in hand MRI. [Methods] We conducted this study on 93 patients, with 32 receiving enhanced MRI and the rest undergoing non-enhanced MRI, between December 2021 and May 2022. We employed the Canon Vantage Gracian 1.5T (MRT-2020/J8) MRI machine for imaging. [Results] Among the 93 cases, 91 cases accurately identified synovitis, while two cases posed challenges in estimating synovitis due to patient movement and artifacts. No significant differences in results were observed when comparing non-enhanced coronal and axial 3D-MIP images, and results were similar between contrast-enhanced and non-contrast images. [Conclusions] Non-contrast 3D-MIP proves to be a valuable tool for easily visualizing synovial lesions in a three-dimensional format and offers cost-effective benefits.

## P3-086

**Association between upper extremity involvement and work disability in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] There is still concern that upper extremity involvement may affect work disability. Here, we investigated the effect of upper extremity involvement on work disability in patients with rheumatoid arthritis (RA). [Methods] The Work Productivity and Activity Impairment (WPAI) questionnaire was obtained annually from RA patients in the Nagahama Rheumatology Cohort at Nagahama City Hospital, from March 2017 to February 2020. The association between work disability and tender joint count (TJC) of the upper extremity was analyzed. [Results] WPAI responses were obtained from 471 patients, and 201 working patients were analyzed. Upper extremity TJC significantly predicted presenteeism (partial regression coefficient [β]=0.0239, $p<0.0001$), even after adjusting for confounding by lower extremity TJC and HAQ-DI in multiple regression analysis. Among the 135 patients with a second WPAI response, Δupper extremity TJC was a significant predictor of Δpresenteeism (β=0.0146, p=0.0387), even after adjusting for confounding by Δlower extremity TJC and ΔHAQ-DI in multiple regression analysis. [Conclusions] Background work disability should be considered, especially in RA patients with a number of affected joints in the upper extremity.

## P3-087

**The effects of glucocorticoid on treatment course in patients with difficult to treat rheumatoid arthritis**

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the effect of concomitant use of glucocorticoid in patients with D2T RA. [Methods] We analyzed 137 patients met D2T RA criteria. We classified subjects as glucocorticoid use group (GC group) or glucocorticoid non-use group (non-GC group). Drug retention rate and disease activity change were evaluated for 24 weeks in each group. In addition, we validated the efficacy of glucocorticoid taper in GC group. [Results] The continuation rate of bDMARDs/JAKi at 24 weeks was not different between GC group and non-GC group (70.8 vs 62.1%, p=0.34). DAS28-ESR at 0, 4, 12, 24 were 5.1, 4.5, 4.5. 4.5 in GC group (p<0.01), and 5.0, 4.6, 4.5, 4.3 in non-GC group (p<0.01). In GC group, DAS28-ESR at 0, 4, 12, 24 were 5.4, 4.8, 4.3. 4.2 in 29 D2TRA patients with GC taper (p<0.01), and 5.0, 4.4, 4.7, 4.7 in 42 D2TRA patients without GC taper (p=0.24). Multivariate logistic regression analysis revealed that high number of past use of bDMARDs/JAKi (ORs;0.15, 95%CI;0.03-0.78, p=0.02) and lymphatic proliferative diseases (ORs;0.001, 95%CI;0.0001-0.76, p=0.04) inhibited the glucocorticoid taper. [Conclusions] High number of past use of bDMARDs/JAKi and lymphatic proliferative diseases were the risk factor to inhibit the glucocorticoid taper in D2TRA patients.

## P3-088

**Examination of diagnostic criteria for frailty: decreased grip strength in patients with rheumatoid arthritis: ~multicenter observational study T-FLAG~**

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Conflict of interest: None

[Objective] To investigate the relationship between Rheumatoid arthritis (RA) patients and decreased grip strength (d-GS). [Methods] Among 692 patients from our observational study with Japanese version of frailty diagnostic criteria (J-CHS), 451 female RA patients were included. GS ≦18 kg was considered to be d-GS. The patients were divided into 287 who met the Treat to Target (T2T) with DAS28-ESR <3.2 and 164 who did not meet T2T with DAS28-ESR ≧ 3.2. The cutoff value of GS for T2T was analyzed by ROC analysis. In the T2T group, robust group (n =71) with a J-CHS score of 0 and a pre-frailty group (n =39) for which only d-GS was met were selected. A cutoff value for pre-frailty was calculated in SARC-F, a diagnostic tool for sarcopenia. [Results] The cut-off value of GS was 16 kg. Compared to the robust group, the pre-frail group was older (71.9 vs. 61.3 years), had a longer disease duration (19.1 vs. 9.5 years), had a higher HAQ-DI (0.19 vs. 0.07), and had a higher SARC-F. (1.59 vs. 0.77), The cutoff value for the pre-frailty was ARC-F: 1.0 (0.674). [Conclusions] RA patients had d-GS despite having good control of disease. As the cutoff values in SARC-F corresponded to the normal group, the criteria of GS for frailty might be too strict for RA patients.

## P3-089

**The effect of central sensitization on D2T-RA using central sensitization inventory**

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Conflict of interest: None

[Objective] Despite the recent proposal of the concept of difficult-to-treat RA (D2T-RA) by EULAR, the involvement of central sensitization in D2T-RA remains unclear. [Methods] We enrolled 240 RA patients (63 males and 177 females) who visited our department between May 2017 and October 2018. Retrospective diagnosis of D2T-RA was performed in accordance with the EULAR definition. CSS (central sensitivity syndrome) was evaluated using the CSI (central sensitization inventory), and the frequency and characteristics of central sensitization in D2T-RA were investigated. [Results] Patient demographics were as follows: age 59.7±14.3 years, disease duration 9.58±7.66 years, and DAS28ESR 2.39±1.07. Among the 240 patients, 30 (12.5%) were diagnosed with D2T-RA. Of these, 3 (10%) patients had CSS (CSI≧40), and all exhibited moderate CSS (50>CSI≧40). Additionally, 8 (26.7%) patients exhibited mild CSS (40>CSI≧30). In the non-D2T-RA group, 15 (7.14%) had CSS, with 13 (6.19%) exhibiting mild CSS. The frequency of mild CSS was significantly higher in the D2T-RA group than in the non-D2T-RA group (p<0.001). [Conclusions] D2T-RA should be treated with caution because of the higher frequency with mild central sensitization compared to non-D2T-RA.

## P3-090

**Comparative study of remission and low disease activity in elderly rheumatoid arthritis patients -the ANSWER cohort study-**

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Conflict of interest: None

[Objective] The primary goal of T2T in rheumatoid arthritis (RA) is remission (CR), and low disease activity (LDA) has been set as an alternative goal in elderly patients. While predictive factors for achievement of CR have been reported in all age groups, those in eldery patients may be different from those in younger patients. We investigated the predictive factors of CR in the elderly. [Methods] We included patients from the multi-center ANSWER cohort database from 2012 to 2022. Patients aged 70 years or older who achieved LDA or less by CDAI within 1 year from b/ts DMARDs initiation were selected. We analyzed predictive factors of CR when comparing CR and LDA groups using multivariate logistic analysis. [Results] 394 patients in the CR group and 707 in the LDA group were selected, and differences were observed in age, duration of disease, RF/ACPA positivity, percentage of abatacept use, and history of b/tsDMARDs use. Predictive factors of CR were duration of disease (OR: 0.997, 95%CI: 0.995-0.998), previous use of b/tsDMARDs (OR:0.770, 95%CI:0.614-0.966), HAQ (OR:0.572, 95%CI:0.453-0.723). [Conclusions] Eldery patients with longer disease duration, more use of previous b/tsDMARDs, and higher HAQ are less likely to reach CR even if they achieve LDA after starting b/tsDMARDs.

## P3-091

**Treatment results of each phase and frequency of D2TRA in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To investigate the treatment results in each phase of RA treatment and the frequency of D2TRA patients. [Methods] 360 RA patients were the subjects of this analysis. The group of patients who achieved remission or LDA in each phase was considered success group (group S), and other patients was considered failure group. We extracted the factors associated with this, and further examined the frequency of D2TRA and related factors. [Results] The group S in Phase 1 was 37.5%. A comparison between the two groups revealed significant differences in background such as age, disease duration, number of tender and swollen joints, DAS28, mHAQ, ACPA and RF, and MMP-3. The group S in Phase 2 was 54.0%, and there were significant differences between the two groups in swollen joints, DAS28, and mHAQ in background, and the type of b/tsDMARDs used in Phase 2. The group S in Phase 3 was 74.2%, and significant differences were observed in swollen joints and DAS28 at the transition from Phase 2 to Phase 3. D2TRA was 6.1% of patients, who had a high mHAQ in background, and a high complication rate at the final follow-up. [Conclusions] Cases with HDA, high mHAQ, or complications are difficult to treat and are likely to end up with D2TRA.

## P3-092

**Evaluation of appetite of patients with rheumatoid arthritis using CNAQ-J (Council of Nutrition Appetite Questionnaire scores for the Japanese)**

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Conflict of interest: None

[Objective] To investigate the relationship between appetite and clinical characteristics of rheumatoid arthritis (RA) patients. [Methods] Ninety-eight patients who were diagnosed with RA or suspected of RA were enrolled into this study. The information regarding disease activity, complications, and treatment were collected at same points of CNAQ-J assessment. Patients were divided into two groups according to CNAQ-J scores as follows; 42 patients whose score were 28 points or less (low score group) and 56 patients over 28 points (high score group). [Results] There were no differences in age, sex, body weight, history of smoking and duration of RA between two groups. The hemoglobin value was higher in high score group (12.2 vs 13.2, p=0.04). The number of tender joints, swollen joints, MMP-3 and CRP level were not different. The usage of glucocorticoids and methotrexate were not differ. However, the usage of immunosuppressant was higher in the high score group. There was a trend in highly usage of biological agents in that group. [Conclusions] Patients with CNAQ-J score less than 28 is reported to be a high risk of developing sarcopenia and frailty. Controlling inflammatory state of RA patients may affect their appetite and contribute to decrease the risk of frailty development.

## P3-093

**The impact of glucocorticoid use on outcomes of rheumatoid arthritis in a multicenter ultrasound cohort study**

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Conflict of interest: None

[Objective] Our objective was to assess the response to biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) in patients who had previously been treated with glucocorticoids (GCs). [Methods] We conducted a prospective multicenter ultrasound study on RA patients treated with b/tsDMARDs. We compared baseline characteristics and 12-month outcomes between two groups: those who received initial GC treatment and those who did not. We used inverse probability weighting (IPW) with propensity scores to account for differences in clinical characteristics and treatments. [Results] Among the 307 RA patients, 160 initially received GCs. They had distinct baseline characteristics such as age, concurrent use of MTX, clinical disease activity, and ultrasound findings compared with those not received GCs. Patients on GCs experienced fewer remissions, both by clinical and ultrasound assessments. Even after adjusting for various factors through IPW, these differences in remission rates remained significant. [Conclusions] RA patients on GCs had higher initial disease activity and a less favorable response to b/tsDMARD treatments compared to those without GCs. The need for GCs may be linked to the poorer b/tsDMARD response through varying clinical conditions.

## P3-094

**The influence of comorbidity and history of breast cancer on control of disease activity in women with rheumatoid arthritis (RA) from the SETOUCHI-RA registry**

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Conflict of interest: None

[Objective] To examine the influence of comorbidity and history of breast cancer on control of disease activity of rheumatoid arthritis (RA) in women with RA [Methods] This was a Single-Center Retrospective Study at our department. The influence of comorbidity or history of breast cancer on RA disease activity was evaluated in 720 RA female patients whose disease activity was evaluated by CDAI by using logistic regression analysis. [Results] A total of 104 cases had a comorbidity or history of solid tumors, of which 24 cases were breast cancer. The average age of patients with breast cancer was 69 years, the time since diagnosis of breast cancer was 12.1 years and the duration of RA was 11.2 years. Compared with the overall population, there was no difference in the use rate of csDMARDs. Although the use rate of b/tsDMARD of all was 59%, the rate of patients with breast cancer was only 17% ($p<0.001$). The rate of achieving CDAI$\leqq$10 was lowest in patients with breast cancer (75%), and the odds ratio of achieving CDAI>10 was 3.03 (95%CI 1.16-7.89). [Conclusions] Because of concerns about the possibility of a breast cancer recurrence over a long period of time, the use of b/tsDMARDs is often refrained from, which was thought to make it difficult to control RA disease activity.

## P3-095

**Longitudinal changes of foot sharp score in rheumatoid arthritis and its related factors**

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Conflict of interest: None

[Objective] To investigate the longitudinal changes of foot sharp score

in rheumatoid arthritis and its associated factors. [Methods] The study included 34 patients with rheumatoid arthritis who had been diagnosed within the past 3 years and had undergone foot X-rays at their initial visit and at 10 or more years after. The study group consisted of 6 males and 28 females. We examined the Sharp Score on foot X-rays (FSS) at the initial visit and at the final follow-up. In addition, we examined the FSS at the final follow-up divided by the duration of rheumatoid arthritis (FSS/year) and its correlation with ACPA, CRP, Mmp-3, RF and foot sharp score at the initial visit to our clinic. [Results] The average age of the 34 patients was 59 years, and the average duration of rheumatoid arthritis was 12.8 years. The average FSS at the initial visit and the final follow-up were 4.1and 18.9, respectively. FSS/year had an average value of 1.5, and among all items, only the initial FSS showed a weak correlation with a coefficient of 0.37 (p=0.04). [Conclusions] The progression of foot deformities in rheumatoid arthritis was correlated with the initial foot Sharp Score. The initial foot Sharp Score may have potential utility in predicting the prognosis of foot deformities in rheumatoid arthritis.

## P3-096

**Successful treatment of refractory rheumatoid pleural effusion with sarilumab**

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Conflict of interest: None

This case report details the successful treatment of treatment-resistant rheumatoid pleural effusion in a 68-year-old male using sarilumab (SAR). Initially, the patient experienced severe joint pain and swelling in multiple areas. Laboratory analysis confirmed the presence of rheumatoid factor and anti-cyclic citrullinated peptide antibodies, leading to a diagnosis of rheumatoid arthritis. The prescribed medications, salazosulfapyridine, provided limited relief. Pleural effusion was confirmed via chest X-ray, with additional tests showing specific characteristics. Prednisolone (PSL) and salazosulfapyridine were initially administered and initially improved symptoms but worsened as PSL dosage decreased to 10 mg/day. The addition of iguratimod was ineffective. Concurrently, the patient faced a prostate cancer diagnosis with a Gleason score of 7 and scheduled for radical prostatectomy. SAR was introduced and led to significant improvements in arthritis and pleural effusion within four weeks. After 14 weeks, pleural effusion resolved, and arthritis remained in remission post-PSL discontinuation. This case underscores the potential benefits of SAR for early intervention in rheumatoid arthritis and pleural effusion management.

## P3-097

**Felty's syndrome complicated with pyoderma gangrenosum and Evans syndrome: favorable response to cyclophosphamide**

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Conflict of interest: None

[Case] A 47-year-old woman, who had a 30-year history of rheumatoid arthritis and long-term treatments with methotrexate (MTX) and infliximab (IFX), was admitted to our hospital because of pancytopenia and pyoderma gangrenosum (PG). IFX was withdrawn 5 years ago. MTX was ceased 2 years ago because of anemia, thrombocytopenia, splenomegaly, and ascites, while leukocytopenia also developed 5 months ago. She developed subcutaneous abscess on the right lower leg, which was refractory to drainage treatment and ultimately developed ulceration after a biopsy, 7 months ago. Positive results for PA-IgG and direct Coombs test along with pancytopenia resulted in the diagnosis of Felty's syndrome and Evans syndrome. PG was diagnosed by skin biopsy, while no evidence of dysplasia in bone marrow. Although initial therapy with prednisolone at 20 mg/day and intravenous infusion of (IV) immunoglobulin therapy provided insufficient efficacy, improvements of leukocytopenia, anemia, and cutaneous ulceration were achieved after administering IV-cyclophosphamide (CY) (500 mg biweekly) concomitantly with MTX. [Conclusions] To the best of our knowledge, this is the first report of Felty's syndrome complicated with Evans syndrome and PG. IV-CY and MTX were useful therapy for this patient.

## P3-098

**Three cases of elderly male who added baricitinib to steroid pulse therapy during acute exacerbation of rheumatoid arthritis-associated interstitial lung disease (RA-ILD)**

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Conflict of interest: None

[Case 1] 79-year-old man, onset of rheumatoid arthritis (RA) at age 62, treated with abatacept and tacrolimus, had interstitial lung disease (ILD) and had its acute exacerbation. Steroid pulse therapy (IVMP) was started, and 4 mg of baricitinib (Bari) was added. He improved, but of infection, died at 8th week. [Case 2] 76-year-old man with RA complidated by mild ILD, dispite the use of prednisolon and tacrolimus, had exacerbation of ILD. IVMP was started, but he was placed on ventilatory management. After 4 mg of Bari was added, he was weaned from the ventilator at 6th week, and is currently on outpatient care without oxygen. [Case 3] 81-year-old man with RA had preceding ILD and it was worsened. IVMP and 4 mg of Bari was started and he had cytomegalovirus reactivation. But he recovered and was transferred to a hospital for rehabilitation. [Clinical Significance] Our three patients all had acute RA-ILD exacerbations that improved once Bari was added to the IVMP. Of the three cases, case 2 was the most impressive. He had another exacerbation when the drug was withdrawn, so we believe that the patient was saved by readministration of the drug. Although the greatest attention should be paid to concomitant infections, Bari may be an option for treat of RA-ILD acute exacerbation.

## P3-099

**A Case of Rheumatoid Arthritis with Overlapping Lymphoproliferative Disease and Primary Lung Cancer**

Takumi Matsumoto
Kin-ikyo Tomakomai Hospital

Conflict of interest: None

[Case] A 77-year-old male with a 30-year history of rheumatoid arthritis (RA). He had been taking 8 mg of MTX orally at our hospital for 12 years. In early September of year X, he noticed swelling on the right clavicle and experienced fever since September 17th of year X. A chest CT scan showed lymphadenopathy in the neck and mediastinum, a tumor measuring up to 7 cm in diameter extending from the right neck to the upper mediastinum. EBUS-TBNA of the mediastinal lymph nodes revealed atypical cells, and immunostaining was positive for CD20 and CD79a, suggesting a B-cell lymphoproliferative disorder. MTX was discontinued, and by December of year X, the mediastinal and left lung tumors had shrunk, but a nodule in the right upper lobe and some mediastinal lymph nodes had enlarged. The biopsy results confirmed primary squamous cell carcinoma of the lung. [Discussion] In the diagnosis of lymphoproliferative disorders, we initially considered the adjacent tumors to be the same pathology, but it turned out to be a concurrent cancer with lung cancer. This led to a three-month delay in the diagnosis of lung cancer. Reports of concurrent cancer in RA are rare, but it is important to be aware of the possibility of concurrent cancer with lymphoproliferative disorders.

## P3-100

**Compliance with Rheumatoid Arthritis Clinical Practice Guidelines in Elderly RA Patients**

Tsuyoshi Watanabe
Department of Orthopaedics, National Center for Geriatrics and Gerontology

Conflict of interest: None

[Objective] To determine whether the guidelines for rheumatoid arthritis treatment are being complied with in elderly RA patients. [Methods] 235 RA patients, 58 males and 177 females were included. Patients were divided into three age groups: young (Y) (<60), semi-elderly (S) (60 to 75), and elderly (E) (75<). The use of MTX, PSL, DMARDs, and compliance with guidelines were compared in each group. The treatment strategy was decided by Shared Decision Making according to the guidelines, and the use of PSL and tsDMARDs was regarded as non-compliance with the guidelines. [Results] Groups Y, S, and E had n (23,73,139), sex (3:20, 18:55, 37,102), BMI (23.0, 23.5, 24.5), RF (54.0, 60.4, 73.5), anti-CCP titer (29.8, 50.2, 114.1), and SDAI (6.06, 6. 63, 7.70), mHAQ (4.75, 4.52, 4.00), MTX use (100%, 38.3%, 78.4%), PSL use (0%, 19.1%, 18.7%), bDMARDs use (17.4%, 8.2%, 24.4%), bDMARDs (17.4%, 8.2%, and 24.4%), tsDMARDs (0%, 6.8%, 31.7%), and guideline compliance (100%, 74%, 50.4%) were observed. [Conclusions] The use of PSL and tsDMARDs was higher in elderly RA patients in groups S and E than in group Y. The use of MTX was significantly lower in group S than in other groups, indicating that MTX was not taken due to complications and adherence.

## P3-101

**Investigation of MTX therapy in elderly RA patients (75 years and older)**

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Conflict of interest: None

[Purpose] Standard rheumatoid arthritis treatment recommends considering MTX upon diagnosis. However, for elderly patients, cautious administration is required. [Method] We studied MTX use in patients aged 75 and above. [Results] In 750 rheumatoid arthritis cases aged 75 or older (34.4% of the total), 329 received MTX. This group consisted of 63 males and 266 females, with an average age of 80 (range: 75-94). Stages: I (60), II (71), III (86), IV (111); Classes: 1 (107), 2 (159), 3 (54), 4 (8). Average MTX dose: 6.2 ± 2.1 mg/week (range: 2-12 mg). Doses: 2 mg (14), 4 mg (83), 6 mg (109), 8 mg (86), 10 mg (27), 12 mg (4). 42.5% received GC (0.5-9 mg/day). 73 cases (22.1%) received bDAMRDs or JAKi, including 47 TNFi, 11 IL6i, 13 CTLA4Ig, and 2 JAKi. eGFR cases: G1 (20), G2 (167), G3a (102), G3b (25), G4 (2), G5 (0). 127 cases required cautious MTX administration or had contraindications; two had severe renal failure. No significant correlations found between MTX dose, age, eGFR, disease activity, or HAQ-DI. [Coclusion] We studied MTX use in patients aged 75 and older. The average dose was 6.2 mg/week, with 63.8% using 6 mg or less. Approximately 40% had eGFR below 60, indicating the need for regular monitoring.

## P3-102

**Cost and effectiveness analysis of DMARDs therapy (annual report from NinJa 2021) -The cost-effectiveness of DMARDs is improving.-**

Yasuo Suenaga[1], Masataka Torigoe[1], Daisaku Kimura[1], Taketo Yoshitama[1], Toshihiro Matsui[2], Shigeto Tohma[3]

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Conflict of interest: None

[Objective] To evaluate the balance between the clinical efficacy of rheumatoid arthritis treatment and its drug costs over time. [Methods] Using data from NinJa, an RA database, from 2002 to 2021, we compared disease activity and the cost of DMARDs. Based on these, a cost-effectiveness analysis was performed and changes over time were examined. [Results] In 2021, 17,181 patients were enrolled; improvement in clinical activity indices such as SDAI continued; and the frequency of biologics use increased slightly to 27.8%. The average cost of DMARDs per patient per year was 495,000 yen, up 10,000 yen from the previous year. The proportion of the cost of biologics continued to decrease to 62.0%, but tsDMARDs accounted for 18.5%. Improvement in effectiveness vs. cost using clinical indicators as effectiveness continues. [Conclusions] Since 2016, the cost-effectiveness of DMARDs remained the same as before the advent of biologics. Since then, costs have remained flat and effectiveness and cost-effectiveness have continued to improve. tsDMARDs combined have the second highest frequency of use after TCZ, yet the average cost per patient is about twice that of TCZs, and further improvements in cost-effectiveness can be expected with the price revisions.

## P3-103

**Comparison of Weekly vs. Biweekly Treatment Outcomes of Etanercept Biosimilar for Rheumatoid Arthritis**

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Toyohashi Municipal Hospital

Conflict of interest: None

[Objective] Etanercept biosimilar (ETN-BS) was marketed as a follow-on product. We use 50 mg pens weekly as well as biweekly if economically difficult, and compared outcomes in rheumatoid arthritis (RA) patients. [Methods] From July 2019 to September 2023, 22 patients were selected who were treated with ETN-BS for at least 1 year, excluding those who changed from the prior product. We classified into 2 groups (weekly and biweekly), and analyzed for patient background, outcomes, reasons for continuation and discontinuation. Patients who changed from biweekly to weekly were considered as discontinuation. [Results] Of the 22 patients, 11 were in the weekly and 11 were in the biweekly. Median age was 60:54 years (p=0.77), median DSA28-CRP was 3.57:3.24 (p=0.56) at start, 6 months: 2.52,1.88 (p=0.13), 12 months: 2.06,1.86 (p=0.43), all observation periods were not significantly different, as was SDAI. While the 12-month continuation rate after treatment was 91:54.5%, there was not significant difference at the last observation. [Conclusions] We compared patients who used ETN-BS from the start of treatment. Patient backgrounds and outcomes were comparable, but there were cases of intensification from biweekly to regular within one year, and biweekly treatment requires careful follow-up.

## P3-104

**Influence of iguratimod on decline of kidney function and associated risk factors in patients with rheumatoid arthritis**

Shunichiro Hanai[1,4], Moe Watanabe[1,4], Nakako Mabuchi[1,4], Soichiro Kubota[1,4], Ryosuke Ito[1,4], Yoshiaki Kobayashi[1,4], Takeyuki Kanzaki[2], Kensuke Koyama[3,4], Daiki Nakagomi[1,4]

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Conflict of interest: None

[Objective] We aimed to examine the risk factors for decline of kidney function among patients with rheumatoid arthritis (RA) who received iguratimod (IGU). [Methods] Changes in estimated glomerular filtration rate 3 months after from IGU administration (delta GFR) in the patients from local registries at our hospitals were measured. We divided the patients into two groups by the rate of delta GFR >15% or <15% and compared the clinical parameters. [Results] Of the 108 patients, 32 (30%) belonged to the delta GFR >15% group. The delta GFR >15% group showed the higher rate of sulfasalazine (SASP) use (47 vs 17%, p<0.005) compared to delta GFR <15% group, but no significant differences were found in baseline age, eGFR and combined use of NSAIDs. Delta GFR were signifi-

cantly higher in the patients with SASP and NSAIDs use than whom without (10.1 vs 5.9, 10.3 vs 5.9, p<0.05, respectively). In binominal regression analysis, the odds ratio of combined SASP use to non-SASP use group for delta GFR >15% was 5.1 (95% CI 1.9-14.0). [Conclusions] SASP or NSAIDs use were identified as risk factors for the decline of kidney function. Combination therapy of IGU with SASP could lead to the eGFR reduction, careful attention should be paid on the renal function.

## P3-105

**Twelve years follow up of patients with rheumatoid arthritis whose onset was over 70 years old**

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Conflict of interest: None

[Objective] Elderly onset rheumatoid arthritis (RA) is on the rise. Patients with elderly onset RA were investigated to confirm long-term results. [Methods] The subjects were 13 patients (male 4, female 9) whose onset of RA were over 70 years and who visited our department in 2 years after onset for the first time from April 2010 to June 2013. Mean age at onset was 77.5±5.5 year. At the first visit, DAS28ESR was 5.9±1.4, CRP was 3.0±2.8 mg/dl, anti-CCP Ab positive cases were 6, and RF positive case were 7. These patients were studied for 10 to 13 years after onset. Death cases were evaluated just before death. [Results] Except for 1 case of bronchiectasis and 1 case of lung cancer diagnosed at initial presentation, MTX was used (2 mg to 12 mg/week). There were 6 deaths and age of death was 87.7±4.2 years. Two patients died of lung cancer and 4 patients died of old age. Disease activity was remission or low just before death. The 6 living patients are 86.0±7.4 years old and the oldest is 100 years old. About the disease activity, 5 cases were remission and 1 case was low. [Conclusions] Patients whose onset of RA were over 70 years were investigated for 10 to 13 years. There were 6 deaths and age of death was 87.7±4.2 years. Disease activity was remission or low when the evaluation was done.

## P3-106

**Morbidly Obese Rheumatoid Arthritis Patient Undergoing Bariatric Surgery: A Case Report**

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Conflict of interest: None

[Background] Obesity contributes to treatment resistance in rheumatoid arthritis (RA). Bariatric surgery is effective for pathological obesity but lacks clinical evidence in RA. This case discusses a RA patient benefiting partially from bariatric surgery. [Case] A 42-year-old female, previously treated with tocilizumab, methotrexate, and steroids, relocated five years ago. At her initial assessment, her weight was 113 kg, BMI 40.5 kg/m², anti-CCP antibody 733, CRP 4.11, and MMP-3 2125.8. Hospitalization resulted in weight reduction through diet and rehab. A switch to sarilumab lowered disease activity, MMP-3 to 93.2. Weight gradually increased to 116 kg a year ago, with renewed pain and joint issues. MMP-3 peaked at 1745.2, CRP at 2.27. Bariatric surgery led to 91.6 kg weight and reduced CRP (0.47) and MMP-3 (438.1) in six months. Joint symptoms improved, and effusion resolved. [Clinical Significance] Bariatric surgery is a promising intervention for pathological obesity-associated RA. Tailoring treatment to individual patients is vital, with bariatric surgery a beneficial option in select cases.

## P3-107

**Differences between Immunology and Orthopedic Departments in Bio/JAK Inhibitor Treatment for Rheumatoid Arthritis: the ANSWER cohort study**

Yuki Etani[1], Kosuke Ebina[1,2], Takaaki Noguchi[2], Yasutaka Okita[3], Kohei Tsujimoto[3], Iku Shirasugi[4], Mai Yamashita[4], Koji Nagai[5], Ayaka Yoshikawa[5], Motomu Hashimoto[6], Tadashi Okano[7], Yuji Nozaki[8], Tetsu Itami[8], Yonsu Son[9], Hidehiko Makino[9], Koichi Murata[10], Takayuki Fujii[10], Wataru Yamamoto[11], Atsushi Kumanogoh[3], Seiji Okada[2]
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Conflict of interest: None

[Objective] The aim of this study was to compare differences in patient background, treatment and course of treatment depending on whether the attending physician is an immunologist or an orthopaedic surgeon. [Methods] The subjects were 4391 cases (immunology: 3402, orthopaedics: 989) newly administered biologics or JAK inhibitors in the ANSWER cohort. Patient backgrounds and treatments were compared. After 24 months, continuation rates and reasons for discontinuation were assessed using Cox proportional hazard models. [Results] Orthopaedic patients were younger (58.4 vs 60.6 years), more female (86.7% vs 81.2%), with higher autoantibody positivity. Steinbrocker classification showed higher Stage in orthopedics (Stage 3 or 4; 62.0% vs 38.6%). No significant differences were found in disease activities. MTX usage was higher in orthopaedics (51.3% vs 40.2%), as were JAK inhibitors (20.7% vs 13.6%), while abatacept usage was lower (6.5% vs 18.8%). Discontinuation due to ineffectiveness was higher in orthopaedics (HR 1.2990; 95% CI 1.11-1.52), while adverse events led to fewer discontinuations (HR 0.7254; 95% CI 0.54-0.98). [Conclusions] Orthopaedic outpatients presented more advanced joint destruction, indicating higher ineffectiveness of biological agents/JAK inhibitors.

## P3-108

**Which mode of action is best for difficult-to-treat rheumatoid arthritis when switching biologics or JAK inhibitors?**

Takuya Tachibana[2], Yutaro Yamada[1], Kenji Mamoto[1], Tadashi Okano[3], Takahito Kojima[1], Shohei Anno[4], Kazuki Orita[4], Takahiro Ida[5], Masahiro Tada[6], Kentaro Inui[7], Tatsuya Koike[8], Hiroaki Nakamura[1]
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Conflict of interest: None

Background/Purpose There are rheumatoid arthritis patients with difficult disease activity control even after using several biologics or Janus kinase inhibitors (BIO/JAKi). Among these D2TRA patients, we investigated the efficacy of switching BIO/JAKi by their mode of action. Methods Total of 185 patients switched to another BIO/JAKi because of being considered as D2TRA. The following BIO/JAKi consists of TNFi (n=20), IL6i (n=32), ABT (n=29), JAKi (n=104). We investigated clinical characteristics and efficacy of following BIO/JAKi for 52 weeks. Results The average age was 62.9, disease duration was 16.1 years at the time of switching (baseline). Retention rate of the following BIO/JAKi at 52w was 60.0%, 56.3%, 51.7%, 48.1%, respectively. DAS28ESR improved from 5.66 to 4.37, 5.19 to 2.78, 4.62 to 4.13, 4.72 to 3.98, and CDAI improved from 27.3 to 12.7, 22.1 to 10.5, 19.2 to 13.6, 20.0 to 12.2, and

MMP3 improved from 185.3 to 119.0, 365.6 to 137.8, 172.3 to 141.7, 287.5 to 110.6, respectively. Conclusion Switching BIO/JAKi was effective for D2TRA regardless of mode of action. IL6i and JAKi were especially effective for patients with high MMP3, whereas TNFi was effective for patients who can use MTX and have high CDAI.

## P3-109

**Comparison of treatment efficacy of second TNF inhibitors and non-TNF inhibitors after first TNF inhibitor failure at our hospital and related facilities**

Ryosuke Koizumi[1,2], Michitomo Sakuma[1], Kensuke Koyama[2,3], Hirotaka Haro[2]
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Conflict of interest: None

[Objective] JCR guidelines recommend switching to non-TNF inhibitors (nTNFi) rather than other TNF inhibitors (TNFi) in patients with inadequate response to TNFi, but the recommendation is weak, and the evidence is insufficient. In this study, we aimed to investigate the efficacy of 2nd TNFi and nTNFi after 1st TNFi failure at our hospital and related institutions. [Methods] 16 RA patients who changed drugs after 1st TNFi failure between 2007 and 2023 at our hospital and related institutions were included, and classified into two groups: 2nd TNFigroup (T group) and nTNFi group (N group). Patient background, survival time of the second drug, drug continuation rate after 1 year, LDA and remission rate, disease activity, and failure rate of the 2nd drug were compared. [Results] Patient background was significantly higher in the T group only for MTX use. There were no significant differences in survival time of the second drug, drug continuation rate after 1 year, LDA and remission rate, and disease activity between the two groups, but the second drug failure rate was 80% in the T group and 33.3 in the N group, p=0.06, showing a tendency for the N group to have lower. [Conclusions] As in previous reports, switching to a nTNFi formulation was considered superior.

## P3-110

**Clinical Outcomes in Patients with Rheumatoid Arthritis using Biologic Drugs and Janus Kinase Inhibitors: a Comparison using Patients' Age**

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Conflict of interest: None

We investigated the background of patients with rheumatoid arthritis (RA) using biologics and Janus kinase inhibitors (JAKs); clinical outcomes were evaluated and compared using patients' age. We investigated the treatment of 62 patients with RA (17 males and 45 females), who had been using biologics or JAKs for >6 months. The mean age and illness duration were 71.2 (44-95) years, and 10 (1-28) years, respectively. Treatment outcomes of patients >75 years (group O) and <75 years (group Y) of age were separately compared. Forty-nine biologic drugs (18 tumor necrosis factor α inhibitors, 22 interleukin-6 inhibitors, and 9 cytotoxic T lymphocyte antigen-4 inhibitors) and 13 JAKs were included. Group Y used more Methotrexate. Overall, usage of immunosuppressive drugs with leflunomide and tacrolimus by group O (15 [58%] patients) was significantly less frequent than that by group Y (30 [83%] patients) ($p$ = 0.04). Monotherapy appeared more prominent in group O ($p$ = 0.05). Comorbidities, such as renal dysfunction and dementia, limit the usage of drugs in elderly patients. Biologics and JAKs are effective options for elderly patients if the type of drug, concomitant medications, and method of use are carefully considered.

## P3-111

**Evaluation of the significance of comprehensive testing for induction of biological DMARDs in inflammatory arthritis**

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Conflict of interest: None

[Objective] Biological DMARDs have superior therapeutic efficacy compared to existing therapies, but cost-effectiveness and persistence remain problems. We examined the implications of short-term hospitalization and comprehensive testing for the use of Biological DMARDs. [Methods] From May 2022 to August 2023, we performed patient education and comprehensive examinations by ultrasonography, physiology, endoscopy, and radiology during short-term hospitalization before the use of biological DMARDs for rheumatoid arthritis and spondyloarthritis. [Results] During this period, 18 patients were hospitalized, with a mean age of 63.7 years. The mean duration of disease at drug induction was 81.6 months, and DAS28CRP was 3.25 (±1.12). There were no active infections or malignancies. 7 patients used TNF inhibitors, 4 IL-6 inhibitors, 1 IL-23 inhibitor, and 1 CTLA4-Ig formulation, respectively. During the observation period after induction, there were no cases of change or discontinuation of the drug of choice and no serious side effects were observed. All 11 patients who were receiving GC at induction received a reduced dose of GC and 4 of them discontinued GC. [Conclusions] We suggest that comprehensive examinations with a short hospitalization for the using of agents has many advantages.

## P3-112

**A survey on the actual situation for self-injection of biological disease-modifying antirheumatic drugs in patients with rheumatoid arthritis**

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Conflict of interest: None

[Objective] To describe the patients' characteristics, health-related quality of life and work productivity in patients with rheumatoid arthritis (RA) who had selected self-injection (SI) of biological disease-modifying antirheumatic drugs (bDMARDs) and those who had not. [Methods] Online questionnaire survey for national monitor panels (November 2022 to January 2023) provided by Medilead Inc. was used to describe the patients' background, proportion of employees, EQ-5D and WPAI in the bDMARDs users treated with SI (SI group) and those without SI (non-SI group), respectively. [Results] Of 139 patients who reported RA as their primary disease (female: 66.9%, mean age: 60.0 years), 40.3% were bDMARDs user, and 69.6% of them selected SI. The proportion of employed patients in the SI group (53.8%) were higher than that in the non-SI group (41.2%). EQ-5D were 0.78±0.12 in the SI group, 0.74±0.22 in the non-SI group, respectively. Absenteeism, presenteeism and overall work impairment by WPAI were 23.5 ± 35.2%, 29.0 ± 22.8% and 42.8 ± 35.9% in the SI group, 0%, 20.0 ± 34.2% and 20.0 ± 34.2% in the non-SI group, respectively. [Conclusions] There were differences in the proportion of employees and WPAI between the SI and non-SI groups, whereas, similar EQ-5D in both groups were observed.

## P3-113

**Efficacy and safety of upadacitinib in patients with rheumatoid arthritis in Niigata Prefecture, Japan (SELECT-NIIGATA study)**

Yuto Tanno[1], Naoki Kondo[2], Satoshi Ito[3], Yoko Wada[4], Yoichi Kurosawa[1], Eriko Hasegawa[1], Ayako Wakamatsu[1], Hiroe Sato[5], Takeshi Kuroda[5], Rika Kakutani[2], Sayuri Takamura[3], Masanori Sudo[3], Asami Abe[3], Daisuke Kobayashi[1], Ichiei Narita[1]
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Conflict of interest: None

[Objective] This study evaluated the efficacy and safety of upadaci-

tinib (UPA) in rheumatoid arthritis (RA) patients in Niigata Prefecture, Japan. [Methods] We retrospectively analyzed 81 RA patients (17 males, 64 females) who started UPA between November 2020 and October 2022. We assessed patients' characteristics, treatment response, continuation rate, and adverse events at 52 weeks after initiation. [Results] The mean age was 66.0±11.4 years, and the mean disease duration was 12.9±9.7 years. Of the patients, 75.3% were RF-positive, 51.9% were positive for anti-CCP antibodies, and 9.9% were negative for both antibodies. The CDAI, DAS28-ESR, and serum MMP-3 levels decreased significantly. Events leading to UPA discontinuation were ineffectiveness in 4 patients, fever in 2 patients, bronchitis, fatigue, CK elevation, stomatitis, and non-compliance in 1 patient each. Other adverse events included herpes zoster in 5 patients, upper respiratory tract infection in 4 patients, liver dysfunction in 3 patients, urinary tract infection, back abscess, and herpes labialis in 1 patient each. [Conclusion] UPA significantly reduced RA disease activity and had a high continuation rate. Serious adverse events were rare, and efficacy and safety were confirmed.

## P3-114

**The status and effectiveness of upadacitinib for patients with rheumatoid arthritis in Tsurumai Biological Communication Registry**

Takaya Sugiura[1], Kenya Terabe[1], Mochihito Suzuki[1], Tatsuo Watanabe[2], Yutaka Yoshioka[5], Yuji Hirano[6], Hisato Ishikawa[8], Yasumori Sobue[8], Yasuhide Kanayama[15], Yosuke Hattori[4], Takefumi Kato[3], Takeshi Oguchi[9], Toki Takemoto[9], Takayoshi Fujibayashi[17], Daizo Kato[10], Tsuyoshi Nishiume[10], Tomonori Kobayakawa[11], Takuya Matsumoto[12], Mihoko Kato[12], Hiroyuki Matsubara[13], Tsuyoshi Watanabe[16], Masahiro Hanabayashi[14], Toshihisa Kojima[4], Nobunor Takahashi[7], Shuji Asai[1], Shiro Imagama[1]

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Conflict of interest: None

Object This study aimed to investigate the status and effectiveness of updacitinib (UPA) treatment for patients with rheumatoid arthritis (RA). Methods A total of 86 RA patients who received UPA treatment were included in the study. We examined the status of UPA treatment in patients at TBCR. We assessed changes in SDAI, the rate of UPA discontinuation, and the incidence rate of herpes zoster infection. Results The mean age of the overall patient population (± standard deviation [SD]) was 67.1±12.8 years, with 86% being female. The mean disease duration was 12.7±11.1 years, and 33% had an eGFR (mL/min/1.73m2) below 60. Concomitant use of MTX/glucocorticoid was 42%/45%. Additionally, 73% of patients had a history of previous treatment with bDMARDs or JAK inhibitors. SDAI scores changed from 22.2±12.6 at baseline to 9.3±9.5 after 4 weeks and 6.3±7.6 after 24 weeks, showing significant improvement. The remission rate at 24 weeks was 44.6%. 11 patients discontinued UPA treatment. The incidence rate of herpes zoster infection was 4.65 (per 100 patient-years). Conclusion Patients treated with UPA had a higher mean age, lower concomitant use of MTX, and a higher history of previous treatment with bDMARDs or JAK inhibitors.

## P3-115

**Differences in the Usefulness of upadacitinib (UPA) in Combination with methotrexate (MTX)**

Hiroto Yamamoto[1], Kenya Terabe[1], Takefumi Kato[2], Toshihisa Kojima[3], Takeshi Oguchi[4], Yasuhide Kanayama[5], Yuji Hirano[6], Takayoshi Fujibayashi[7], Tsuyoshi Watanabe[8], Nobunori Takahashi[9], Daizo Kato[10], Hisato Ishikawa[11], Hiroyuki Matsubara[12], Yosuke Hattori[3], Masahiro Hanabayashi[13], Toki Takemoto[4], Tatsuo Watanabe[14], Yutaka Yoshioka[15], Tsuyoshi Nishiume[10], Takuya Matsumoto[16], Mihoko Kato[16], Tomonori Kobayakawa[17], Yasumori Sobue[11], Shuji Asai[1], Shiro Imagama[1]

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Conflict of interest: None

Object This study aimed to investigate the effectiveness of concomitant methotrexate (MTX) in upadacitinib (UPA) treatment for rheumatoid arthritis (RA). Methods A total of 86 RA patients were divided into non-concomitant MTX group (N group) and concomitant MTX group (M group). We investigated the change of SDAI and the rate of discontinuation. Results 50 were in N group and 36 were in M group. Patients in N group were a significantly higher proportion of previous bDMARDs/JAK inhibitor treatment (N: 88%, M: 53%) and the rate of eGFR (mL/min/1.73m2) below 60 was N: 43%, M: 19%. Although there were not significant differences, the mean age was higher in N group than in M group (N: 69.3±10.8, M: 64.0±12.6). Mean SDAI significantly decreased in both groups (N: 20.9±12.4 to 6.9±7.3, M: 9.2±12.9 to 5.6±7.3). The patients who were discounted were one patient in N group and three patients in M group while there were no significant differences between the two groups by Cox Hazard models analysis. The patients with herpes zoster were three in N group, and two in M group. Conclusion There were no significant differences in the effectiveness of UPA between the concomitant MTX or not. These results suggested that UPA will be a useful treatment for RA patients who are intolerant to MTX.

## P3-116

**Characteristics and Outcomes of Patients with Rheumatoid Arthritis in Japan Treated with Upadacitinib in a Real-World Setting**

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Conflict of interest: Yes

Objectives To describe characteristics and outcomes of patients (pts) with rheumatoid arthritis (RA) treated with upadacitinib (UPA) in Japan. Methods Data were drawn from the Adelphi RA Disease Specific Pro-

gramme™, a cross-sectional survey of rheumatologists and their RA pts currently receiving UPA ≧ 6 months in Japan. Physicians provided clinical data and Pts completed PROs. All data were analysed descriptively. Results Rheumatologists (n=46) reported that UPA pts (n=99) had a mean [SD] age of 63.4 [14.0]. Of UPA pts with ≧ 1 prior AT use (n=66), 65.2% had prior use of a TNFi, 39.4% a JAKi, 34.8% IL-6 and 25.8% CTLA4. At UPA initiation, 37.4% pts had moderate/high (29.3%/8.1%) DAS28 and 62.7% had moderate/severe pain (47.5%/15.2%). At follow-up, 97.9% of patients were in remission/low disease activity (LDA) (54.5%/43.4%), 97.0% had mild/no pain (50.5%/46.5%) and 92.9% had mild/no fatigue (43.4%/49.5%). Pts reported mean [SD] scores of 39.2 [9.4] on FACIT-Fatigue (n=79), 0.8 [0.72] on J-HAQ-DI (n=79) and 0.794 [0.17] on EQ-5D-5L (n=76). Conclusion This analyses of real-world data on Japanese patients with RA receiving UPA ≧6 months showed that UPA is an efficacious therapy, with 97.9% patients in remission/LDA, 97.0% with mild/no pain and 92.9% with mild/no fatigue.

## P3-117

**Discontinuation of methotrexate in rheumatoid arthritis patients achieving clinical remission by treatment with upadacitinib plus methotrexate (DOPPLER study) -study protocol and patient demographics report-**

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Conflict of interest: Yes

[Objective] To evaluate changes in disease activity after the addition of upadacitinib (UPA) in rheumatoid arthritis (RA) patients refractory to methotrexate (MTX) and to determine whether clinical relapse can be avoided after discontinuation of MTX in those who achieve clinical remission. [Methods] This study is an interventional, single-arm clinical trial. It will include a total of 155 RA patients with at least moderate disease activity while on MTX. Patients will receive UPA, and MTX will be discontinued for those who achieve clinical remission at week 24. The primary endpoint is the proportion of patients who sustain a DAS28-CRP ≦3.2 until week 48. We will also conduct musculoskeletal ultrasound and analyze serum biomarkers. Patient enrollment will continue until March 31, 2025; thus, the study is still ongoing. We analyzed patient demographics for the enrolled cases. [Results] We have evaluated 49 cases available for analysis of patient demographics. The median age of the patients was 66 years, with 77.6% being female. Among them, 81.6% had rheumatoid factor, 73.5% had anti-CCP antibody, and the median MTX dose was 10 mg/week. The median DAS28-CRP was 4.7, while the median DAS28-ESR was 5.28. [Conclusions] We showed the study protocol and the demographics of the enrolled patients.

## P3-118

**Short-term results of Upadacitinib in patients with rheumatoid arthritis refractory to multiple biologics/JAK inhibitors**

Yuma Saito, Yuji Hirano
Toyohashi Municipal Hospital

Conflict of interest: None

[Objective] To evaluate the short-term results of upadacitinib (UPA) in rheumatoid arthritis (RA) patients with multiple drug failure of biologic agents (Bio)/JAK inhibitors (JAKi) in the Toyohashi RA Database (TRAD). [Methods] 12 RA patients who used UPA after December 2021 and could be observed for at least 24 weeks were included. Patient background, disease activity, methotrexate (MTX) use, adverse events and continuation rates were examined. [Results] The mean age of the patients was 71.4 years. The mean duration of disease was 16 years, MTX was used in 3 patients. 75% of patients were on their fourth or more Bio/JAKi drug, 2 were on their third drug. 83.3% were difficult-to-treat (D2TRA) cases, according to the EULAR definition. The mean DAS28-CRP was 3.91 at initiation, 4 weeks: 2.23 ($p<0.05$), 12 weeks: 2.9 ($p=0.08$), 24 weeks: 2.07 ($p<0.05$). Mean SDAI was 21.4 at initiation, 4 weeks: 7.18 ($p=0.049$), 12 weeks: 10.14 ($p<0.05$), 24 weeks: 5.05 ($p<0.05$). Adverse events occurred in 4 patients (33%), and discontinuation occurred in 3 patients (83%) at 6 months. [Conclusions] Although UPA improved disease activity in Bio/JAKi multidrug-refractory patients, including many D2TRA patients. Because of adverse events in 33% of patients, the course of the disease should be carefully monitored.

## P3-119

**Efficacy and safety of switching to JAKi (upadacitinib) low-dose monotherapy in 19 patients with rheumatoid arthritis in remission with b-DMARDs**

Kenji Souda
Murakami Clinic

Conflict of interest: None

[Objective] In this study, we switched from b-DMARDs to JAKi's upadacitinib (Upa) based on Shared Decision Making (including the possibility of lower cost and its side effects), and examined its efficacy and safety. [Methods] Nineteen patients in remission with b-DMARDs were switched to Upa 7.5 mg daily or every other day and observed for about 2 years. [Results] Almost all patients had better quality of life. 1 patient had herpes zoster. 2 patients had hemopenia. 4 patients increased dose to 15 mg. 1 patient returned to original b-DMARD. One patient returned to b-DMARD. Many patients on concomitant prednisolone were able to reduce or discontinue the dose. [Conclusions] Although JAKi has been used in clinical practice for 10 years, its use is still infrequent, probably due in part to the high cost of the drug. In this study, we found that a small dose of 7.5 mg of Upa (about one-fourth of the dose every other day) was sufficient to control the disease from a cost perspective, and that MTx is difficult to use in elderly patients, but MTx-free Upa monotherapy is useful. In the case of bDMARDs, spacing/tapering has already been tried, and switching to a small dose of JAKi may be an option.

## P3-120

**Evaluation of efficacy and safety of JAK1/2 inhibitor baricitinib in treatment algorithm phase 2**

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Conflict of interest: None

[Objective] We evaluated the efficacy and safety of baricitinib in phase II of the treatment algorithm. [Methods] The subjects were 191 patients who met the ACR/EULAR RA classification criteria and started receiving baricitinib. Continuation rate in Phase II and Phase III of the JCR treatment algorithm, CDAI improvement rate were evaluated. [Results] Of 191 patients treated with baricitinib (28 men, 163 women, mean age at start of treatment 62.0+/-13.0 years), 93 patients (48.7%) were in the phase II initiation group. In the phase II initiation group, treatment continuation rate (89.7% at 26 weeks, 84.4% at 52 weeks, Log-rank p=0.002) and CDAI improvement rate (85.0% at 26 weeks, 95.5% at 52 weeks, p<0.0001). The number of patients with insufficient treatment response (48) was higher in the phase III group (67%, p=0.0131), and the number of 139 patients who achieved low CDAI disease activity at week 12 of baricitinib treatment was significantly higher in the phase II group (p =0.0076). The 31 patients who discontinued the study due to adverse events were related the majority were over 65 years of age or had at least one CV risk. [Conclusions] We found that the introduction of baricitinib in phase II of the treatment algorithm significantly improved disease activity.

## P3-121

**Investigation of the efficacy of baricitinib and the factors contributing to improvement of DAS28CRP in patients with rheumatoid arthritis switched to baricitinib**

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Conflict of interest: None

[Objective] To investigate the efficacy of baricitinib (BAR) and factors contributing to improvement in disease activity indices such as DAS-28CRP in patients with rheumatoid arthritis (RA) switched BAR. [Methods] We examined changes in DAS28CRP, SDAI, changes in each of the components of DAS28CRP, and in blood concentration of MMP-3, after 3 months of treatment in RA patients (3 males and 17 females) who switched to BAR. [Results] The mean DAS28CRP significantly decreased from 3.07 before treatment to 2.70 after 3 months from baseline, SDAI from 14.8 to 11.2, and serum concentration of MMP-3 from 206.5 (ng/dl) to 110.5. The number of swollen joints significantly improved from 5.6 before treatment to 4.0 and the general vas (PGA) from 28.9 to 20.9. The number of tender joints, CRP, and blood sedimentation rate improved, but not significantly. The pain VAS significantly improved from 26.3 to 22.7. [Conclusions] Disease activity by DAS28CRP showed remission in 10 patients and low disease activity in 3, showed effectiveness of BAR treatment in RA switch cases. Both PGA and pain VAS improved with BAR administration, suggesting that this improvement in pain may have contributed to BAR efficacy.

## P3-122

**The long-term efficacy of disease activity and safety of treatment with low dose baricitinib in elderly rheumatoid arthritis patients with inadequate response to methotrexate therapy**

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Mie University Graduate School of Medicine, Mie, Japan

Conflict of interest: None

[Objective] The therapeutic effect of low-dose baricitinib (JAK1/2 inhibitor) on elderly rheumatoid arthritis (RA) patients was investigated. [Methods] Twelve RA patients aged 65 years or older who had insufficient MTX effect started treatment with baricitinib 2 mg/day and were able to follow up until 52 weeks later were included. The continuation rate, therapeutic effect and adverse effects up to 52 weeks of treatment were evaluated. [Results] The patients were 9 females and 3 males, with an average age at the start of baricitinib treatment of 74.5 years. The disease activity of DAS-ESR/SDAI/CDAI before treatment was 4.3/13.6/12.8. Baricitinib was discontinued in 2 patients due to gastric discomfort and thrombocytosis 2 weeks after treatment. In other 10 patients, hepatic function increased, leukocyte depletion, cold, ingrown toenail, dizziness and stone cholangitis were observed during the administration period, requiring temporary suspension of medication in some cases. But they continued to treat with baricitinib 2 mg/day until 52 weeks, and their disease activity was improved significantly. [Conclusions] Low-dose baricitinib for elderly RA patients may be an efficacy and safety option, but adverse events should be noted in the early stages.

## P3-123

**Efficacy and safety of Baricitinib 2 mg with and without reduced renal function**

Mirai Hozumi[1], Takanori Ito[1], Sho Higuchi[1], Yukina Yokoyama[1], Yui Amari[1], Mizuki Kato[1], Mitsuru Watanabe[1], Tatsuo Watanabe[2], Yoichiro Haji[1]
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Conflict of interest: None

[Objective] Baricitinib (BAR) 2 mg is mainly used in rheumatoid arthritis (RA) patients with reduced renal function (RRF), but its efficacy on BAR 2 mg is unclear. In this study, we investigated it. [Methods] RA patients, treated with BAR 2 mg until October 1, 2023, were divided into two groups: RRF group (eGFR <60 mL/min/1.73 m2) or not. We analyzed for CDAI remission at the last visit, continuation rate, and presence of complications. [Results] 43 patients were divided into two groups: 22 in the RRF and 21 in the non-RRF group. There were no differences in age (76 vs. 59 years, 86% vs. 76% female), disease duration (median 79 vs. 33 months, p=0.08), RF/ACPA positivity (82% vs. 71% RF, 64% vs. 76% ACPA), and history of biologic agent (64% vs. 57%). Disease activity (CDAI) at baseline was intermediate in both groups (median 11 vs. 21, p=0.5). Efficacy was similar in BAR use duration, persistence rate, and remission rate (median 10 vs. 14 months p=0.4, 73% vs. 56%, 36% vs. 23%). Inadequate response discontinuation; 3 in the RRF group and 8 in the non-RRF group. Safety; 5 and 3 developed infectious diseases during the observation period, respectively. [Conclusion] In this study, there was no significant effect of impaired renal function on the efficacy or safety of BAR 2 mg.

## P3-124

**Efficacy of once-daily baricitinib 2 mg in patients with rheumatoid arthritis, a single-center study**

Sho Higuchi[1], Mitsuru Watanabe[1], Takanori Ito[1], Mirai Hozumi[1], Yukina Yokoyama[1], Yui Amari[1], Mizuki Kato[1], Tatsuo Watanabe[2], Yoichiro Haji[1]
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Conflict of interest: None

[Objective] Baricitinib (BAR) is recommended for adult rheumatoid arthritis (RA). Low-dose BAR is reported to be effective, but the efficacy and drug survival are uncertain. [Methods] We retrospectively collected data of patients who initiated BAR 2 mg and evaluated the disease activity score based on CDAI at 24 weeks, MTX reduction, and the drug retention rate. [Results] 43 patients were included. Median age was 73 years, 35 (81.4%) were female, median duration of disease was 63.0 months, 27 (62.3%) were on MTX, 23 (53.5%) were on b/ts DMARDs, 22 (51.2%) had coexisting CKD, and median CDAI was 13.0. LDA based on CDAI was achieved in 88.9% of patients and remission was achieved in 61.1%. MTX dose was reduced in 19 patients (73.1%) and discontinued in 5 patients (18.5%). The median duration of BAR exposure was 10.0 months and the most common reason for discontinuation was ineffectiveness (73.3%). The retention rate was 76.4% in b/ts DMARDs naïve patients. The continuation rate for patients with ILD comorbidity was 66.7% (4/6), and 72.7% (16/22) in patients with CKD. [Conclusion] Low-dose BAR was appropriate for b/ts DMARDs naïve patients. The efficacy is suggested in patients with comorbidities such as ILD or CKD.

## P3-125

**Long-term efficacy and safety of Baricitinib (2 mg) in patient with rheumatoid arthritis in a routine care**

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Conflict of interest: None

[Objectives] Baricitinib (BAR) is a JAK inhibitor that has been prescribed in a routine care in Japan since 2017. There are a few studies that have examined the efficacy of BAR begun at one-half dose (2 mg) in RA patients in a routine care. In this study, we investigated the long-term efficacy of BAR in RA patients. [Methods] RA patients treated with BAR for longer than 3 years were included in this study. We retrospectively reviewed the efficacy (DAS28-CRP), discontinuation of BAR therapy and adverse event in one-half dose (2 mg group) and typical dose (4 mg group), respectively. [Results] Twenty-three (2 mg group) and fifteen (4 mg group) patients were included in this study. Mean age was 66 and 68 years old and concomitant methotrexate rates are 74% and 93% (2 mg and 4 mg groups, respectively). Mean DAS28-CRP was 3.9 and 3.6 at baseline, and 1.3 and 1.3 at 3 years (2 mg and 4 mg groups, respectively). The number of patients who withdrew from BAR was nine (2 mg group) and six (4 mg group). Serious adverse event is none in two groups. [Conclusion] Typical dose (4 mg) but also one-half dose (2 mg) of BAR was effective in RA patients in a routine care. This study provides support for the possible use of one-half dose of BAR in RA patients.

## P3-126

**Outcome of treatment with Baricitinib for difficult-to-treat RA arthritis at our hospital**

Ayaka Takahashi, Kiichiro Ando, Atsushi Imamura
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Conflict of interest: Yes

[Objective] In the past, there were no effective treatments for RA, which often resulted in joint deformities, bedridden, and a decline in ADLs. In recent years, however, with the advent of DMARDs and biological agents such as bDMARDs, it has become possible to achieve remission by starting treatment before the appearance of bone destruction. On the other hand, there are a certain number of patients with D2T-RA who show little improvement even with bDMARDs. We report here the results of a study of our D2T-RA patients treated with Baricitinib, a tsDMARD, with good results. [Methods] Mean age at Baricitinib induction: 72.7±10.12 years, mean CRP: 1.90±2.36 mg/dl. One male and 10 female patients were included in the study. The mean CRP at 12 weeks after introduction of Balicitinib was 1.95±3.00 mg/dl, but arthralgia and extra-articular symptoms were markedly improved. It has been 1-4 years, and the clinical symptoms have improved and no serious side effects have been observed. [Conclusions] In this study, Baricitinib showed high clinical efficacy and usefulness in RA patients who were refractory to MTX and bDMARDs after treatment. However, since tsDMARDs have only been on the market for a short period of time, further studies are needed on their long-term safety and other aspects.

## P3-127

**The efficacy of baricitinib at 1 year in patients with rheumatoid arthritis in our institution. (2nd report)**

Yayoi Hashiba[1], Kota Imaizumi[1], Masayuki Murai[1], Kazuyoshi Kubo[1], Atsushi Matsuoka[2], Hiroshi Kuroda[2], Toshihiko Hidaka[1]
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Conflict of interest: None

[Objective] To assess the efficacy of baricitinib (BARI) in patients with rheumatoid arthritis. [Methods] Thirty-three RA patients were initiated BARI in our institution from May 2018 to May 2023, and 30 of them were continued BARI over three months. DAS28-CRP and CDAI were assessed at the point of 0,1,2,3,6,12 months. [Results] DAS28-CRP / CDAI after initiation of BARI decreased as follows; DAS28-CRP/CDAI 0 month: 33.95/18.13, 0.5 month: 2.89/11.40, 1 month: 2.50/8.70, 2 months: 2.48/6.93, 3 months: 2.21/7.06, 6 months: 2.35/7.33, 12 months: 2.24/6.60 with significant difference (respectively, $p<0.01$/$p<0.01$) 2 weeks later onward. Remission rate of DAS28-CRP/CDAI was as follows; 0 month: 13%/3%, 3 months: 70%/53%,6 months: 70%/53%, 12 months: 67%/43% and under low disease activity rate was as follows; 0 month: 23%/27%,3 months: 77%/80%,6 months: 73%/77%, 12 months: 70%/83%. [Conclusions] These data indicate that BARI therapy can be expected to have sustained efficacy from the initial stage.

## P3-128

**A study of patients undergoing dose reduction or treatment switch based on safety considerations after initiating treatment with JAK inhibitors**

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Conflict of interest: None

[Objective] To examine patients undergoing dose reduction or treatment switch based on safety considerations after initiating treatment with JAK i. [Methods] To date, 178 patients have been treated with JAK i. This study included 53 patients who had been treated with BARI (20), PEFI (3), UPA (20) or FIL (10) and subsequently underwent dose reduction or treatment switch based on safety considerations. [Results] The reasons for dose reduction or treatment switch included liver and kidney function test abnormalities in 17 and 16 patients, respectively, and other adverse events in 19 patients. Specifically, liver function test abnormalities were observed in 6 patients treated with BARI, 9 with UPA, and 2 with FIL, while kidney function test abnormalities were observed in 7 patients receiving BARI, 3 receiving PEFI, 3 receiving UPA, and 3 receiving FIL. Other adverse events included elevated CK levels in 4 patients, precancerous conditions/solid cancer in 3, decreased total lymphocyte counts in 3, and dizziness in three. [Conclusion] Safety profiles differed among JAK i, suggesting that each inhibitor has different issues. Further, kidney function test abnormalities were observed for all JAK i, suggesting such abnormal values should be given particular attention.

## P3-129

**Treatment status of RA patients who have been receiving JAK inhibitors for more than 3 years at our clinic**

Toshiharu Okuda
Okuda Orthopedic Clinic

Conflict of interest: None

[Purpose] Since November 2014, our hospital, which is an orthopedic clinic, has been administering JAK inhibitors to rheumatoid arthritis patients (RA). We have investigated the status of treatment. [Method] The subjects were 65 casesem who had been using JAK inhibitors for the first time for more than 3 years. The mean age was 66.7 years, and the JAK inhibitors used were tofacitinib (TOF) in 31 cases, baricitinib (BAR) in 30 cases, upadacitinib (UPA) in 4 cases, and bionaive cases in 23 cases. There were 42 patients who changed from biologics. Of these cases, we investigated the continuation status of the first JAK inhibitor in 51 cases whose status could be confirmed after 3 years. [Results] 26 patients (TOF 10 / BAR 14 / UPA 12) continued on the first JAK inhibitor. There were 11 cases (TOF 4/BAR 6/UPA 1) who changed to another JAK inhibitor within 3 years. There were 12 patients who changed to a biologic agent, and 9 patients requested a change to a TNF agent before using a JAK inhibitor. Among the bionaive patients (19 patients), all patients continued to take JAK inhibitors (change 4). [Conclusion] The 3-year continuation rate of JAK inhibitors was high in bionaive patients, but in some patients treated with biologics, the drug was changed at an early stage.

## P3-130

**Janus kinase inhibitors suppress vascular endothelial growth factor-induced angiogenesis in human endothelial cells**

Kensuke Wada[1], Shinya Hayashi[1], Toshihisa Maeda[2], Naoki Nakano[1], Tomoyuki Kamenaga[1], Masanori Tsubosaka[1], Kensuke Anjiki[1], Kemmei Ikuta[1], Yuma Onoi[1], Shotaro Tachibana[1], Tsukasa Matsubara[2], Ryosuke Kuroda[1]
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Conflict of interest: None

[Object] The Janus kinase (JAK)/signal transducer and activator of

transcription (STAT) signaling pathways play an important role in angiogenesis. The present study aimed to compare the therapeutic effects and mechanism of tofacitinib (TOF), baricitinib (BAR), and peficitinib (PEF) on angiogenesis induced by vascular endothelial growth factor (VEGF). [Methods] Human umbilical vein endothelial cells (HUVECs) were treated with VEGF, including TOF, BAR, or PEF. The viability, migration, and tube formation of the HUVECs were evaluated and tube formation including JAK2 or JAK3 selective inhibitors (JAK2-I, JAK3-I) were also evaluated. Additionally, STAT3 phosphorylation in HUVECs stimulated with VEGF and the suppression by JAK inhibitors were evaluated using western blotting. [Results] TOF, BAR, and PEF suppressed VEGF-induced cell viability and tube formation. JAK3-I suppressed VEGF-induced tube formation more than JAK2-I. VEGF-induced cell migration was suppressed by TOF and PEF but not by BAR treatment. VEGF-induced STAT3 phosphorylation was inhibited by TOF, PEF, and JAK3-I, but not BAR and JAK2-I. [Conclusions] VEGF-induced angiogenesis in HUVECs was suppressed by JAK inhibitors, especially TOF and PEF. The JAK3/STAT3 signaling pathway may be essential for VEGF-induced angiogenesis.

## P3-131

**Reason of discontinuation of JAK inhibitor for rheumatoid arthritis in our hospital: From the NOSRAD registry**

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Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan

Conflict of interest: None

[Objective] To consider the reason of discontinuation of JAK inhibitor for rheumatoid arthritis in our hospital: From the NOSRAD registry [Methods] 1517 patients of rheumatoid arthritis who introduced bDMARDs or JAK inhibitor before August 2022 were included in this study. [Results] The average age at the start of administration of abatacept (70.3±11.5 years old) and JAK inhibitor (68.9±13.2 years old) were significantly higher than TNF-α inhibitor (56.7±15.7 years old) and anti-IL-6 receptor antibody (61.8±15.8 years old). Usage rate of MTX in TNF-α inhibitor (64.8%) was significantly higher than other medicines. Primary failure of anti-IL-6 receptor antibody, and Secondary failure of anti-IL-6 receptor antibody and JAK inhibitor were significantly lower. In Adverse event, rate of herpes zoster in JAK inhibitor was higher than other medicines. Rate of malignant disease was no difference in these medicines. [Conclusions] LPD was occurred 4 cases in TNF-α inhibitor, 3 cases of these used MTX. However 2 cases developed LPD in JAK inhibitor did not use MTX. So I think these mechanism was possibly difference.

## P3-132

**Investigation of continuation rate and safety of Janus kinase inhibitors - Comparison of hepatic metabolizing type and renal excreting type using propensity score matching -**

Ikkou Hirata[1], Nozomi Nitanda[3], Hiroki Oba[1,2,4], Ryo Hazue[1,6], Ryo Rokutanda[5], Ryohkan Funakoshi[1,6]
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Conflict of interest: None

[Objective] Janus kinase inhibitor (JAKI) side effects such as infections including herpes zoster have been cited as a safety concern. In an outpatient pharmacist study, there appeared to be a difference in persistence rates and adverse effects between hepatic and renal excretion JAKIs. Therefore, we conducted a retrospective study using propensity score matching. [Methods] Subjects were patients aged 18 years or older using JAKI from January 2014 to September 2022. The endpoints were the continuation rate of JAKI for 52 weeks and side effects. The comparison was made between hepatically metabolized and renally excreted JAKI. [Results] The 247 patients included 59 Upa, 13 Tofa, 170 Bari, and 5 Fil. The continuation rate of hepatic metabolism and renal excretion, at 52 weeks was 64% vs. 64%of 90 patients ($p = 1.00$). The side effects were 30 vs. 23 ($p = 0.33$). The infection was 25 vs. 6 ($p < 0.001$). Discontinuation due to infection was 13 vs. 3 ($p < 0.05$). Risk factors for JAKI discontinuation were use of 5 or more drugs, adverse events, and dyslipidemia. Risk factors for infection were identified as hepatic metabolic JAKI, chronic kidney disease, and unvaccinated against herpes zoster. [Conclusions] Continuation of JAKI is important to reduce the drug dose and reduce side effects.

## P3-133

**Medical economics of JAK inhibitors**

Masahiko Miya
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Conflict of interest: Yes

[Objective] In phase 2 of the Rheumatoid Arthritis Clinical Practice Guidelines 2020 Drug Treatment Algorithm, the use of bDMARDs should be considered over JAK inhibitors from the perspective of long-term safety and medical economy. [Methods] We investigated the cost-effectiveness of antirheumatic drugs in terms of health economics in patients with rheumatoid arthritis, including periods of biologic-free or JAK inhibitor-free periods. [Results] JAK inhibitors were less cost-effective than anti-IL-6 receptor antibodies, but were more cost-effective than anti-TNF antibodies. JAK inhibitors are less expensive than anti-TNF antibodies and are not less cost-effective. [Conclusions] JAK inhibitors are more cost-effective than anti-TNF antibody preparations, and medical economics is not a reason not to choose JAK inhibitors. JAK inhibitors are as useful as biologics.

## P3-134

**Study on Long-Term Administration Continuation of Golimumab**

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Conflict of interest: None

[Objective] Examine the characteristics of 20 patients administered golimumab for over 10 years and investigate its long-term continuous effects. [Methods] The average age and duration of the disease was 67.5 and 105 months, and the average period of golimumab administration was 111 months. As prior treatments, 17 patients had been on methotrexate, 3 on biological agents, and 1 on a JAK inhibitor. Disease activity at the time of golimumab administration, as well as 3 months, 6 months, 1 year, 3 years, 6 years, and at the final observation and mTSS at the time of administration and the final observation was assessed. [Results] The DAS28-ESR before and at the final observation of golimumab administration significantly decreased from 5.2 to 3.4; the CDAI: from 20.3 to 9.9. ; CRP (mg/dl): from 2.6 to 0.9 (P<0.01), mTSS/y significantly decreased from 7.1 at baseline to -0.05 (1 year), and 0.40 (final) (P<0.01). There were many cases related to bone marrow edema observed by MRI, but joint destruction's progression was limited over the long term. Adverse events occurred in 3 cases, but there were no discontinuations due to these. [Conclusions] The long-term continuous effects of golimumab were confirmed.

## P3-135

**The impact of multi drug resistance factor (MDR1) on the efficacy of JAK inhibitors**

Yuma Onoi[1], Shinya Hayashi[1], Naoki Nakano[1], Masanori Tsubosaka[1], Tomoyuki Kamenaga[1], Kensuke Anjiki[1], Kemmei Ikuta[1], Shotaro Tachibana[1], Toshihisa Maeda[2], Ken Tsumiyama[2], Keiko Funahashi[2,3], Ryosuke Kuroda[1], Tsukasa Matsubara[2,3]
[1]Department of Orthopaedic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan, [2]Matsubara Mayflower Hospital, Kato, Japan, [3]Research Institute of Joint Disease, Kobe, Japan

Conflict of interest: None

[Object] Janus kinase inhibitors (JAK-i) have excellent therapeutic efficacy for rheumatoid arthritis (RA), however, some patients do not respond to the treatment. This study aimed to examine the influence of the MDR1 on the effect of JAK-i in vitro using human Synovial fibroblast-like cells (RA-FLS). [Methods] Human RA-FLS was used as a primary culture system. MDR1 expression was evaluated by RT-PCR and compared in two groups: high and low expression groups. RA-FLS were seeded in plates and exposed to JAK-i (Tofacitinib, Baricitinib, Peficitinib, Upadacitinib, and Filgotinib) and Bucillamine at clinical blood concentrations. Two hours later, RA-FLS were stimulated with 100 ng/ml IL-6 and sIL-6R each, and 24 hours later, cell proliferation was evaluated by WST assay and expression levels of ICAM-1, VCAM-1, VEGF, MCP-1, and MMP-1 by RT-PCR. [Results] No significant differences were observed between MDR1 high and low groups in RA-FLS cell proliferation and expression levels of ICAM-1, VCAM-1, VEGF, MCP-1, and MMP-1 for any of the five JAK-i types, whereas significant differences were observed for Bucillamine (High group, 1.32, 3.29, 2.33, 2.08, 2.11, 1.46; Low group, 1,19, 2.60, 1.68, 1.65, 1.29, 1.07; $p<0.05$). [Conclusions] The effect of JAK-i may not be affected by MDR1 expression.

## P3-136

**The clinical course of 15 RA patients treated with peficitinib**

Shinsuke Yamada, Kazuo Fukumoto, Tomohiro Kuwamoto, Ryuhei Ishihara, Masao Katsushima, Ryu Watanabe, Motomu Hashimoto
Department of Clinical Immunology, Osaka Metropolitan University of Medicine

Conflict of interest: Yes

[Objective] To investigate the clinical course after the introduction of PEFI. [Methods] The course of DAS28 (CRP), HAQ, and various blood test findings were statistically analyzed for 12 patients who continued taking PEFI for one year. [Results] All patients were started on the usual dose (150 mg/day), and in three patients the dose was reduced to 100 mg/day when the disease was stable. There were no discontinuations due to adverse events, but one primary and one secondary disorder were observed. 15 patients had a median age of 67.0 years and eGFR of 69.4 mL/min/1.73 m2. 6 were BIO/JAK naive, 6 were on one drug, 3 on two or more drugs, and 3 on two or more drugs. Of the 12 patients who took the drug for at least one year, 11 achieved clinical remission after one year. In addition, HAQ scores improved significantly after one year in patients over 65 years of age. On the other hand, serum IgG decreased significantly after 1 year, and eGFR showed an unstable course with no significant change after 1 year but significant decreases after 12 and 24 weeks. [Conclusions] PEFI may be a useful treatment option for elderly patients and patients with CKD complications, but careful follow-up is required regarding renal function and immune status.

## P3-137

**Experience of a 93-year-old Patient with Rheumatoid Arthritis who had been treated with Peficitinib for more than one year**

Keio Ayabe, Akira Inoue, Wataru Iriyama, Yurina Iwasaki
Keiyu Orthopedic Hospital

Conflict of interest: None

[Objective] We report a case of rheumatoid arthritis in a 93-year-old patient who had been treated with Peficitinib for more than 1 year. [Case] [Course] The patient is a 93-year-old single woman. She had chronic hepatitis C, osteoporosis, chronic kidney disease, hypertension, and chronic gastritis. The results of the blood test at the time of visit were as follows: anti-CCP antibody: 722.9U/mL, RF: 51U/mL, CRP: 1.62 mg/dL, ESR: 81 mm/h, MMP-3: 460.4 ng/mL, eGFR: 39.9mL/m$^2$/1.73$^2$. The disease activity was so high, DAS28ESR: 6.07, SDAI: 36.62, that the patient entered the examination room in a wheelchair. He was started onSASP1000 mg/day and PSL 6 mg/day, but her symptoms did not improve, so we discussed intensification of treatment and added Peficitinib 50 mg/day, and then gradually increased the dose of Peficitinib. One year after the administration of Peficitinib, the disease activity has remained in remission with Peficitinib 100 mg/day and PSL 5 mg/day, and the unstable lymphocyte count has stabilized at 1000/μL, and she is able to take a walk every day. [Conclusion] We have experienced cases in which pain improved and ADL could be maintained by taking JAK inhibitors in selected old patients.

## P3-138

**A case of rheumatoid arthritis in which PCP and CMV infection developed simultaneously while using JAK inhibitors**

Erika Iguchi[1], Atsuko Tsujii[1], Yanakawee Siripongvutikorn[1], Kurumi Yamamoto[1], Akira Nishigaichi[1], Maiko Yoshimura[1], Akihiko Nakabayashi[1], Hyota Takamatsu[1,2], Shiro Ohshima[1,2]
[1]NHO Osaka Minami Medical Center, Osaka, Japan, [2]NHO Osaka Minami Medical Center, Osaka, Japan

Conflict of interest: Yes

[Case] 69-year-old female [Progress] Developed rheumatoid arthritis in her 40s and is currently being treated with UPA7.5 mg/day + MTX 8 mg/week + PSL 2 mg/day. On September Y-4, X, she developed a fever. September Y-3 Cough appeared. She visited our hospital on September Y. Blood tests revealed an increased inflammatory response, high β-D glucan and LDH values, and a chest CT scan revealed ground-glass opacities in both lung fields. She suspected PCP and started treatment with sulfamethoxazole trimethoprim + PSL 30 mg/day+micafungin hydrate. On the fourth day of illness, she was also found to be positive for CMV antigen and was started on ganciclovir. She was discharged from hospital on the 24th day of illness. [Discussion] The clear risk of PCP and CMV infection due to JAK inhibitors is not known. In this case, PCP and CMV infection developed simultaneously under conditions where JAK inhibitors were being used, but at half the dose. We will examine the clinical characteristics of this patient in conjunction with other cases in which PCP and CMV infections developed during use of JAK inhibitors at our hospital. [Clinical Significance] We believe that it is important to accurately understand the risk of opportunistic infections in order to use JAK inhibitors appropriately.

## P3-139

**Two cases of malignant rheumatoid arthritis whose lower leg ulcers improved after filgotinib treatment**

Tomo Oyakawa
Orthopedics, Nakagami Hospital, Okinawa, Japan

Conflict of interest: None

[Objective] I report two cases of malignant rheumatoid arthritis (MRA) whose lower leg ulcers improved after filgotinib (FIL) therapy. [Case] #1 76-year-old woman she was diagnosed with left lower leg ulcer 21 years ago. She was diagnosed MRA. Steroid pulse therapy, leukocyte ablation therapy, two skin grafts, pedicled flap grafting, and vein ligation were perfomed, but leg ulcer recurred. Treatment with abatacept, tocilizumab, and sarilumab was also ineffective. Three months after FIL therapy, granulation and epithelization of the ulcer were observed. #2 58-year-old woman combined with systemic lupus erythematosus. Both lower leg ulcer appeared 17 years ago. Infliximab was introduced, but discontinued due to side effects. Leg ulcer improved with the introduction of prednisolone (PSL) and etanercept (ENT), but it recurred 2 years ago. she was referred to our hospital one year ago. I judged ENT with the second invalidity. Leg ulcer was improved after FIL therapy in four months and epithelized. [Conclusion] Corticosteroids, immunosuppressants, biological agents, and plasma exchange therapy have been reported as treatments for rheumatoid vasculitis. I experienced cases in which FIL was effective for treatment-resistant leg ulcers. It may be effective for treatment-resistant MRA.

## P3-140

**A case of pulmonary mucormycosis developed while using filgotinib for rheumatoid arthritis**

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Hospital

Conflict of interest: Yes

[Case] A woman in her 60s. She developed RA at the age of 40 and was resistant to treatment with csDMARDs, so she was treated with tocilizumab (TCZ) at the age of 44. Her RA went into remission. Before using TCZ, her chest HR-CT revealed lesions suggestive of non-tuberculous mycobacteria, but no bacteria were detected. At the age of 58, she experienced secondary failure of TCZ and was switched to adalimumab, which was insufficiently effective. At the age of 61 she was switched to the JAK inhibitor FIL, and she went into remission again. When she was 62 years old, she was diagnosed with pulmonary mucormycosis. She was treated with posaconazole and showed improvement. During her course, she contracted bacterial pneumonia twice, which improved with antibiotics. When she stopped taking FIL, her immunoglobulin (Ig) levels were almost normal, but 1 year later, they all decreased to 429 mg/dL IgG, 68 mg/dL IgA, and 17 mg/dL IgM, indicating that she had immunodeficiency. [Clinical Significance] To date, there have been no reports of pulmonary mucormycosis occurring while using FIL. JAK inhibitors are a useful option for D2TRA, but as with biologics, caution must be taken against opportunistic infections. The patient remained immunocompromised 1 year after FIL withdrawal.

## P3-141

**A case of rheumatoid arthritis with herpes zoster meningitis during remission maintenance with baricitinib**

Ayano Ando[1], Tatsuhiko Wada[1], Nao Tsugita[1], Nana Kinoshita[1], Yosuke Sakamoto[1], Shunsuke Kyoda[1], Eri Shishido[1], Keisuke Ikeda[1], Yosuke Iwadate[1], Hirotomo Asakura[1], Risa Shindo[1], Kazuma Ino[1], Yoshiro Kanayama[1], Takumi Muramatsu[1], Junichi Kondo[1], Kosuke Shimode[1], Jun Okada[1], Yasuhiro Hasegawa[1], Tomoki Tanaka[1], Yu Matsueda[1], Yoshiyuki Arinuma[1], Sumiaki Tanaka[1,2], Kenji Oku[1], Kunihiro Yamaoka[1]
[1]Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, [2]Division of Rheumatology, Kitasato University Medical Center

Conflict of interest: None

A 52-year-old woman who developed rheumatoid arthritis 27 years ago came to our hospital with headache, fever, and back pain. She has been on concomitant abatacept (ABT) for the past 12 years due to persistent intermediate disease activity despite oral methotrexate 8 mg/week. ABT was replaced by baricitinib (BAR) last year. Five days ago, back pain and a symptomless blister appeared on the right thigh. The dermatologist diagnosed herpes zoster (HZ) and started treatment with amenamevir (ANMV). Later, however, high fever, headache, and vomiting appeared. The patient was diagnosed with disseminated HZ and aseptic meningitis based on a positive varicella-zoster virus (VZV) DNA quantification test in cerebrospinal fluid (CSF). BAR was withdrawn, and after 1 week of treatment with acyclovir, headache and nausea disappeared, and the patient was discharged. Two months later, VZV DNA in CSF became negative. HZ developing in the head and neck region is a known risk for progression to meningitis. In the present case, however, the shingles developed in the lumbar region. Lower-than-expected cellular immunity and low CSF transferability of ANMV may have been involved. It was thought necessary to consider drug selection based on CSF transferability when developing HZ under JAK inhibitors.

## P3-142

**A case of SAPHO syndrome with soft density zone in paravertebral body and osteosclerosis in multiple vertebral bodies on thoracic spine MRI**

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Department of General Medicine, Gifu University Hospital, Gifu, Japan

Conflict of interest: None

[Case] 61-year-old man [Chief complaint] Back pain [Current medical history] The patient became aware of nocturnal back pain 10 years ago and visited his local doctor. He was referred to our orthopedic surgery department because thoracic contrast-enhanced MRI showed a soft area with contrast enhancement effect in front of the vertebral body at the Th4-9 level and multiple osteosclerosis images in the frontal part of the vertebral body at the same level. The soft tissue biopsy of the paravertebral body was performed thoracoscopically, but no bacteria, including acid-fast bacilli, were detected in the biopsy. [Progress] The diagnosis of SAPHO syndrome was made based on the diagnostic criteria of SAPHO syndrome. Four months later, a CT scan of the chest showed no change in the multiple sclerosis of the vertebral body, but the paravertebral soft-tissue density area had decreased. [Clinical Significance] Spinal involvement in SAPHO syndrome is relatively common, occurring in about 1/3 of all cases, and 16-44% of patients have no skin symptoms, making the diagnosis difficult when spinal or joint lesions are present alone or without skin lesions. SAPHO syndrome should be considered when soft density areas are present in the paravertebral bodies and osteosclerosis in multiple vertebral bodies.

## P3-143

**A case of pustulotic arthro-osteitis treated with guselkumab during treatment of SLE**

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Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: None

[Case] A 49-year-old woman with polyarthralgia, hypocomplementemia, thrombocytopenia, and positive for anti-dsDNA antibody was diagnosed with SLE in 2010. Treatment with prednisolone 30 mg/day was started, and after 2017 the patient was in remission with prednisolone 1 mg/day. On September 2022 skin rash appeared and was diagnosed as palmoplantar pustulosis by a dermatologist. An ultrasound examination of the joints showed active sternoclavicular arthritis, which led to the diagnosis of pustulotic arthro-osteitis. There was no evidence of focal infection around her teeth, sinusitis, or tonsillitis. Although the arthritis improved with topical therapy and oral NSAIDs, the skin rash did not improve. So, treatment with guselkumab was started and the skin rash improved. During treatment, the patient did not show any exacerbation of SLE. [Discussion] There have been few cases of pustulotic arthro-osteitis combined with SLE reported to date. There are no reports of guselkumab being used for SLE. However, there have been reports that IL-12 and ILI-23 may be involved in the pathogenesis of SLE, and a clinical trial of utekinumab was conducted. We report a case of pustulotic arthro-osteitis during treatment of SLE, in which we used guselkumab and had a good course of treatment.

## P3-144

**A case of ulcerative colitis with worsening of spondylitis by vedolizumab, alpha4beta7 inhibitor**

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Conflict of interest: None

[Case] A 30's man who had experienced low back pain was diagnosed with ulcerative colitis (UC) in X-1 year. Treatment with mesalazine was started, but the intestinal symptoms did not improve. Filgotinib was added, but the treatment effect was insufficient, and the drug was switched to vedolizumab, an α4β7 inhibitor. After switching to vedolizumab, bowel symptoms tended to improve, but low back pain worsened, and he was referred. MRI showed fused sacroiliac joints and active inflammatory spondylitis. CT-guided biopsy was performed to rule out infection, etc., and since infection, etc. were unlikely, UC-related spondyloarthritis was diagnosed. The patient was switched to upadacitinib, because vedolizumab was considered to have exacerbated spondylitis, and spinal and intestinal symptoms improved, as well as MRI findings of spondylitis, and he remains in clinical remission. [Conclusion] Although vedolizumab, an α4β7 inhibitor, is attracting attention as a therapeutic drug for UC, it has recently been reported that vedolizumab is not effective for UC-related

SpA symptoms or may worsen SpA symptoms in some cases. We would like to review and discuss previous reports on the effects of vedolizumab on UC and SpA, as well as the characteristics and mechanisms of some cases of worsening SpA.

## P3-145

**Extreme clavicular osteitis in a patient with ulcerative colitis-related spondyloarthritis**

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Conflict of interest: None

A 32-year-old man, who had been diagnosed with ulcerative colitis (UC) at the age of 21, was referred to us because of sharp pain in the right clavicle for a month. He had been treated with ustekinumab, vedolizumab, tofacitinib, and filgotinib sequentially, but with insufficient efficacy. On examinations, there was a pain on the right clavicle and the second costosternal joint, but there was no swelling. CT of the chest revealed the swelling of soft tissue around the right clavicle, and the budging right clavicle was surrounded by linear ossifications. MRI of the chest revealed high-intensity lesions in the right clavicular bone, surrounding soft tissues and adjacent muscles, left clavicle, and sternal manubrium. Because osteomyelitis or bone tumor was suspected, bone biopsy was performed. The culture of the bone biopsy specimen was negative, indicating that osteomyelitis was unlikely. Histopathology of the biopsied bone revealed proliferation of osteocytes, suggesting new bone formation. The patient was diagnosed with UC-related spondyloarthritis, because of the episode of enthesopathy and the presence of refractory UC. Both the clavicular pain and the UC were improved markedly by the treatment with infliximab. Extreme clavicular osteitis is rare in UC-related spondyloarthritis.

## P3-146

**Two cases of Campylobacter enteritis associated reactive arthritis developed during disease outbreak of Campylobacter food poisoning**

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Conflict of interest: None

[Cases 1 and 2] In June X year, 21 year-old female students attended a meeting and later a social gathering, and ate together in large numbers. Some were fed semi-raw chicken. Several days later, several of the participants of the social gathering, including the two patients, developed pyrexia, abdominal pain, and diarrhea, and stool culture revealed that they had Campylobacter food poisoning. The patient was treated with antibiotics, and symptoms of enteritis improved. At least 2 of these patients started to complain of arthralgia at 3 weeks after the recovery of enteritis symptoms. Recalling that there had been a lecture on ReA in a student lecture, they suspected ReA on their own and visited our department. Increased CRP and ESR were observed. Enthesitis was also observed. Thus, ReA was diagnosed after excluding other diseases. They were treated with NSAID and low-dose PSL, and the symptoms improved. For HLA typing, Case 1 and 2 were found to have HLA-B27, and HLA-B7 and B44, respectively. [Conclusion] Even in recent years when hygienic environment is improved, food poisoning occurs, and classic ReA can occur in some cases. Since students sometimes learn by themselves, it is necessary to continue the education and dissemination activities of ReA for accurate early diagnosis.

## P3-147

**Succcessful treatment with upadacitinib for Inflammatory Bowel Disease-related Spondyloarthritis with IgA nephropathy**

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Conflict of interest: None

[Case] A 10s' -years-old man was diagnosed with Crohn's disease at the age of 11 months. Infliximab was started at X-15 year. But at X-1 year, he was switched to ustekinumab (UST) due to development of skin rush. At X year, he developed inflammatory back pain. In addition, abnormal urinalysis was noted for the first time and UST was withdrawned. On his admission, renal function was normal range. Urinarysis showed proteinuria and hematuria. MRI STIR demonstrated high-intensity areas along the sacroiliac joint, suggesting IBD-Related SpA. Renal biopsy revealed IgA nephropathy (IgAN), Upadacitinib was initiated, and then, his symptoms, laboratory and imaging findings improved with normalized urinary finding. [Discussion] Although UST, an anti-IL12/23 inhibitor, is noted as a treatment for IBD, It has recently been reported that UST could induce secondary IgAN as paradoxical reaction. In addition, JAK inhibitors have recently been recognized as a new therapeutic strategy for IBD-related SpA, and may be effective in IgAN as in the present case. These might suggest common pathogenesis between SpA and IgAN, and therapeutic potential of JAK inhibitor for IgAN.

## P3-148

**A case of psoriatic arthritis that developed systemic lupus erythematosus early after administration of ixekizumab**

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Conflict of interest: None

[Case] 51 year old female [Chief complaint] Fever/arthritis [History of current illness] The patient was diagnosed with psoriatic arthritis (PsA) in year X-9. In November of year X, ixekizumab was introduced. Two weeks later, she developed a fever of 38 degrees and developed arthritis, and was admitted to the hospital for further investigation. [Course after admission] Measurement of her autoantibodies revealed high levels of anti-nuclear antibody (640x) and anti-dsDNA antibody. In addition, a kidney biopsy revealed findings consistent with lupus nephritis type III, and the patient was diagnosed with systemic lupus erythematosus (SLE) as it met the 2019 ACR/EULAR SLE classification criteria. She received treatment with immunosuppressive treatment and her symptoms and data improved. [Discussion] There are few reports of anti-IL-17 antibody preparations. Increased interferon production due to cytokine shift has been reported as the mechanism of onset of drug-induced lupus by TNF inhibitors, but the mechanism of induction by anti-IL-17 antibody preparations is not clear. Here, we will discuss the relationship of ixekizumab administration to the SLE pathology in this case using serum before and after administration and past literature reports.

## P3-149

**A case of challenging diagnosis in spondyloarthritis**

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Conflict of interest: None

[Case] A 17-year-old female initially diagnosed with sacroiliitis presented with persistent lower back pain. Despite the absence of extra-articular symptoms, inflammatory back pain and suggestive imaging indicated axial spondyloarthritis, initiating pharmacological intervention. Development of diarrhea led to a diagnosis of ulcerative colitis upon gastroenterology referral. Anti-TNF-α therapy was implemented due to aggravated sacroiliitis, followed by a successful switch to JAK inhibitors, resulting in improvement of both arthritis symptoms and ulcerative colitis. [Clinical Significance] The concept of spondyloarthritis is gradually gaining recognition, yet its diagnosis often requires significant time. Reports suggest that 10-20% of patients with axial spondyloarthritis progress to ankylosis if treatment is delayed, highlighting the importance of early diagnosis. Furthermore, extra-articular symptoms may not necessarily manifest con-

currently with arthritis, as seen in this case. Understanding the disease concept is essential for early diagnosis and timely intervention, emphasizing the need for comprehensive literature review.

## P3-150

**A case of a boy with juvenile spondyloarthritis diagnosed after cervical fusion**

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Conflict of interest: None

The case is a 15-year-old boy. From around the age of 10, he began to notice limited range of motion in his neck. At the age of 14, he started complaining of frequent headaches, so he visited a local neurosurgical clinic, where neck X-rays and cervical MRI revealed cervical vertebrae fusion, and he began rehabilitation. But half a year later, this was a facet joint fusion, rather than the fusion of the vertebral bodies that is normally seen in vertebral bodies, and because the fusion was observed not only in the cervical vertebrae but also in the lower thoracic vertebrae, he was suspected some kind of bone system disease, and he was introduced to our hospital. Blood tests suggested the presence of chronic inflammation, and an MRI of the sacroiliac joint revealed evidence of sacroiliitis. He had no psoriasis-like skin findings, so we diagnosed juvenile spondyloarthritis and started treatment. In adults, ankylosis of the cervical facet joints may occur before the appearance of ligament osteophyte formation and ankylosis in the lumbar vertebral body, but within our search, we were unable to find any reports of this in children. We report a case of a child with cervical facet joint ankylosis, which was discovered after cervical fusion and was later diagnosed as spondyloarthritis.

## P3-151

**A case report: severe mono-coxoarthritis in patient with spondyloarthritis**

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Conflict of interest: None

[Chief complaint] Severe right coxalgia [Present Illness] Right hip pain and sacroiliac joint pain since around May 2020, which was alleviated with NSAIDs. In November 2021, He had pain in the right trochanteric region, but it improved with injections. Since April 2022, the patient was referred to our hospital because of right hip pain and increased CRP. [Past history] None. No history of inflammatory lower back pain. [Findings] Severe pain when passively moving the right hip joint when flexed and adducted; X-P showed no abnormality in the hip joint, but Grade 2 findings were found in both sacroiliac joints. MRI showed bone marrow edema and periarthritis in the right hip joint. White blood cell count: 10,100, CRP: 5.93, otherwise blood analyze was within normal. HLA-B27 positive. [Course] Steroid injection was performed three times under ultrasonography, but there was no effect. Upatacitinib (15 mg) treatment was started, and within the first week, the CRP became negative and the symptoms were relieved. [Discussion] It is not uncommon for patients with axial spondyloarthritis to present first with hip pain. Steroid administration under echocardiography was ineffective, and administration of upatacitinib was early effective.

## P3-152

**A case of psoriatic arthritis preceded by joint destruction**

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Conflict of interest: None

A 61-year-old woman visited our hospital with bilateral hip pain. Physical examination revealed tenderness in bilateral knee, hip, and back pain. Venous blood sample showed that CRP was 0.09 mg/dl, RF was 8.0 IU/ml, MMP-3 was 30 ng/ml, ACPA was <0.6U/ml, HLA-A24, A26, B52, B61 were positive. Joint space narrowing in right knee of lateral and bilateral hip joint, bony proliferation at distal phalanx, and osteosclerosis of bilateral sacroiliac joints were found in X-ray or CT. MRI showed no bone edema in spine or sacroiliac joint. No enthesitis or synovitis were found in joint ultrasonography. We suspected spondylarthritis because of her multiple joint destruction and bony proliferation. In this case, we start NSAIDs. Total hip arthroplasty and total knee arthroplasty was performed for biratelar hip and right knee. Five years after joint pain, anthema appeared in bilateral lower legs. Pathological results revealed that this anthema was psoriasis. It was generally known that arthritis appeared after the onset of skin symptoms. However, previous studiy reported that 2.1% patients with psoriasis were arthritis precedent type. Diagnosis of arthritis precedent psoriasis is very difficult. Imaging evaluation is important in the diagnosis of psoriatic arthritis.

## P3-153

**A case of reactive arthritis after COVID-19 infection**

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Conflict of interest: None

A 72-year-old woman presented with polyarthralgia. Four months before, she had COVID-19 infection, and her symptoms improved spontaneously after 3 days. Three months before, polyarthralgia occurred and gradually worsened. Physical examination revealed moderate swelling of the affected joints. CRP was eleveted to 4.25 mg/dL. The serological tests were all normal. HLA typing analysis were A24, B54 and B61 positivity. 18F-FDG PET/CT revealed significant FDG accumulations in the intervertebral ligament of the neck and the tendon attachments of the affected joints. Based on above findings, she was diagnosed with reactive arthritis (ReA) after COVID-19 infection (post-COVID ReA). She was initially treated with prednisolone 10 mg/day and salazosulfapyridine 1000 mg/day. His polyarthralgia improved, and the CRP level normalised. ReA is acute aseptic arthritis occurring 1 to 4 weeks after a distant infection in a genetically predisposed individual and is classically considered a sub-type of spondyloarthritis. COVID-19 is accepted as one of the new causative agents of ReA. In our case, the positivity of HLA-A24 and HLA-B61 might be a genetic predisposition to the development of post-COVID ReA. Clinicians should be aware that COVID-19 infection has been added to the list of causes of ReA.

## P3-154

**A case of gouty arthritis of the DIP joint with Pencil-in-Cup-like deformity and marked improvement of the deformity**

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Conflict of interest: None

[Introduction] We report a case of progressive joint destruction caused by gouty arthritis of the DIP joint of the finger, which subsequently improved markedly. [Case] Male in his early 70s developed gout in the left 1st MTP joint 8 years ago, and subsequently developed redness and swelling in the left DIP joint of 4th finger. A synovectomy was performed and he was diagnosed with a tophus gout, so he was referred to our hospital. US showed inflammation in the nail bed and extensor tendons of the left 4th fingers. XP and HR-pQCT showed osteophyte formation, bone erosion, and a pencil-in-cup-like deformity. He was treaeted with colchicine and febuxostat. One year after, HR-pQCT showed a clear joint space in the left 4th finger DIP joint, and 4 years later, improvement of bone erosion. [Conclusions] In patients with hyperuricemia, high levels of extravascular uric acid form crystals in joints, etc. His initial US showed inflammation of the extensor tendon and HR-pQCT showed a pencil-in-cup deformity, suggesting that the patient also had peripheral SpA. The high concentration of uric acid in the plasma exudated by tendinitis and enthesitis repeat-

edly deposited crystals around the joint, suggesting the possibility that gouty arthritis developed.

## P3-155

**A case of calcium pyrophosphate crystal deposition disease with multiple nodules**

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Conflict of interest: None

[Case] A 72-year-old male suffered from polyarthralgia 11 years ago. He was hospitalized to the neurosurgical hospital with putaminal hemorrhage. His articular symptoms worsened in the admission and he was referred to our hospital. He presented with high fever and sever pain in both PIP joints, wrists, knees and ankles. Multiple subcutaneous nodules with slight tenderness were observed in both PIP joints, right DIP joint, both wrists and left MTP joint. ESR was 106 mm/h and CRP was 27.32 mg/dL. RF and anti-CCP Ab were both negative. Radiological examinations of left knee joint demonstrated a linear calcification in the articular cartilage. He was performed a biopsy from the nodular lesion of his right wrist. Microscopic examination of the nodule with polarized light revealed extensive deposition of crystals as calcium pyrophosphate dehydrate (CPPD). A diagnosis of nodular pseudogout was made. He was treated with NSAIDs, but the symptoms were continued. Steroid and MTX were administrated and his symptoms improved. This case is classed to chronic inflammatory arthritis with CPPD according to 2011 EULAR recommendations for CPPD. We report a rare case of CPPD deposition with multiple nodules of peripheral joints including literature reviews.

## P3-156

**Lifehacks for preventing recurrent arthritis; less kneeling, light tools for carrying at job, and avoid fish with anisakis**

Eiko Tauchi
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Conflict of interest: None

52 year Japanese male construction worker suffered from reccurent arthritis. He has been gout since 1994. His visit had been irregular and had frequent gout attack. His medicine had been never less than low dose steroid + colhichicine 0.5-1.5 mg +high dose NSAIDS and antihyperuricemia medicine. Recently, he experienced 2 attacks of his left knee on July 2022 and March 2023. MRI image showed chronic arthritis. Left knee joint aspiration showed aseptic arthritis with CPPD and gout crystals with increased leukocyte. On the diagnosis of crystal induced arthrtis, intra articular steroid injection was done, and incresed dose of oral steroid and NSAIDS were pescribed. Alongside with increased antiuricemic medicice, we asked him stop drinkig, and stop overuse of the knee, because it was thoght to be the cause of CPPD. Still he had knee arthralgia on July 2023. After he enjoyed seasonal raw bonito with alcohol, he had severe abdominal pain, vomitting and diarrhea. Later he had left knee arthralgia. His RAST value of anisakis was 11.7Ua/ml, and he had anisakis allergy, eventually thoght to be a cause of steroid withdrawal. We suggest him to avoid fish with anisakis, then later he has no attacks and also on less steroid. As this case was quite informative, we report here.

## P3-157

**Current status of osteoporosis treatment and ongoing secondary fracture prevention management in patients with proximal femur fractures at Showa University Koto Toyosu Hospital**

Kosuke Sakurai
Showa University Koto Toyosu Hospital

Conflict of interest: None

[Objective] To clarify the current status of continuous management for secondary fracture prevention at Showa University Koto Toyosu Hospital. [Methods] This study included hospitalized patients who underwent surgery for proximal femur fracture between April 2022 and March 2023. A retrospective survey assessed secondary fracture prevention expenses, patient characteristics at admission, and osteoporosis treatments before and after admission. [Results] The study involved 41 patients with a median age of 82 years. 29 were female, and five had received osteoporosis treatment before admission. 21 patients qualified for ongoing management fees related to secondary fracture prevention. A comparison between patients with and without these fees revealed no differences in terms of age, sex, renal function, or the number of medications taken upon admission. Among the eligible patients, five received bisphosphonate (Bis) alone, 11 received active vitamin (Vit) D alone, and 5 received a combination of Bis and VitD. Among those who did not qualify for the fees, nine had not undergone testing and received medications, nine had not received medications, and two had not been tested. [Conclusions] We advocate for active intervention in osteoporosis treatment for patients with femur fractures.

## P3-158

**Five-year efficacy of anti-RANKL antibody denosumab in patients with rheumatoid arthritis**

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Conflict of interest: None

**[Objective]** To evaluate the 5-year efficacy of denosumab, an anti-RANKL antibody, in patients with rheumatoid arthritis (RA) using bone mineral density and bone metabolism markers. **[Methods]** In rheumatoid arthritis patients on initial denosumab treatment at our institution, the bone mineral density of the distal radius (R), lumbar spine (L), and femoral neck (FN), serum TRACP-5b, and BAP were measured at the start of treatment and after 5 years of treatment, and 17 patients were retrospectively evaluated. **[Results]** The mean age of the 17 patients was 78.9±8.25 years, and the male-to-female ratio was 3 males to 14 females. The mean bone mineral density of R, L, and FN and serum TRACP-5b and BAP after 5 years of denosumab treatment (at the start of treatment vs. after 5 years of treatment) were R 70±0.23% vs. 72±0.27% (p=n. s) for all patients, L 81.9±0.17% vs. 95.6±0.19% (p=0.03), FN 66.8±0. 13% vs 68.5±0.13% (p= n.s.), TRACP-5b 597.0±352.5 mU/dL vs 366.7±209.0 mU/dL (p= n.s.), BAP 12.9±3.75 μg/L vs 9.13±2.00 μg/L (p=0.004). **[Conclusions]** Five years of denosumab treatment showed a trend toward improvement in bone mineral density, with significant improvement in the lumbar spine. In addition, a significant improvement in BAP was also observed in serological findings.

## P3-159

**Study of 3-year administration of anti-RANKL antibody denosumab to RA patients for the purpose of suppressing the progression of bone erosion**

Toshiharu Okuda
Okuda Orthopedic Clinic

Conflict of interest: None

[Purpose] There were 108 patients with RA who had been receiving denosumab (DMB) for more than 3 years at our hospital. We will report on the investigation of the therapeutic effect on cases in which DMB was used. [Methods] Subjects were 53 RA patients (9 males/99 females, average age 68.5 years) who had bone erosion confirmed by XP and were administered DMB. For these cases, measurements of bone density (lumbar vertebrae, proximal femur/neck, radius), bone metabolism markers (TRAP-5b, BAP), and XP tests were performed at every 6 months for 3 years. [Results] In 45 patients whose bone density was measured every 6 months for all 3 years, At the start and at 36 months, lumbar spine %YAM (Mean±SD) was 85.6±13.4, 94.4±15.3, proximal femur %YAM was 75.4±14.2, 78.7±14.2, femoral neck %YAM was 76.1± 13.7, 79.7±13.5, radial %YAM was 65.8±19.5, 68.4±19.7, and significant increases were observed at all sites. The trends in bone metabolism markers (average values) at the start, at 6, 12, and 36 months, TRAP-5b (mU/dL) was 421.5,

244.2, 271.2, and 307, and BAP (μg/L) was 13.3 and 8.7. [Conclusion] Significant increases in bone density were confirmed at all sites after 3 years of DMB administration. All bone metabolism markers showed a significant decrease from an early stage.

## P3-160

**Effects of initial treatment of osteoporosis by bisphosphonates or denosumab on bone mineral density with biological agents or JAK inhibitors in rheumatoid arthritis**

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Conflict of interest: None

[Objective] The aim of this 1-year retrospective study was to evaluate the differences in outcomes of bisphosphonate (BP) or denosumab (DMAB) with golimumab (GLM), abatacept (ABT), baricitinib (BAR), or upadacitinib (UPA) in rheumatoid arthritis. Bisphosphonates and denosumab has long half-life in bone, and these can affect bone metabolism after we change to another drug in osteoporosis. Therefore, only patients who received initial treatment for osteoporosis were included. [Methods] We investigated patients treated with GLM, ABT, BAR or UPA which are common at our hospital. There was a total of 29 patients whose BMD were measured. Patients were divided into GLM and BP treated group (6 cases), ABT and BP group (4 cases), ABT-DMAB group (8 cases), BAR-DMAB group (6 cases), UPA and BP group (5 cases). We measured bone mineral density (BMD) of the lumbar 2-4 vertebrae (L-BMD) and total hip (H-BMD) at baseline and 1 year. [Results] There were no significant differences in the percent changes in 5 groups. The highest percent change was L-BMD in UPA-BP (median 108%), and the lowest percent change was H-BMD in UPA-BP (median 98%). [Conclusions] GLM and ABT, BAR, UPA are said to have an effect on osteoclasts. BP and DMAB are thought to increase BMD similarly even under that influence.

## P3-161

**Efficacy of romosozumab for glucocorticoid-induced osteoporosis in patients with rheumatic diseases**

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Division of Rheumatology, Department of Internal Medicine, Toho University School of Medicine

Conflict of interest: None

[Objective] To evaluate the efficacy of romosozumab (ROMO) in glucocorticoid-induced osteoporosis (GIO). [Methods] Patients with rheumatic diseases who had not previously received osteoporosis treatment and were newly treated with prednisolone (PSL) 15 mg/day or more were randomly assigned to receive either ROMO, denosumab (DMAb), or bisphosphonate (BP). We measured bone mineral density (BMD) of the lumbar spine (L2-L4), femoral neck and total hip every 6 months and bone turnover markers every 3 months after initiation of glucocorticoid therapy. [Results] Eleven patients were assigned to the ROMO group, 14 to the DMAb group, and 14 to the BP group. The mean percent change of lumbar spine BMD from baseline at 12 months was greatest in the ROMO group among the three groups (ROMO: 5.9±5.4%, DMAb: 4.3±4.9%, BP: 0.9±4.9%). Serum BAP level, a bone formation marker, slightly increased in the ROMO group, but decreased in the DMAb group. Serum NTx and TRACP-5b, bone resorption markers, and urine pentosidine, a bone quality marker, decreased in all groups. The cumulative frequency of new fractures tended to be lower in the ROMO group (ROMO: 9.1%, DMAb: 7.1%, BP: 14.3%). [Conclusions] ROMO increased lumbar spine BMD and tended to prevent new fractures, suggesting that ROMO is effective in GIO.

## P3-162

**The therapeutic effects of Romosozumab on patients with rheumatoid arthritis and osteoporosis, and its relationship with exercise habits**

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Clinic Quest for Rheumatology & Well-Being, Mito, Japan

Conflict of interest: None

[Objective] We explored the relationship between rheumatoid arthritis (RA), osteoporosis, exercise habits, and Romosozumab's effectiveness in our clinic, with a focus on elderly women with severe osteoporosis coexisting with RA [Methods] Sixty RA patients diagnosed with osteoporosis received one year of Romosozumab treatment. We examined YAM changes and exercise habits before treatment. Patients were categorized into remission (SDAI < 3.3, 33 patients) and non-remission (SDAI > 3.3, 27 patients) groups [Results] In the remission group, the YAM change rate was 11.0% in the lumbar spine, 4.1% in the femoral neck, and 6.1% in the proximal thigh, and 14 patients performed exercise. SDAI was 1.38 → 1.44. YAM change rate in the non-remission group was 12.9% in the lumbar spine, 3.2% in the femoral neck, and 4.2% in the proximal thigh. There were 6 exercise participants. SDAI was 7.33 → 2.66 The remission group had a higher proportion of exercise participants, and the improvement rate of femoral bone density was particularly excellent. [Conclusions] Long-term RA management often involves a risk of complications and reduced quality of life. Achieving and maintaining clinical remission is vital for effective osteoporosis management and the overall well-being of patients.

## P3-163

**Comparative study of the effects of romosozumab on rheumatoid arthritis patients using TNF alpha inhibitors, non-TNF alpha inhibitors, and csDMARDs alone**

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Department of Orthopaedic Surgery, Kohnan Kakogawa Hospital

Conflict of interest: None

[Objective] We compared the clinical effects of romosozumab (ROMO) between the groups of rheumatoid arthritis (RA) patients using tumour necrosis factor (TNF) alpha inhibitors, non-TNF alpha inhibitors, or csDMARDs alone. [Methods] We enrolled the RA patients (n=42) who received ROMO in our hospital for 12 months from 2019 to 2022. We devide them into 3 groups including TNF alpha inhibitor user (A), non-TNF alpha inhibitor user (B), and only csDMARDs user (C). We evaluated perioperative changes (Δ) in the BMD (at lumbar spine and femoral neck), TRACP-5b, and BAP. [Results] Mean age of 42 patients including 3 men and 39 women is 69.7. A/B/C group included 13/14/13 patients. Mean TRACP-5b was 267/327/333 mU/dl, mean BAP was 10.7/14.8/13.6μg/l, mean BMD at lumbar spine was 0.967/1.110/0.885 g/cm$^2$, and mean BMD at femoral neck was 0.547/0.562/0.636 g/cm$^2$. Mean ΔTRACP-5b was 3.38/-41/-0.8 U/dl, mean ΔBAP was 1.99/0.34/1.58 μg/l, ΔBMD at lumbar spine was 0.072/0.026/0.062 g/cm2, ΔBMD at femoral neck was -0.025/0.008/0.015 g/cm$^2$. ΔBMD at femoral neck of A was significantly lower than other groups. (P=0.02) [Conclusions] These data suggest that clinical effects of ROMO in RA patients using TNF alpha inhibitor might be lower than the effects of them using non-TNFα inhibitor and csDMARDs.

## P3-164

**A Study of the Efficacy and Safety of Romosozumab in Patients with Rheumatoid Arthritis after 12 Months of Treatment**

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Toyota kosei Hospital

Conflict of interest: None

Purpose: Romosozumab is an effective osteogenesis-promoting agent for patients with severe osteoporosis. However, the efficacy and safety of romosozumab in patients with RA-complicated osteoporosis have not been adequately investigated. In this study, we investigated the efficacy and safety of romosozumab on BMD of rheumatoid arthritis patients after 12 months of treatment. Methods: Eighteen postmenopausal women who could be followed up to 12 months after starting romosozumab were included. The study included patient age, BMI, renal function, corrected Ca, duration of RA, and DAS28-CRP, with the baseline point of romosozumab initiation. The primary outcome was assessed by BMD and DAS28-CRP after 12 months. Results: The mean age of the patients was 70.8±7.5 years, mean BMI was 18.8±23.15, mean eGFR was 84.6±37.9mL/min/1.73m2, mean Ca was 9.4±0.4 mg/dl, and mean duration of RA was 18.1±17.1

years. All patients completed the 12-month observation period from the start of romosozumab use without any adverse events. ΔBMD at 12 months was 7.9±6.9% for the lumbar spine and 3.5±3.1% for the total hip. Conclusions: Our results suggest that romosozumab therapy may be effective and safe to use in patients with RA-associated osteoporosis.

## P3-165

**Therapeutic effects of romosozumab from the acute phase in patients with the new onset of osteoporotic vertebral fractures**

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Conflict of interest: None

[Objective] We had examined effects of romosozumab (RMAB) from the acute phase in patients with the new onset of osteoporotic vertebral fractures (OVF). [Methods] 28 patients (5 men, 23 women, average 78.2 years old) had been diagnosed at the new onset of OVF, and treated with RMAB. They had put on their own corset, performed blood tests before every RMAB, and measured bone density every six months. [Results] 28 patients had 36 OVF. 25 of them had injury histories. The days until RMAB introduction were 7.9 days after the onset. The bone density increased rates of lumbar vertebrae were average 10.2% at 6 months, 18.4% at 12 months, and of proximal femur were average 4.3% at 6 months, 7.1% at 12 months from the baseline. P1NP were increased 39.8% and TRACP5b were inhibited 26.6% at 3 months from the baseline. We had used combination osteoporotic drugs with RMAB in 96.4%. We had evaluated bone unions of OVF with CT and a standing-up position and decubitus position of the side radiographic appearance. 78.6% of OVF had got their bone unions at the time of RMAB completion. There were no cases of new fragile fracture onset. [Conclusions] We had introduced RMAB from the acute phase on the onset of OVF. We had got bone unions of OVF and good effects of the bone density.

## P3-167

**A case of acromegaly diagnosed during the course of treatment for 25 years of erosive osteoarthritis**

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Conflict of interest: None

[Case] A 58-year-old woman presented with arthralgia in her fingers since X. She had bilateral DIP and PIP arthritis, treated with NSAIDs for erosive OA. In X+21, she had joint replacement surgery. In X+23, she developed SAH and was admitted to the hospital, her first visit. Acromegaly (GHoma) was suspected due to a positive Fist sign. Her medical history revealed persistent headaches since X+5, secondary amenorrhea since X+6, and a history of ureteral stones in both X+6 and X+21. She had numbness in her fingers at X+20, an enlarged lip at X+21, and was diagnosed with colon polyps and glucose intolerance in X+22. She also noted changes in ring and shoe sizes, snoring, and depression. She showed facial changes, voided dentition, and excessive sweating. Lab tests showed a significantly elevated IGF-1 level at 444 ng/mL. Endocrinological evaluation including OGTT and pituitary adenoma findings on MRI confirmed OA associated with GHoma. [Discussions] Delayed GHoma diagnosis leads to complications and worse prognosis. GHoma treatment doesn't affect arthropathy but improves headache, atherosclerotic disease, malignancy, and prognosis. This case highlights OA could be clue to diagnosis of GHoma, emphasizing the importance of early diagnosis and treatment for prognosis improvement.

## P3-168

**A case of systemic lupus erythematosus (SLE) requiring tracheotomy due to laryngeal edema**

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Conflict of interest: None

[Case] 39-year-old male [History of present illness] When he was hospitalized for acute enteritis in January X, laboratory findings showed 160 times anti-nuclear antibody, anti-Sm antibody, and hypocomplementemia. In April X, he was re-hospitalized with butterfly-shaped erythema, Cre 1.98 mg/dl, urinary protein 2.9 g/gCr, and urinary casts. He was diagnosed with SLE and administrated MMF, PSL, and HCQ. Renal function showed a tendency to improve with treatment. On the 32nd hospital day, he presented with dyspnea, and laryngoscopy revealed severe laryngeal edema. Tracheotomy was performed due to airway construction. The PSL dosage was increased to 40 mg and oral agents were discontinued. Laryngoscopy on the 36th hospital day showed improvement in laryngeal edema, and the tracheal foramen was closed on the 51st hospital day. The DLSTs of the discontinued agents were all negative, and he was considered to have laryngitis associated with SLE. [Discussion] Laryngeal lesions associated with SLE are known to be rare organ disorders. Although they have been often reported to occur at the initial onset or during an active exacerbation of SLE, it should be noted that airway clearance may be necessary in the process of improving lupus nephritis as in this case.

## P3-169

**A case of iatrogenic immunodeficiency primary central nervous system lymphoma related to mycophenolate mofetil in systemic lupus erythematosus**

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Conflict of interest: None

A 43-year-old woman urgently presented to our hospital with fever, impaired consciousness, right upper and lower extremity paralysis, and motor aphasia. She was diagnosed with SLE 26 years ago based on lupus nephritis, skin erythema, arthralgia, fever, positive anti-nuclear antibodies, positive anti-dsDNA antibody, and low complement. She had a history of taking AZA and TAC for relapse. On admission, she was treated with PSL 11 mg/day, TAC 3 mg/day, MMF 1,750 mg/day, and BLM 200 mg/week. Head MRI showed a relatively well-defined mass in the left frontal lobe with an internal T2 low-signal area with an extensive T2-enhanced area around the tumor reflecting brain edema. She got a craniotomy, and pathology revealed iatrogenic immunodeficiency primary central nervous system lymphoma related to MMF and DLBCL. The primary lesion didn't exist below the neck on CT. After RTX-high-dose MTX and RTX-high-dose Ara-C, she underwent an autologous peripheral blood stem cell transplant in February X-1 and went into complete remission. We describe the 15th case of iatrogenic immunodeficiency primary lymphoma related to MMF. In our case, the head MRI 3 months earlier showed no abnormalities, and the tumor enlarged rapidly in a few months. We have to recognize the risk of this lymphoma in MMF use.

## P3-170

**A case of elderly-onset SLE with fever of unknown origin in need of differential diagnosis from drug-induced lupus**

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Conflict of interest: None

A 74-year-old man presented with anorexia and elevated inflammatory markers (CRP: 13 mg/dL). Initial treatment with antibiotics did not improve his condition, introducing to our hospital. Further investigation revealed leukopenia, pleurisy, proteinuria/hematuria, and positive direct

Coombs test, suggesting SLE. Despite of negative anti-ds-DNA antibody, positive anti-DNA and ss-DNA and histone antibodies were observed. Rare cases of statin-induced DIL with renal and hematologic abnormalities indicated diagnosis of SLE. We started to treat with high-dose corticosteroids (0.8 mg/kg) as elderly-onset SLE on the 8th day. After additional medications (mycophenolate mofetil, tacrolimus, belimumab, and hydroxychloroquine) were introduced and corticosteroids were gradually decreased, the patient was discharged without fever after 66th days. Distinguishing between elderly-onset SLE and DIL is crucial, because most of the patients with the DIL recover after discontinuation of the suspected drug. We have reported a case of elderly-onset SLE that required differential diagnosis from DIL based on negative anti-ds-DNA antibodies and positive anti-histone antibodies.

## P3-171

**The case of Behcet's disease who developed SLE after COVID-19**

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Conflict of interest: None

Case A 62 year-old man who had medical history of Behcet's disease. He had been treated with infliximab and cyclosporine. He was diagnosed with covid-19 complicated by disseminated intravascular coagulation, pleural effusion, and pericardial effusion. Uveitis due to Behcet's disease flared up. He was treated with remdecivir and thrombomodulin. Fever had been also remained after initiation of treatment, then a close examination was performed. He was diagnosed with SLE based on elevating anti-DNA antibody, anti-SS-A antibody, positive direct Coombs, low CH50, thrombocytopenia, and serositis. He was treated by prednisolone 30 mg/day, but his symptoms had remained. And PSL was increased up to 50 mg/day. Although uveitis had improved, but other symptom remained with presenting low C3. Cyclosporine 200 mg/day was added for treatment forward SLE and uveitis. Then pleural effusion was improved. After starting use of hydroxychloroquine, he was discharged from the hospital. Discussion The relationship between viral infection and the development of SLE has been reported. covid-19 may also contribute to the development of SLE, but there are few reports. This is a rare case of a patient with an underlying Behcet's disease who developed SLE with flare-up of uveitis after covid-19.

## P3-172

**A Case of SLE occurring post-Vaccination of COVID-19**

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Conflict of interest: None

[Clinical Significance] We recently experienced a case of SLE that developed after receiving the initial two doses of the novel COVID-19 vaccine. [Case] 18-year-old female, 17-year-old, received two initial booster vaccinations of the COVID-19 vaccine during the COVID-19 pandemic. Immediately after the second vaccination, the area around her ears became reddish-purple and she visited a local doctor. This was due to the material of the mask. Two months after the 2nd vaccination, she developed scattered redness on both palms without itching or pain. In the 3rd month, multiple arthralgia appeared. Xray was performed at another hospital and no abnormalities were found. She also noticed morning-stiffness and palm edema and both legs hurt and it was difficult to go up and down the stairs. Discoid eruptions and skin biopsy consistent with SLE, a painless linear ulcer on the soft palate, lymphocytes 1158/μL, ANA 1:320 (Sp.), anti-ds-D-G antibodies (EIA) 87, and anti-DNA antibodies (RIA) 27, were diagnosed with SLE. She had hypocomplementemia and was judged to have disease activity. On the same day, mPSL 12 mg/d was started, tapering gradually discontinued 6 months. One month later, HCQ 200 mg/d was introduced, reducing 100 mg/d in the first year of starting HCQ.

## P3-173

**Neuropsychiatric systemic lupus erythematosus in a chronically hospitalised patient with schizophrenia**

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Conflict of interest: None

A 67-year-old woman with a 35-year schizophrenia history presented with pancytopenia. Serology was positive for the anti-nuclear antibody, anti-ds-DNA antibody, and anti-platelet-associated IgG antibody. Her haemoglobin, platelet, and white blood cell counts were 7.7 g/dL, 3.2 $\times 10^4$/μL, and 2000/μL, respectively. The brain magnetic resonance imaging revealed sporadic punctate hyperintense areas in the cerebral white matter. Single photon emission computed tomography showed decreased blood flow from the parietotemporal association area to the temporal lobe. Accordingly, systemic lupus erythematosus (SLE) with neuropsychiatric SLE (NPSLE) was diagnosed. Oral prednisolone (40 mg/day) was started, and laboratory findings, including pancytopenia improved. No relapses were reported during the 2-year follow-up. Psychiatric symptoms are rarely reported as the first and isolated feature of SLE, although many patients experience psychiatric symptoms before being diagnosed with SLE. In many NPSLE cases, there is a considerable delay between the first psychiatric and the first physical symptoms. In particular, psychiatric symptoms such as schizophrenia are self-reported by patients, making it difficult to differentiate them from other psychiatric disorders.

## P3-174

**A case of Systemic Lupus Erythematosus (SLE) with prolonged Activated Partial Thromboplastin Time (APTT) and complications of Antiphospholipid Antibody Syndrome (APS) emerged subsequent to transitioning from belimumab to anifrolumab**

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Conflict of interest: Yes

CASE: A 36-year-old woman diagnosed with Systemic Lupus Erythematosus (SLE) since age 12, featuring lupus nephritis and no history of pregnancies. Notably, she exhibited skin ulcers, ear skin shedding, and cranial alopecia. At 32, belimumab treatment proved ineffective, leading to a transition to anifrolumab at age 35, resulting in marked improvements in her skin condition. Notably, laboratory assessments showed a prolonged activated partial thromboplastin time (APTT). The patient tested positive for lupus anticoagulant on two separate occasions, leading to the diagnosis of antiphospholipid antibody syndrome. Discussion: Around 30-40% of patients with SLE exhibit the presence of antiphospholipid antibodies. Anifrolumab operates by inhibiting type I interferon, which subsequently affects B-cell-activating factor (BAFF). Notably, BAFF induction is mediated by type III interferon from various cell sources, potentially sustaining its activity. In this case, the contrasting mechanisms of action between anifrolumab, a type I interferon receptor antibody, and belimumab, an anti-BAFF antibody, likely contributed to the development of antiphospholipid antibody syndrome. It may be necessary to watch for the emergence of new diseases after using Anilflorumab.

## P3-175

**A case of systemic lupus erythematosus developed during follow-up of Gossypiboma**

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Conflict of interest: None

[Case Report] The case is a 40-year-old woman. She gave birth by cesarean section in X-12 year, and a wire and gauze were left behind, forming a Gossypiboma. The mass had increased over time and she was scheduled for tumor resection surgery. Since June of X-1 year, she had been visiting a dermatologist with a generalized skin rash. She had a fever of 38 degrees and gained 6 kg in weight since late July X year. she devel-

oped respiratory distress and visited a surgeon on August 2. She had polyarthralgia and generalized edema, and was referred to the Department of Rheumatology. Based on fever, polyarthritis, myocarditis, pericarditis, positive antinuclear antibody, positive anti-RNP antibody, hypocomplementemia, and hypergammaglobulinemia, a diagnosis of SLE was made. She was treated with prednisolone, mycophenolate mofetil, hydroxychloroquine, and various therapies for heart failure, and her symptoms became mild. [Clinical Significance] Gossypiboma is a medically-induced tumor that arises when cloth gauze or towels used during surgery are left behind in the body. It generally forms granulation and often presents with local symptoms, but in this case, it may have triggered a systemic autoimmune disease, and we report this case with a review of the literature.

## P3-176

**A case of ruptured inferior pancreaticoduodenal artery (IPDA) aneurysm with gastrointestinal bleeding in systemic lupus erythematosus (SLE)**

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Conflict of interest: None

A 69-year-old woman was hospitalized with a diagnosis of cerebral infarction at a local hospital on May 8th, 202X. Since she developed fever, laboratory data suggesting inflammation and pericardial effusion, she was transferred to another hospital, followed by a diagnosis of SLE. She was treated with intravenous methylprednisolone pulse therapy followed by oral prednisolone (PSL) and intravenous cyclophosphamide (IVCY). For further treatment, she was re-transferred to our hospital. With gradual reduction of oral PSL, she received additional IVCY twice in the course. She suddenly had bloody stool on October 29th. Plain CT revealed an abdominal mass in the duodenum. Subsequent gastrointestinal endoscopy revealed reddish mucosa with narrowing of the duodenum, but could not identify the origin of bleeding. After contrast-enhanced CT identified bleeding at the duodenal mass, she was emergently treated with endovascular embolization for ruptured IPDA aneurysm. Arterial aneurysm is a rare complication of SLE, compared to thromboembolism. Previous reports show that arterial aneurysms are formed at unusual sites in SLE. In the case of gastrointestinal bleeding, arterial aneurysms should be suspected in a patient with SLE. Contrast-enhanced CT is useful in the detection of bleeding site.

## P3-177

**A case of late onset SLE presenting with marked serious edema**

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Conflict of interest: None

A 73-years old woman who presented 1 month prior with serious edema visited our hospital. Computed tomography showed the pericardial and thoracoabdominal effusions, then laboratory investigation revealed positivity of both anti-nuclear antibody (1:320, homogeneous and speckled patterns) and anti-ds-DNA antibodies, hypocomplementemia and proteinuria. The diseases related with heart, kidney and cancer were contradictory as far as we investigated. She was diagnosed as late onset SLE, treated with prednisolone 40 mg (0.6 mg/kg), hydroxychloroquine, tacrolimus and cyclophosphamide. Her weight decreased 20 kg as improvement of edema and both pleural and cardiac effusions, however, ascites and hypocomplementemia were persisted. The upper gastrointestinal endoscopy revealed the esophageal varices, and the elevation of liver enzymes was observed persistently, therefore, we suspected her of having the liver cirrhosis following the autoimmune hepatitis. The diagnosis of SLE which emerged to elderly is difficult in comparison to young, because the typical symptoms of SLE tend to lack. The present case was hard to determine because the patient lacked typical SLE symptoms other than severe edema and serositis, in addition liver cirrhosis complicated her condition.

## P3-178

**A case of myositis induced by dupilumab in a patient with systemic lupus erythematosus**

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Conflict of interest: None

CASE PRESENTATION: A 37-year-old female diagnosed with SLE 25 years ago, and was treated with prednisolone (PSL) and tacrolimus. Five years ago, she started experiencing skin itching and blood tests showed an increase in eosinophil count and slightly elevated CRP. In March, two years ago, she was started on dupilumab. In early April, she developed muscle pain in both upper arms and thighs. Her CRP was 10.4 mg/dL, and CPK was 590 U/L. Muscle biopsy revealed muscle fiber degeneration and infiltration of inflammatory cells into the muscle sheaths. She was diagnosed with myositis and treated with PSL. However, her symptoms relapsed during the course of treatment, so mycophenolate mofetil (MMF) was added. PSL was gradually tapered, but her skin itching worsened. Therefore, dupilumab was restarted in early May. However, muscle pain reappeared at the end of May, with an increase in CPK and CRP. PSL and MMF were increased again, and her symptoms improved. CLINICAL SIGNIFICANCE: The patient experienced drug-induced myositis, which is considered to be caused by dupilumab. Although there have been no reports of myositis caused by dupilumab, particular attention should be paid to the appearance of myositis symptoms, especially in patients with underlying autoimmune diseases.

## P3-179

**A case of paroxysmal nocturnal hemoglobinuria with systemic lupus erythematosus**

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Conflict of interest: None

Paroxysmal nocturnal hemoglobinuria (PNH) is a hematopoietic stem cell disorder characterized by complement-mediated hemolytic anemia. The coexistence of systemic lupus erythematosus (SLE) and PNH has been rarely reported. Here we report a case of PNH which developed in a 34-year-old woman with SLE. At the age of 28, she was diagnosed with SLE because of nephritis, serositis and pancytopenia. As secondary thrombotic thrombocytopenic purpura occurred subsequently, she was treated successfully with cyclophosphamide and high-dose prednisolone (PSL) in combination with plasma exchange. Her disease had been stable for years with low-dose PSL, mycophenolate mofetil, tacrolimus and hydroxychloroquine. From one year ago, thrombocytopenia and macrocytic anemia were worsened with negative Coombs test and negative anti-dsDNA antibodies. Serum haptoglobin turned to be undetectable. While belimumab was administrated for possible recurrence of SLE, it was ineffective. Besides hemosiderinuria suggesting intravascular hemolysis, flow cytometry analysis with peripheral blood showed the deficiency of CD55 and CD59 in both red blood cells and granulocytes. Finally, the diagnosis of PNH was made. Our case taught that cytopenia in SLE would not always be caused by immune-mediate mechanism.

## P3-180

**A case of systemic lupus erythematosus with right brachial plexitis**

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Department of Immunology, Osaka University Hospital

Conflict of interest: None

[Case] 45-year-old female. She was a patient at our hospital because of suspected Sjögren's syndrome (SjS). On X-30, she was admitted to the previous hospital with sudden onset of right hand paralysis. Muscle weakness in the right forearm, high STIR signal on brachial plexus MRI and

demyelination in the radial nerve area on needle electromyography suggested right brachial plexitis. Peripheral neuropathy due to systemic lupus erythematosus (SLE) was suspected based on SjS or anti-dsDNA antibodies and hypocomplementaemia, and the patient was treated with steroid pulse therapy at the previous hospital on X-7. She was transferred to our hospital on X day. Since a definitive diagnosis of SjS was not reached due to the absence of abnormalities on lip biopsy, the diagnosis of brachial plexitis associated with SLE was made in this case. Since motor function improved, immunosuppressive therapy was considered effective, and induction remission therapy with rituximab was administered. The patient was discharged on the 68th day of her illness because of improvement in motor function of the right hand. Clinical significance: Brachial plexitis due to SLE is very rare, and this case was successfully treated with immunosuppressive therapy. We report this case with a review of the literature.

## P3-181

**A Case of refractory lupus nephritis treated with rituximab and belimumab following renal biopsy**

Gen Yamagiwa, Shuzo Yoshida, Takaaki Ishida
Amanokawa Hospital

Conflict of interest: None

[Case] A 76-year-old man. In July X, he was urgently admitted to a nearby hospital due to lower leg edema and difficulty in moving. Because increased CRP, positive for anti-nuclear, anti-RNP antibodies, and hypocomplementemia, lupus nephritis was suspected. Renal biopsy was considered difficult due to poor ADL and retention of pleural and ascitic fluid, so treatment initiated with mycophenolate mofetil and tacrolimus, following a steroid pulse, yielded no improvement, and pancytopenia was observed, resulting in discontinuation of concurrent medications and reliance on a single steroid. Subsequently, the patient developed an stroke, transferring to our hospital. Referred to our hospital, after renal biopsy, started tacrolimus, RTX, and belimumab. Steroid dose gradually reduced, no nephrotic syndrome remission, but discharged for outpatient treatment. [Discussion] This is a case of refractory lupus nephritis in which renal biopsy was performed and treatment was performed with belimumab and rituximab. If remission is not achieved, treatment must be strengthened as it is strongly associated with decreased ADL and life prognosis due to complications of nephrotic syndrome. Kidney biopsy should be actively considered to provide a rationale for administering rituximab or belimumab.

## P3-182

**Clinical course of systemic scleroderma patients treated with rituximab**

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Conflict of interest: None

[Objective] Rituximab (RTX) showed effectiveness for dermal sclerosis of systematic scleroderma (SSc) patients. RTX for SSc patients could have been used from September 2021 in Japan. We evaluated clinical course of SSc patients treated with RTX. [Methods] Seven patients were enrolled who had been treated with intravenous RTX (375 mg/m2) once per week for 4 weeks. The assessment of dermal sclerosis, esophageal lesion, Raynaud's phenomenon, interstitial lung disease (ILD), and chronic pseudoenteric obstruction (CIPO) at both 0 weeks and 24 weeks were performed in this study. [Results] Dermal sclerosis in 7 patients, esophageal lesion in 5 patients, Raynaud's phenomenon in 7 patients, ILD in 4 patients, and CIPO in 3 paitients were seen at 0 weeks. 24 weeks after starting RTX, changes in dermal sclerosis (improved in 1, unchanged in 3, and worsened in 3), esophageal lesion (improved in 2 patients, unchanged in 2 patients, and worsened in 1 patient), raynaud's phenomenon (improved in 3, unchanged in 4), ILD (unchanged in 3 and worsened in 1), and CIPO (improved in 1, unchanged in 1, and worsened in 1) were observed. [Conclusions] In this report, RTX was showed effectiveness for Raynaud's phenomenon of SSc patients, suggesting that it may also effective for vascular lesion in SSc.

## P3-183

**Effectiveness of rituximab for skin sclerosis in patients with systemic sclerosis, especially that associated with autoimmune polyendocrine syndrome (APS) type 2**

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Conflict of interest: None

[Objective] To examine the efficacy of rituximab for skin sclerosis in systemic sclerosis (SSc). [Methods] We retrospectively examined the efficacy of rituximab for skin sclerosis in 3 patients with SSc treated between 2021 and 2023 and followed up for over 6 months at Nagaoka Red Cross Hospital. [Results] Case 1: A 25-year-old male. SSc, myositis and Sjögren's syndrome associated with APS type 2 (type 1 diabetes and autoimmune thyroiditis). Interstitial lung disease (ILD) (-). Although the modified Rodnan total skin thickness score (mRSS) at the first visit was 5 points, it progressed rapidly during 2 months, reaching 13 points, and pulmonary function tests revealed a decreased vital capacity (VC) (%VC 62.3%) due to sclerosis of the anterior chest skin. Therefore, we started RTX therapy. At one year after the start of RTX therapy, the mRSS was 4 points and %VC had improved to 73.5%. Case 2: A 66-year-old female. Anti-Scl70 (+), ILD (+). The mRSS had decreased from 30 points to 26 at one year after the start of RTX therapy. Case 3: A 66-year-old male. ILD (+). The mRSS had decreased from 11 to 6 points after 6 months of RTX therapy. [Conclusions] RTX was effective for skin sclerosis in 3 patients with SSc, being especially effective for SSc associated with APS type 2.

## P3-184

**A case of systemic scleroderma that responded to rituximab for a calcified skin lesion that required repeated surgery**

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Conflict of interest: None

A 68-year-old woman presented to her previous physician with skin induration and phalanges. She was diagnosed as having systemic scleroderma and started treatment with prednisolone (PSL) 10 mg/day. However, when the PSL was tapered off, the interstitial pneumonia worsened, and the patient was referred to our hospital. 20 mg/day of PSL was increased to induce remission, and 50 mg/day of azathioprine was added to start tapering off the PSL. Thereafter, calcified lesions with swelling and pain appeared on the fingers and toes, and a total of five calcified lesions were surgically removed. However, the calcified lesions continued to appear and were sometimes accompanied by ulceration, so bosentan and tocilizumab were used, but with no effect. The calcified lesions worsened, and the patient was admitted to our department for intensified treatment. Rituximab 375 mg/m2/week was administered for a total of 4 times as intensified treatment. Thereafter, the pain in the fingers and toes showed a tendency to improve, and the patient was able to progress without surgery. We report a case of systemic scleroderma in which rituximab was effective in treating a calcified skin lesion that required repeated surgery, with a discussion of the literature.

## P3-185

**A case of systemic sclerosis in which glucocorticoids and rituximab were effective in treating progressive toe gangrene**

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Conflict of interest: None

Case: A 76-year-old woman with a history of celiac artery stent noticed skin tightness and reduced grip strength for the past two years. She was hospitalized for pleural effusions, peritoneal effusions, and left toe ulcers. She tested positive for anti-centromere antibodies and was transferred to our hospital. On admission, she displayed widespread skin sclerosis, Raynaud's phenomenon, and gastrointestinal dysmotility, leading to a diagnosis of diffuse cutaneous systemic sclerosis. Autoantibodies such as anti-phospholipid antibodies and ANCA were negative. Gangrene in her

left big toe, middle toe, and little toe's tips, along with dark purple skin changes on the forefoot, prompted treatment with calcium channel blockers, intravenous alprostadil, and antibiotics. Although a percutaneous angioplasty and two antiplatelet drugs were added, toe gangrene progressively worsened, affecting all left toes. The initiation of glucocorticoids and rituximab promptly stopped the expansion of gangrenous areas.

## P3-186

**Successful Treatment of Generalized Edema in Systemic Scleroderma with Tocilizhmab: A Case Report**

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Conflict of interest: None

A 74-year-old woman has regularly attended to this hospital with a diagnosis of systemic scleroderma. She had been well until three months before current evaluation, when she realized dyspnea on exertion. She was admitted to our department as the symptom gradually worsened. Ascites and leg edema was identified. Ascites puncture revealed no malignant cells. She had remained undiagnosed in spite of laboratory data and imaging studies. Fever appeared, and serum CRP, IL-6, and VEGF levels were elevated, but a diagnosis of POEMS syndrome or TAFRO syndrome was not made. She was discharged after starting diuretics, but she was readmitted two months later because of the progression of fluid retention and exhaustion. Based on the findings of high serum IL-6 and VEGF levels, we suspected that the patient was suffering from inflammatory and fluid retention pathology with a background of immunological abnormalities. We introduced tocilizumab. Not only fever and tiredness but also systemic fluid retention have improved. The patient was discharged without flare-up. Systemic scleroderma is an autoimmune disease with a variety of symptoms, and IL-6 may be a therapeutic target when the patients present with generalized edema associated with an inflammatory pathology.

## P3-187

**A case of sudden skin hardening and fulminant myocarditis and scleroderma renal crisis during the course of diffuse systemic scleroderma**

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Conflict of interest: None

A 47-year-old woman was referred to our department in August X-1 for swelling of the fingers of both hands. She was diagnosed as diffuse systemic scleroderma and followed up having mRSS of 6. PSL 3 mg/day was introduced in February, X. In March, X, she was hospitalized due to respiratory distress; echocardiography on the second day showed a decrease in EF to 62% and a large amount of pericardial sac fluid. The patient was judged to have pericarditis, and PSL 0.5 mg/kg was started on the 5th day the illness. On the 6th day, the patient was diagnosed with fulminant myocarditis based on systolic blood pressure of 60 mmHg, echocardiography showing a decreased EF of around 5%, and troponin T4.508 ng/ml. Steroid pulse, plasma exchange therapy, IVIg, and PSL 1.0 mg/kg were then started. Cardiac function improved to about 35% EF, and mRSS rose to 51 points. However, her renal function worsened rapidly, and she was placed on dialysis on the 25th day of the illness, but continued dialysis became ineffective; she died on the 57th day of the illness. Pathological autopsy revealed scleroderma in kidney and fibrosis in myocardium. Conclusion: Rapid progression of skin hardening represents risk for scleroderma in kidney and may be associated with fulminant myocarditis.

## P3-188

**A case of scleroderma renal crisis sine scleroderma with rheumatoid arthritis**

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Conflict of interest: None

[Case] A 70-year-old woman was admitted for progressive renal dysfunction. She had a 7-year history of seropositive rheumatoid arthritis currently treated with methotrexate, tacrolimus, and golimumab. The laboratory findings were significant for marked anemia and thrombocytopenia (Hb 9.0 g/dl and Plt 39000/μl), renal impairment (serum creatinine 3.87 mg/dl). Undetectable haptoglobin, negative coombs and schistocytes suggested thrombotic microangiopathy. Scleroderma renal crisis was suspected for hypertension (180/110mmHg), Raynaud's phenomenon, telangiectasia and positive antinuclear antibody, in spite of no skin sclerosis or negative results of anti-centromere/SCL70/RNP polymerase III/RNP antibody. Kidney biopsy was executed after thrombocytopenia ameliorated with administration of ACE inhibitors and revealed mucinous intimal thickening and onion-skin lesions of interlobular arteries and arterioles partly with fibrinoid necrosis. RP11/RP155 antibody was also proved positive for another assay. A diagnosis of scleroderma renal crisis sine sclerosis was finally made. [Clinical Significance] Scleroderma renal crisis sine sclerosis has been rarely reported. Diagnosis should be carefully made with pathology and detection of specific autoantibody in multiple assays.

## P3-189

**A case of a patient with systemic scleroderma with severe electrolyte abnormalities due to hypomagnesemia associated with malabsorption syndrome**

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Conflict of interest: None

[Case] A 43-year-old woman was diagnosed with Raynaud's phenomenon around age 30, chronic vomiting, diarrhea, reflux esophagitis, gastrointestinal peristalsis, and skin sclerosis. In February X-1, she had hypokemia and potassium supplementation was started. In July X, she had decreased appetite, painful muscle spasm of limbs, and increased urinary K excretion. The symptoms worsened and the patient was brought to our hospital on July 27. Blood samples were taken and revealed hypocalcemia, acidosis, hypomagnesemia, hypokalemia, and hyperphosphatemia. Hypomagnesemia due to malabsorption syndrome and prolonged use of PPIs was considered to be the cause of the severe electrolyte abnormalities. After admission, various electrolytes were corrected, erythromycin and metoclopramide were started to promote gastrointestinal peristalsis, and intestinal antiflatulents were used to treat abnormal bacterial growth. [Conclusions] Periodic Ca and Mg measurements are recommended in scleroderma patients with malabsorption disorders. In addition, there is a risk of hypoglycemia due to long-term oral administration of PPIs. The results of this study were particularly significant in patients with reflux esophagitis due to scleroderma who were taking PPIs for a long time.

## P3-190

**Two cases of Systemic Sclerosis with double positive of disease specific autoantibodies**

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Conflict of interest: None

[Case 1] An 81-year-old woman was referred to our hospital because of knee joint pain. She was diagnosed with diffuse cutaneous systemic sclerosis (SSc) with skin sclerosis and anti-topoisomerase I antibody (ATA) and anti-centromere antibody (ACA) positive. She developed interstitial pneumonia and a digital ulcer, treated with antifibrotic agents, peripheral vasodilators, and platelet aggregation inhibitors. [Case 2] An XX-year-old woman was referred to the hospital because of dry cough and abnormal shadow with chest x-ray. She was diagnosed as localized cutaneous SSc due to positive ACA and finger sclerosis. Anti-RNA polymerase III antibody (ARA) are also detected in our hospital. The lung lesions were non-progressive on imaging and the serum KL-6 level tended to decrease with time, so we did not use medication and followed up with chest CT images. [Clinical Significance] Disease-specific antibodies in SSc are normally exclusive, and overlapping cases of ATA and ACA have been reported in 0.5% to 5.6% of cases. The overlap of ARA and ACA is even rarer, and this is the fourth case reported in Japan as far as our search indicates. Our cases were also milder than the ARA-single-positive case. Antibody overlap in SSc does not necessarily lead to overlap or severity of the disease.

## P3-191

**Clinically Isolated Aortitis: Single Center Experience**

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Conflict of interest: None

[Objective] Clinically isolated aortitis (CIA) refers to inflammation of the aorta without signs of systemic vasculitis or infection. We aimed to assess the clinical features and prognosis in a cohort of patients with CIA. [Methods] We retrospectively reviewed medical records of Japanese patients diagnosed with IA at our hospital between April 1, 2013 and September 30, 2023. IA was defined pathologically in resected aortic tissue or radiologically by CT scans. Data were collected on clinical features and prognosis. [Results] Among 16 patients with IA, 5 patients with CIA were identified. The median age at diagnosis was 66 (range, 56-88) years; 4 (80%) of them were female. Four patients were diagnosed following aortic surgery; 3 of them had multinucleated giant cells. The median duration of follow-up was 0.62 years (range, 0.27-6.67). One patient died within 4.2 months of surgery; another patient was diagnosed with Giant cell arteritis after 7.5 months. The other 3 patients remain under outpatient care without any signs of systemic vasculitis. [Conclusion] Although patients with CIA are at an increased risk for subsequent aortic events and developing systemic aortitis, some may be stable after aortic surgery alone.

## P3-192

**Evaluation of the usefulness of tocilizumab in the treatment of large vessel vasculitis in our hospital**

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Conflict of interest: None

[Objective] TCZ is the only biological agent approved in Japan for the treatment of TAK and GCA, and clinical trials have shown a reduction in relapse and steroid dose. In this study, we investigated the use of TCZ in our hospital to examine its efficacy in clinical practice. [Methods] TAK and GCA patients who were initiated on TCZ at our hospital from Sep 2017 to Aug 2023 were included, and prognoses such as relapse and large-vessel complications under TCZ use and changes in steroid dosage were evaluated retrospectively. [Results] 11 patients with TAK and 14 patients with GCA were included, and the duration of illness was significantly longer in the TAK group than in the GCA group (44 vs. 6 months). Relapse after TCZ induction was 3 in the TAK group and 3 in the GCA group, including 2 deaths due to exacerbation of large vessel complications. In both TAK and GCA groups, there was a significant negative correlation between the duration of TCZ and the dosage of prednisolone ($r=-0.62$, $p=0.043$ for TAK group; $r=-0.59$, $p=0.026$ for GCA group). On the other hand, no correlation was found between the duration of TCZ and the number of relapses. [Conclusions] The results of this study suggest that TCZ may contribute to steroid reduction in both TAK and GCA treatment in clinical practice.

## P3-193

**An example of adult large vessel vasculitis after SARS-CoV-2 infection**

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Conflict of interest: None

[Case] A 73-year-old man [Current medical history] The patient was hospitalized with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at another hospital and recovered on day 7. Although respiratory symptoms improved, he had fever over 38 °C again from day 15. Blood test results showed C reactive protein (CRP) 18 mg/dL. He had persistent fever and high CRP levels despite antimicrobial therapy. Blood culture results were negative. CT and 18F-fluorodeoxyglucose positron emission tomography on day 27 showed elevated 18F-FDG uptake in the arterial wall, ranging from the ascending aorta to the abdominal aorta. On day 35, he was referred to our hospital due to suspected large vessel vasculitis (LVV). At the time of referral to our department, the peak of fever had decreased to less than 38°C and CRP was also decreased (7.3 mg/dL). He exhibited no visual impairment. Magnetic resonance imaging of the brain and orbit was unremarkable for inflammatory lesions. We followed the clinical course with only acetaminophen. By day 48, fever gradually improved, and CRP decreased (0.82 mg/dL). [Discussion] We experienced a case of LVV after SARS-CoV-2 infection. It should be noted that LVV after SARS-CoV-2 infection may improve without immunosuppressive treatment, as in this case.

## P3-194

**A case of suspected vasculitis based on cuffing around superior mesenteric artery, which turned out to be pancreatic cancer**

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Conflict of interest: None

[Case] 74-year-old male presented constipation and anorexia after the common cold. Since right lower abdominal pain also appeared, plain CT and upper endoscopy were performed, but no abnormality was found. Contrast enhanced CT (CECT) and PET-CT revealed cuffing around superior mesenteric artery (SMA). Suspected vasculitis or perivasculitis, he was admitted to our hospital for further examination. CRP and ANCA were negative, and IgG4 was within normal range. Re-performed CECT showed a 15 mm-sized tumor in the uncinate process of pancreas, which presented low enhancement at the early phase and gradual enhanced over the late phase. Endoscopic biopsy demonstrated atypical glandular epithelial cells with foamy gland pattern, therefore he was diagnosed with pancreatic ductal adenocarcinoma. Surgery was not possible due to adhesion between tumor and artery. Best supportive care was selected because of patient's wishes. [Discussion] The typical image of pancreatic cancer is low enhancement mass at the early phase and/or dilation of main pancreatic duct. However, it has been reported that some pancreatic cancers only present with cuffing around the celiac artery or SMA, which require differentiation for vasculitis or IgG4 related diseases due to similarity of images.

## P3-195

**A case of diverse cardiovascular lesions during treatment of ulcerative colitis**

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Conflict of interest: None

<Case> A 58-year-old man was treated for ulcerative colitis (UC). Prednisolone (PSL) was added due to worsening of intestinal symptoms, and discontinued. Subsequently, he developed fever in the 38°C range, elevated inflammatory response. Contrast-enhanced CT showed thickened vessel walls in the ascending aorta, and FDG-PET/CT showed increased FDG accumulation in the right atrial wall, leading to the diagnosis of aortitis syndrome and pericarditis related to UC. He also had complete atrioventricular block and later underwent pacemaker implantation. Pulse therapy with mPSL was started on the second day. CT showed dissection of the ascending aorta, and a standby ascending aortic replacement was performed. Vascular pathology of the ascending aorta showed inflammatory cell infiltration and from the outer to the tunica media, which was thought to be Takayasu arteritis (TA). Thereafter, the patient was treated with oral upadacitinib, chest symptoms and inflammatory response improved, PSL was gradually reduced. <Conclusions> This is a rare case of UC complicated by a variety of cardiovascular lesions, including TA, complete atrioventricular block, and pericarditis. We report the mechanism of the development of this series of lesions, including a review of the literature.

## P3-196

**Clinical characteristics of eosinophilic granulomatosis with polyangiitis treated with mepolizumab at our hospital**

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Conflict of interest: None

[Objective] The relapse of eosinophilic granulomatosis with polyangiitis (EGPA) often occurs during the tapering of glucocorticoids (GCs) and its sparing approach might be beneficial. The purpose is to elucidate clinical characteristics of EGPA treated with mepolizumab (MPZ). [Methods] We examined patients with EGPA, who admitted to our hospital between May 2008 and Oct 2023. Background, Clinical symptoms and laboratory data were examined between patients with MPZ and those without MPZ (non-MPZ). We also evaluated the GC-sparing effects in patients with MPZ. [Results] 1) 23 patients (51.7±19.0 years old, 9 males/14 females) were evaluated. MPZ group (14 patients) was significantly younger than non-MPZ group (p=0.006). 2) There was no difference about the damaged tissues between MPZ and non-MPZ group. The proportion of MPO-ANCA positive patients was significantly lower in MPZ group (p=0.018). 3) MPZ was administered mainly due to the relapse of EGPA (42.9%) and the reduction of GCs (35.7%). 7 patients with MPZ reduced the dose of GCs from 9.6 mg/day to 4.4 mg/day in one year. [Conclusions] The characteristic features of MPZ group were early onset and lower frequencies of positive MPO-ANCA. MPZ was administered mainly during the maintenance of EGPA at our hospital, which could reduce GCs doses.

## P3-197

**Remission induction therapies and their outcome with ANCA-Associated Vasculitis (AAV) in our department**

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Conflict of interest: None

[Objective] To clarify remission induction therapies and their outcomes in patients with AAV in our department. [Methods] From 2013 to 2021, we reviewed clinical data of AAV patients who received induction therapy in our department for two years, from their medical records retrospectively. We defined remission as those who had Birmingham Vasculitis Activity Score (BVAS) less than 1, prednisolone use less than 10 mg/day, and absence of flare-up. [Results] We found 29 microscopic polyangiitis (MPA) patients, 10 granulomatosis with polyangiitis (GPA), and 9 eosinophilic granulomatosis with polyangiitis. Median age of each AAV patients was 72, 64 and 68 years old, and males were 29, 60 and 33%, respectively. MPO-ANCA (positive, %): 100/25/44, PR3-ANCA (%): 0/75/0. Median score of BVAS before therapy was 14, 16 and 14, respectively. At 52 weeks, patients in remission of MPA, GPA and EGPA in corticosteroids (CS) +IVCY group and CS group were 1/0/1 case and 10/1/0 cases, respectively. Over 50% of GPA cases resulted in recurrence. Patients with MPA and GPA who were not in remission had diabetes mellitus (67 and75%) and infection (56 and 50%), respectively. [Conclusions] The remission rate was lower in patients with diabetes and infections.

## P3-198

**A Case of microscopic polyangiitis (MPA) complicated by large and medium vessel vasculitis: utility of lower limb arterial echo examinations and PET-CT**

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Conflict of interest: None

[Case] An 82-year-old woman was referred to our hospital for suspected interstitial pneumonia (IP) due to persistent cough and dyspnea. NSIP on chest CT and elevated MPO-ANCA (30.2 IU/mL) led to a diagnosis of MPA. Immunosuppressive therapy was not started because of negative CRP and unchanged IP images. Two years later, she began having fever and right lower limb myalgia with worsening of cough and dyspnea. She was admitted to our hospital in August of X year. CRP rose to 8.10 mg/dL and MPO-ANCA to 55.8 IU/mL, and PET-CT indicated large vessel vasculitis. MRI showed high signal areas in T2-weighted fat suppression images in both lower leg muscles, suggesting medium vessel vasculitis. Initiation of 60 mg of PSL and rituximab rapidly improved her symptoms and normalized CRP. Three weeks later, the findings of MRI disappeared and interestingly arterial echo showed normalized blood flow. The dose of PSL was tapered according to the protocol of reduced-dose group in the PEXIVAS trial (N Engl J Med 2020; 382:622-631) without recurrence. [Clinical Significance] MPA is primarily a small vessel vasculitis but can coexist with large and medium vessel vasculitis. In addition to PET-CT, non-invasive arterial echography was useful not only for diagnosis but also for evaluation of treatment.

## P3-199

**Clinical Significance of Mepolizumab in patients with Eosinophilic Granulomatosis with polyangiitis**

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Conflict of interest: None

[Objective] We examined the treatment and problems with eosinophilic granulomatosis with polyangiitis (EGPA). Clinical utility and problems of mepolizumab for EGPA Five patients with EGPA were given mepolizumab 300 mg S.C. once a month. Two cases were women. Three preceding allergic diseases were accompanied by chronic eosinophilic rhinosinusitis with nasal polyp (CRSwNP) and bronchial asthma. 3 positive cases of MPO-ANCA. Mononeuritis multiplex was observed in 4 cases. The maximum average of eosinophils was 5,290. Steroids administered from PSL 50 mg. After continuation of mepolizumab, mononeuritis multiplex was relieved and steroid tapering was possible in all five cases. However, in 2 out of 3 patients with CRSwNP re-enlargement of the nasal polyp, nasal obstruction, and odor disturbance occurred when the PSL was ta-

pered to less than 5 mg. [Conclusions] It is considered to be a point to be noted in the process of aiming for steroid termination when treating EGPA.

## P3-200

**Successful early glucocorticoid reduction with mepolizumab combination in a case of eosinophilic granulomatosis with polyangiitis complicated by appendiceal cancer**

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Conflict of interest: None

The case was 69 years old, male. He developed bronchial asthma in 20XX-11. In May 20XX, He was referred to our hospital due to purpura of the extremities, polyneuritis, and eosinophilia. Although laboratory findings were negative for both MPO-ANCA and PR3-ANCA, a skin biopsy showed necrotizing vasculitis with eosinophilic infiltration, and he was diagnosed as having eosinophilic granulomatosis with polyangiitis (EGPA). Rapid progression of neuropathy and acute cerebral infarction in the left capsule were observed, and treatment with high-dose glucocorticoid (GC) was started. In addition, colonoscopy revealed cecum cancer (cT2N0M0), which was indicated for surgery. Early GC reduction was required due to surgery for cecum cancer, combination of mepolizumab was initiated from day 11. The dose of GC was reduced to PSL 10 mg/day in 6 weeks, surgery for cecum cancer was performed on day 80. The patient had no postoperative recurrence of EGPA, treatment with high-dose immunoglobulin therapy was stared for residual neurological symptoms. In addition to GC therapy, cyclophosphamide pulse therapy or rituximab are often used as induction remission therapy for severe EGPA. Combination use of mepolizumab was considered to be a useful option for early GC reduction in EGPA.

## P3-201

**Tocilizumab in patient with treatment-resistant microscopic polyangiitis with aortitis**

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Conflict of interest: None

A 68-year-old woman was hospitalized with fever, leg pain, upper limb numbness, right leg motor paralysis, and antibiotic-resistant pneumonia. Laboratory tests revealed hematuria, proteinuria, and MPO-ANCA 120 U/mL, leading to the diagnosis of microscopic polyangiitis. She was started to treat with intravenous methylprednisolone pulse followed by oral prednisolone (PSL) 1 mg/kg and rituximab (RTX). Myalgia, nephritis, and mononeuritis multiplex were improved with reduced-dose glucocorticoid taper regimen, but CRP was elevated again. PSL was increased to 0.5 mg/kg and tapered more slowly. On day 45, she was discharged. On day 200, when PSL was 10 mg, she was readmitted because of pericardial effusion. We diagnosed relapse, and added avacopan and RTX, but neither pericardial effusion nor CRP improved. On day 270, contrast-enhanced CT revealed aortitis. PSL was increased to 1 mg/kg and added pulse cyclophosphamide. MPO-ANCA was improved, but CRP was not. FDG-PET revealed accumulation of aorta and pulmonary artery. After Tocilizumab was started, CRP was normalized, and on day 498, we confirmed the disappearance of pericardial effusion and reduction in aortic wall thickening. We report a case of treatment-resistant microscopic polyangiitis with aortitis that responded to tocilizumab.

## P3-202

**Two cases of microscopic polyangiitis with severe liver dysfunction caused by avacopan**

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Conflict of interest: None

Case 1: A woman in 80s was referred to our department with edema of both lower legs, general malaise, and renal dysfunction. MPO-ANCA 361 IU/mL, MPA was diagnosed, and mPSL 500 mg, IVCY400 mg, PSL 25 mg, and avacopan 60 mg were used in combination. Two months later, hepatic impairment appeared, and avacopan was discontinued. Liver function normalized after one month. Case 2: A man in 60s who was diagnosed with MPA 9 years ago, was in complete remission with PSL alone, and completed PSL administration 6 months ago. MPO-ANCA was positiveized, MPA was considered to be a relapse and the combination of PSL 30 mg and avacopan 60 mg was resumed. 4 months later, MPO-ANCA 4.1 IU/ Although mL tended to improve, hepatic dysfunction appeared, and liver function normalized one month after discontinuation of avacopan. Discussion: Abacopan as a selective C5a receptor inhibitor is expected to reduce side effects by early reduction of steroids, but the method of administration has not been established. Immediately after marketing surveillance reported 37.5% of hepatobiliary disorders, but the pathogenesis and countermeasures are unknown. We report two suggestive cases in which MPA normalized liver function approximately one month later without recurrence due to discontinuation of treatment.

## P3-203

**A case of MPO-ANCA positive Granulomatosis with polyantiitis with myocardial disorder**

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Conflict of interest: None

64 years-old female visited an otorhinolaryngologist for hearing loss of left ear in April, X. She was diagnosed with otitis media with effusion, so she was treated. The symptom was improved, but relapsed with headache in July. One day, she felt sudden back discomfort and cold sweat, so she visited the emergency department in our hospital. The blood sumpling showed elevation of CPK and BNP level and Troponin positive. Chest X ray showed congestion and electro-cardiogram showed novel right bundle branch block. She admitted and under went cardiac catheterization, but no epicardiac coronary artery occlusion was detected. Cardiac MRI showed late gadlinium enhancement in septal and posterior wall, and myocarditis was suspected. She had left sensorineural hearing loss, redness of the left nasal mucosa, redness and swelling of the left external auditory canal, and evidence of otitis media. A biopsy was performed. Blood test showed high CRP level and MPO-ANCA positive. Left peripheral facial nerve paralysis developed, at the same time lung and renal disorder was observed. We started steroid therapy. The biopsy of nasal and ear showed granuloma and necrotizing vasculitis, so we diagnosed GPA and added rituximab. Myocardial disorder of GPA is rare. We report this case with some discussion.

## P3-204

**A case of polyarteritis nodosa presenting with acute abdomen**

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Conflict of interest: None

On X-17, he became aware of fatigue, and watery diarrhea, abdominal pain, and fever in the 40°C range appeared on the following day. On X-8, acute abdominal pain appeared, and he visited the emergency department again. Abdominal CT showed a severed middle colonic artery and increased lipid concentration in the mesentery, and the patient was admitted to the previous hospital on the same day with a diagnosis of mesenteric hematoma. He was transferred to our hospital on Xth. The diagnosis of polyarteritis nodosa (PAN) was made based on fever, scattered purpura on both lower legs, refractory hypertension, persistent elevated inflammatory response, and multiple aneurysms in the region of the superior mesenteric artery on arteriography. Steroid pulse therapy was started, followed by PSL 0.8 mg/kg/day and intravenous cyclophosphamide 900 mg/dose (500 mg/m$^2$). After the start of treatment, fever and abdominal symptoms improved, and the inflammatory reaction became negative on the 8th day of

treatment. [Clinical Significance] Abdominal vascular lesions caused by PAN often have a poor prognosis, and early diagnosis and therapeutic intervention may improve the prognosis. Abdominal angiography is recommended when this disease is suspected.

## P3-205

**Avacopan use in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis syndrome**

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Conflict of interest: None

[Objective] We conducted a retrospective analysis of Avacopan use in AAV patients. [Methods] Eight AAV patients were subjected for the study. Four were granulomatosis with polyangiits (GPA), three were microscopic polyangiitis (MPA), and one was categorized as unclassifiable vasculitis. The mean age was 71±18 year-old, one male and seven female. GPA patients were positive for MPO-ANCA in three, PR3-ANCA in one. All MPA patients were positive for MPO-ANCA. Duration of Avacopan use was one to six months. [Results] The BVAS changed from 5.4±4.8 to 2.9±3.2 after Avacopan use. In three cases who used Avacopan more than three months, one case reached remission, and the other two attained partial remission. The case that attained remission was early systemic GPA in whom Avacopan was only used. The one case of partial remission was multi-drug resistant GPA that already used six immunosuppressive agents including IVCY and RTX. Serious adverse events were experienced in two cases, in which severe liver dysfunction was observed. However, both patients were fully recovered without any sequela. [Conclusions] Avacopan might be useful in multidrug-resistant AAV cases, and is able to use as a single agent of immunosuppressive medication in early systemic AAV.

## P3-206

**A case of suspected exacerbation of Pseudomonas aeruginosa pneumonia by Avacopan**

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Conflict of interest: None

[Case] An 85-year-old woman visited our hospital complaining of fever and dyspnea. She had chronic bronchitis and bronchiectasis with *Pseudomonas aeruginosa*. She was admitted to our hospital with a relapse of ANCA-associated vasculitis due to acute kidney injury, elevated inflammatory response, and elevated MPO-ANCA. After the commencement of prednisone and Avacopan, bronchiectasis and pneumonia were exacerbated. Although Antibiotics were administered, the pneumonia worsened again within a week. She was diagnosed with a pulmonary pyogenic disease caused by *Pseudomonas aeruginosa* and was treated for 4 weeks. PSL was tapered down to 10 mg. However, one week after discontinuing the antibiotics, the pneumonia worsened again. In this case, Avacopan may be involved in exacerbating the Pseudomonas aeruginosa infection, and the Pseudomonas infection subsided after discontinuing Avacopan and administering antibiotics. [Discussion] It has been reported that C5a receptor-deficient mice cannot eliminate *Pseudomonas aeruginosa* that has invaded the lungs and died. The anti-C5 antibody eculizumab has been reported to be susceptible to infection by capsular bacteria. The course of this case and data from mice suggest that Avacopan may exacerbate Pseudomonas aeruginosa infection.

## P3-207

**Urinary retention as first presentation of granulomatosis with polyangiitis successfully treated with TMP-SMX monotherapy**

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Conflict of interest: None

[Case] A 66 year old man [Present history] One month ago, he developed urinary retention and was diagnosed with benign prostatic hyperplasia (BPH). Three weeks ago, he developed nasal obstruction and was referred to our clinic for suspected granulomatosis with polyangiitis (GPA) because of positive PR3-ANCA. [physical exams] SpO2 98%, otitis media and mild dyspnea [test results] Cr 0.88 mg/dl, Na 132 mmol/l, CRP 5.35 mg/dl, HbA1c 8.1%, βDglucan and T-spot negative, PR3-ANCA ≧ 350 U/ml, U-OB (2+), Chest Xp; mass lesion in the right lower lobe, sputum culture; negative, prostatic pathology; granulomatosis [Clinical Coarse] He was diagnosed with GPA, but diabetes was poorly controled and glucocorticoid (GC) might worsen it. His general condition being well, he was started on TMP-SMX 3 tablet/wk, which was titrated up to 2 tablets/day. His symptoms and laboratory data improved. [Clinical Significance] Even if BPH was initially suspected, it is important to measure ANCA if systemic symptoms are present. In this case, his symptoms and organ function were stable, and his diabetes mellitus was poorly controlled. In these conditions, TMP-SMX monotherapy rather than combination with GC might be considered as a the first-line treatment.

## P3-208

**A case of ANCA-negative eosinophilic granulomatosis with polyangiitis complicated by myocarditis successfully treated with intravenous immunoglobulin**

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Conflict of interest: None

[Case] A 77-year-old man developed bronchial asthma 2 years before. He suffered from nasal obstruction and was diagnosed with eosinophilia by his family doctor. One month later, he developed abdominal pain with persistent eosinophilia, so he was referred to our hospital for suspected EGPA. Blood tests showed CRP 4 mg/dl and hypereosinophilia (5800/ul) with negative MPO-ANCA. He also had elevated troponin I, and his echocardiography showed diffuse hypokinesis. Contrast-enhanced MRI showed enhancement in his myocardium, and myocardial biopsy revealed lymphocytic infiltration. We diagnosed EGPA complicated by myocarditis. We started high-dose prednisolone 60 mg/day (1.0 mg/kg) after methylprednisolone pulse treatment (1g, 3 days). MRI showed persistent myocarditis, so we administered high-dose intravenous immunoglobulin (IVIg) therapy. After that, his cardiac contraction and contrast enhancement on MRI improved. [Clinical Significance] EGPA causes various organ lesions due to vasculitis. Myocarditis is a fatal and recurrent complication in ANCA-negative patients. We successfully treated him with IVIg, so we report this case with the literature review.

## P3-209

**A case of a young woman treated with steroid and rituximab plus avacopan for recurrent ANCA-associated vasculitis localized to the central nervous system and spinal cord**

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Conflict of interest: None

(Clinical course) A 29-year-old female visited our hospital complaining of nausea and numbness in the left side of her body in December of X-1 year. MRI showed a high-intensity area on the right side of the medulla oblongata. She was treated with steroid pulse therapy as a diagnosis of CNS localized AAV because MPO-ANCA was revealed positive, and her symptoms improved. PSL were tapered and discontinued in June of X year, but dizziness and numbness in the right hand appeared 1 week later. Brain MRI showed no abnormal findings. Steroid pulse therapy was initiated as an outpatient. The numbness improved after pulse therapy, but numbness in the left upper limb appeared after shifting to PSL 30 mg. Cervical MRI showed C3 level spinal cord high-intensity area, indicating

the causative lesion. She was admitted in July of X year. After admission, PSL 60 mg, RTX 375 mg/m2, and avacopan were administered and the numbness gradually improved. PSL are currently being tapered on an outpatient. (Discussion) CNS-localized AAV is a unique type of AAV, and spinal cord involvement in particular is rare. The patient was a young woman but relapsed even with moderate-dose steroids, so RTX and avacopan were used. There have been few reports of the use of avacopan in CNS lesions, and we report this case.

## P3-210

**A case of subarachnoid hemorrhage (SAH) during remission induction therapy for mononeuritis multiplex due to eosinophilic granulomatosis with polyangiitis (EGPA)**

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Conflict of interest: None

[Case] 64-year-old woman [Chief complaint] Drop foot [History] Eosinophilic pneumonia, bronchial asthma [Current medical history] 4 months before admission, dizziness, headache, fever, and abnormal sensation in the lower limbs appeared. MPO-ANCA was positive, so she was diagnosed as EGPA. She was treated with PSL 20 mg and mepolizumab 300 mg monthly, but her symptoms did not improve. Also drop foot appeared, so she was referred to our department. After examinations, we diagnosed polyneuropathy due to EGPA and started IVCY added to high-dose steroid therapy. The symptoms improved partly, but headache appeared on the 4th day, and left paresis and truncal ataxia appeared on the 13th day. Head MRI showed SAH in the right parietal lobe, infarction, and multiple vascular stenoses in cerebral arteries. She was transferred to the hospital for rehabilitation on the 78th day without any worsening. [Discussion] AAV with SAH is reported to have a low incidence of cerebral aneurysm, which was consistent with this case. CNS involvement, including SAH, is high mortality rate, and immunosuppressive therapy, such as IVCY, is recommended for severe organ involvement. The headache in this case may have been a prodromal symptom of CNS involvement, and it is presented as an instructive case.

## P3-211

**Short-term utility of avacopan after remission inductiontherapy with rituximab in elderly patients with ANCA-associated vasculitis**

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of avacopan (AVA) early after initiation in elderly ANCA-associated vasculitis (AAV) patients. [Methods] Patients were included in this study who were diagnosed with AAV from November 2022 to September 2023 and started AVA after remission induction therapy with corticosteroids and rituximab. We evaluated maintenance rate of remission (BVAS ≧50% improvement from baseline) after starting AVA at 12 weeks and the detail of adverse events. [Results] Seven patients (age mean: 69.7 years, median: 71 years) were included who were diagnosed with microscopic polyangiitis. Five patients of rapidly progressive glomerulonephritis, 3 of interstitial pneumonia (IP) or alveolar hemorrhage, 1 of myositis, 1 of otitis media, and 1 of mononeuritis multiplex were identified as active lesions. Five patients received steroid pulse therapy. The average initial dose of prednisolone (PSL) was 53.3 mg/day. When starting AVA, all patients had below PSL 30 mg/day and duration from initial treatment was 24 days on average. Five patients met remission at starting AVA and 4 (80%) remained at 4 weeks. In one patient, liver dysfunction with suspected adverse events occurred. [Conclusions] Efficacy and safety of AVA in early stage were suggested in elderly AAV patients.

## P3-212

**The successful experience of tocilizmab treatment for polyarteritis nodosa 2 patients**

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Conflict of interest: None

[Background] PN has many recurrence cases, and immunosuppressants are often used, but there are situations where it is difficult to use due to liver dysfunction. There have been some cases of TCZ treatment for PN, and the experience of TCZ treatment for PN 2 patients with alcoholic hepatitis is reported. [Case 1] A man with alcoholic hepatitis in his 30s. PN diagnosis from skin biopsy with lower limb pain. After steroid pulse therapy + cyclophosphamide pulse, the dose was reduced from 1 mg/kg PSL treatment. CRP negativity could not be maintained, and AZP was used in combination, but transaminase elevation was observed, and TCZ 162 mg was administered, CRP negative, PSL was reduced and discontinued. [Case 2] A man with alcoholic hepatitis was diagnosed with skin type PN. Although adjusted with PSL10 mg~20 mg, CRP negativity could not be maintained, and transaminase elevation was observed while AZP and MTX were used in combination. TCZ was administered, and CRP was negative, and the dose could be reduced. [discussion] In cases of abnormal liver function such as elevated transaminases such as alcoholic hepatitis, it is difficult to select conventional treatments, but TCZ combined use has gained valuable experience in controlling the disease.

## P3-213

**A case of polyarteritis nodosa (PAN) complicated by multidrug-resistant Pseudomonas aeruginosa infection in both lower leg ulcer sites**

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Conflict of interest: None

[Case] 84-year-old woman [Medical history] She was diagnosed with cutaneous PN and referred to our department due to worsening leg ulcers and numbness in both upper extremities; she was diagnosed with PAN and started steroid therapy. Her symptoms improved after treatment, but both lower extremity ulcers worsened and she was admitted to our hospital. [Clinical Course] Pseudomonas aeruginosa was detected in the ulcer and the patient was treated with antimicrobials, steroid pulse therapy, and IVCY. After completion of antimicrobial therapy, the inflammatory response increased and Pseudomonas aeruginosa was detected in the ulcer; IVCY was discontinued, steroids were tapered, and antimicrobial therapy was continued. The patient did not deteriorate after completion of antimicrobial therapy. [Objective] PAN causes inflammation of the walls of medium and small arteries, leading to organ ischemia and infarction, which are often fatal. On the other hand, immunosuppressive therapy increases the risk of infection, and infection is reported to be the most common cause of death in patients with PAN. In this report, we describe a case of multidrug-resistant Pseudomonas aeruginosa infection in bilateral leg ulcers associated with PAN that was difficult to evaluate and treat.

## P3-214

**A case of polyarteritis nodosa diagnosed early due to the appearance of testicular pain after hospitalization**

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Conflict of interest: None

[Case] A 44-year-old male with no previous medical history. He had persistent fever, and was referred to our hospital after his doctor found high inflammatory response and liver damage. When he came to our hospital, there was no physical abnormality to be noted except for a fever and hypertension. On the evening of hospitalization, he had a pain in the right testicle. Contrast-enhanced CT showed increased lipid concentrations around bilateral testicular arterioles, abdominal angiography showed multiple small aneurysms in the hepatic artery, wall irregularity in the superior

mesenteric artery and in the right testicular artery from the middle. We diagnosed as probable PAN. PSL 0.8 mg/kg/day and IVCY 500 mg/m$^2$ x 6 times were started. After initiation of treatment, the inflammatory response and hepatic LDL improved rapidly. Follow-up CT performed on the 43rd day showed that the increased lipid concentration around the spermatic cord had disappeared. [Clinical Significance] A testicular pain is an important physical finding that can rule in medium-sized vasculitis, including PAN. In this case, testicular pain appeared immediately after hospitalization, and we were able to promptly diagnose and treat the patient by performing an examination assuming PAN at an early stage.

## P3-215

**A case of polyarteritis nodosa caused by bilateral epididymitis**

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Conflict of interest: None

[Case] A 48-year-old man visited his family doctor because of the onset of fever and left scrotal pain around August of X year. He was diagnosed as epididymitis and prescribed antibiotics, but his symptoms did not improve. He was referred to our urology department in September X. His symptoms included fever, elevated CRP, bilateral epididymitis, arthralgia, muscle pains, and weight loss. MRI and ultrasonography indicated bilateral epididymitis. Head MRI, MRI angiography, PETCT, and upper and lower endoscopy showed no abnormal findings. A biopsy of the left epididymis was performed, and findings suggestive of vasculitis. The diagnosis of polyarteritis nodosa ("PAN") was made, because it met the ACR criteria for classification, although it did not meet the Japanese diagnostic criteria. Prednisone 50 mg/day was started, CRP and symptoms improved. [Discussion] It has been reported that about 60-80% of autopsy cases of patients with PAN have findings of suspected vasculitis in the scrotum, and testicular pain is also included in the ACR criteria for PAN classification. However, the diagnostic criteria for PAN used in Japan criteria do not include scrotal symptoms, which may lead to a doctor's delay if there are few findings other than scrotal symptoms.

## P3-216

**Three cases of muscle biopsy to diagnose ANCA-associated vasculitis (AAV)**

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Conflict of interest: None

Background We report three cases in which AAV was suspected and muscle biopsy was performed. Case 1 A woman in her 70s. A month before admission, fever, myalgia, and muscle weakness appeared. Serum CRP levels and MPO-ANCA titers were elevated while serum CK levels were normal. MRI showed T2-weighted high signal areas in bilateral iliopsoas muscles. A muscle biopsy revealed perivascular inflammation. Case 2 A man in his 80s. A month before admission, fever, weakness and pain of lower limbs, and jaw claudication appeared. Serum CRP levels and MPO-ANCA titers were elevated. MRI showed T2-weighed high signal areas in the masticatory muscles and bilateral iliopsoas muscles. A muscle biopsy revealed perivascular inflammation. Case 3 A man in his 60s. Three months before admission, numbness of lower limbs appeared, and he lost 18 kg. Serum CRP levels and MPO-ANCA titers were elevated and mononeuropathy multiplex was observed. MRI showed T2-weighed high signal areas in hamstring. A muscle biopsy showed no findings of vasculitis, but a nerve biopsy showed perivascular inflammation. Clinical importance Muscle biopsy is a relatively safe method to obtain pathological specimens. Muscle biopsy may be considered when renal or skin biopsy is not applicable.

## P3-217

**case of eosinophilic granulomatosis with polyangiitis in which mepolizumab influenced the titer of MPO-ANCA**

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Kuwana City Medical Center

Conflict of interest: None

[Objective] The efficacy of mepolizumab to MPO-ANCA-positive eosinophilic granulomatosis with polyangiitis (EGPA) is controversial, and the influence on MPO-ANCA is unclear. In We report a case of EGPA in which MPO-ANCA remained negative after starting mepolizumab, increased after discontinuation of the drug, and decreased after restarting it. [Case] 72-year-old woman suffering bronchial asthma, purpura, multiple mononeuropathy, and MPO-ANCA positive (457 U/mL) was diagnosed with EGPA in year X-10. Induction therapy with glucocorticoids (GC) was performed, but peroneal nerve palsy remained. In year X-5, She relapsed and was referred to our department. Re-induction therapy was conducted and GC was tapered off. By year X-1, GC was discontinued. In September of the year, she underwent surgery for lumbar scoliosis and degenerative scoliosis at another hospital, and mepolizumab was discontinued at that time. In December of the same year, increaseing of MPO-ANCA was observed, which continued until January year X, and then showed decreasing. [Conclusions] This is an interesting and suggestive case to think about the association between eosinophil / IL-5 and MPO-ANCA in EGPA.

## P3-218

**Eosinophil activation in active granulomatosis with polyangiitis**

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Conflict of interest: None

[Objective] Neutrophil extracellular traps (NETs) are involved in the pathogenesis of granulomatosis with polyangiitis (GPA). Septum ANCA can activate eosinophils to induce eosinophil extracellular traps (EETs). However, the role of eosinophils in GPA is not known. [Methods] Serum concentrations of ECP, Galectin10, CitH3 and MPO were retrospectively examined in 25 patients with active GPA and 27 with remission. Additionally, the association between disease activity (BVAS) and conventional markers such as ANCA and CRP was also evaluated. [Results] The serum concentrations of ECP, Galectin10, CitH3, ANCA and CRP in active GPA were significantly higher than those in remission AAV. BVAS was associated with ECP and Galectin-10 ($r=0.783$, $P<0.001$, $r=0.774$, $P<0.001$, respectively). Elevated serum ECP and Galectin-10 were identified as factors associated with the active phase using multivariate analysis with eosinophil count and the amount of GC as a covariate. ROC analyses for ECP and Galectin10 for discriminating between active disease and remission revealed AUC of 0.972, with a sensitivity of 96.3% and specificity of 92%, AUC of 0.923, with a sensitivity of 85.2% and specificity of 91.3%, respectively. [Conclusions] The activation of eosinophils is important for disease activity.

## P3-219

**Eosinophilic granulomatosis with polyangiitis: three patients presenting with hypocomplementemia and increased serum IgG4 levels**

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Conflict of interest: None

[Case 1] A 75-year-old man with a 6-year history of bronchial asthma (BA) developed foot drop along with purpura, resulting in the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) based on eosinophilia. He additionally had increased serum IgG4 levels, hypocomplementemia (hypo-com), thickened bronchial wall, and multiple lymphadenopathies, pathologically where IgG4/IgG ratio of plasma cells presented >70%, leading to the diagnosis of IgG-related disease (IgG4-RD). [Case 2] A 72-year-old woman with a 2-year history of BA was diagnosed with

EGPA because of purpura and numbness on the lower limbs along with eosinophilia. She had serum IgG4 level, hypo-com, and multiple lymphadenopathies, whose histology was negative result for IgG4 staining. [Case 3] A 58-year-old woman, who developed BA 1.5 months prior to the onset of purpura, fever, and ankle arthritis, as well as eosinophilia, was diagnosed with EGPA. She had no evidence of IgG4-RD, despite increased serum IgG4 levels and hypo-com. [Conclusion] Increased serum IgG4 levels could be often observed in EGPA, despite hypo-com being rarely shown. It is necessary to properly determine the comorbidity of IgG4-RD by assessing relevant pathological lesions.

## P3-220

**A case of Goodpasture syndrome in which rapid renal dysfunction was observed after steroid treatment started as organizing pneumonia**

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Conflict of interest: None

[Case] 70-year-old woman [history of present illness] Two weeks ago, she had slight fever and fatigue. She was prescribed antibiotics, but there was no improvement. Her chest CT revealed infiltrative shadows in both upper lobes and right lower lobe. The bronchoalveolar lavage fluid of bronchoscopy revealed no hemosiderin phagocytic macrophages, although she occasionally had bloody sputum. Blood test showed that antinuclear antibody and ANCA was negative. She was started on prednisolone 40 mg/day as organizing pneumonia. Although respiratory symptoms and imaging findings improved, rapid renal dysfunction was observed, and she was found to be positive for anti-GBM antibodies. She was diagnosed with Goodpasture syndrome. On the same day, plasma exchange therapy and steroid pulse therapy were started, and cyclophosphamide pulse therapy and hemodialysis were combined. She was discharged from the hospital after weaning from hemodialysis. [Clinical Significance] Initially, the patient was thought to have idiopathic organizing pneumonia, but she was later diagnosed as secondary organizing pneumonia associated with vasculitis. We report this case as it is thought to be highly suggestive in considering the causes and differential diagnosis of organizing pneumonia.

## P3-221

**A case of microscopic polyangiitis resulting in RPGN after resection of thymoma**

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Conflict of interest: None

[Case] A 56-year-old woman presented with multiple joint pains; she was referred to our department with positive ANA, MPO-ANCA, and urine occult blood and protein. Chest CT showed a 37*29 mm mass with contrast effect in the anterior mediastinum, which was diagnosed as thymoma. Renal biopsy showed necrosis and adhesions of the vascular loop wall in some glomeruli, but no evidence of crescent formation or sclerotic glomeruli. At this time, there was no evidence of AAV and were no serious organ complications, so a decision was made to proceed with surgical treatment for thymoma. After delays due to COVID-19, robot-assisted thymectomy was performed. After discharge, the patient experienced fatigue and anorexia, and a short-term decrease in renal function and an increase in urinary protein and occult blood were observed. MPA was diagnosed together with RPGN, and remission-induction therapy was performed using PSL and RTX. [Discussion] Thymoma is known to be associated with a variety of autoimmune diseases, some of which can be expected to improve after removal of the thymoma. The combination of thymoma and AAV is rare, and the impact of thymectomy on the disease course is uncertain, so we consider this case to be informative for clinicians.

## P3-222

**Eosinophilic granulomatosis with polyangiitis after dupilumab administration in patients with eosinophilic chronic rhinosinusitis**

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Conflict of interest: None

A 40-year-old woman presented fever, cough, and nasal congestion. She was diagnosed with eosinophilic pneumonia and eosinophilic sinusitis because of increased eosinophils in bronchoalveolar lavage fluid and eosinophil infiltration in the sinus tissue ten months before she visited our hospital. She was started on 40 mg prednisolone (PSL), and the lung shadow and thickening of the sinus mucosa improved. PSL was tapered and stopped two months before she visited our department. Because the thickening of the sinus mucosa worsened, Dupilumab was started 16 days before her visit. Two days later, she experienced pain, numbness, and purpura distal to both ankle joints. Eosinophils in the peripheral blood increased from 2000-3000/μL to 9000/μL, a new pulmonary infiltrate appeared, and C-reactive protein increased. PSL 15 mg was started 9 days before the visit. Nerve conduction studies revealed peripheral neuropathy and a skin biopsy showed extravascular infiltration of eosinophils. The patient was diagnosed with EGPA in our department, and then started PSL 45 mg. The eosinophil count quickly decreased, and the purpura, pulmonary infiltrate shadow, numbness, and pain disappeared. The patient's disease is stable, and PSL is being tapered off with the addition of mepolizumab.

## P3-223

**A case of granulomatosis with polyangiitis (GPA) resulting in perforation of the gastrointestinal tract during treatment due to difficulty in diagnosis**

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Conflict of interest: None

[Case] A 65-year-old man developed fever and myalgia in April, X-2. In January X, he showed positive PR3-ANCA (11 U/L) but no organ involvement, so the diagnosis was not made. PET-CT showed FDG-accumulated lesions in intramural lymph nodes. Suspecting malignant lymphoma, a laparoscopic lymph node biopsy was performed on the third day. On the 4th day, an emergency endoscopy was performed due to massive hematochezia. Bleeding from an exposed jejunal vessel was found, and clipping was performed. Multiple ulcers were observed in the proximal jejunum. On the 5th and 6th days, the patient had hematochezia every day and underwent clipping again. Based on the multiple nodules in the lung, multiple ulcers in the small intestine, and positive PR3-ANCA, a diagnosis of granulomatosis with polyangiitis (GPA) was made, and steroid pulse therapy and high-dose therapy were started. On the 14th day, there was perforation of the gastrointestinal tract, and emergency surgery was performed. From the 19th day, the patient was treated with rituximab and discharged from the hospital. Abacopan was introduced and he has been doing well since then. [Clinical Significance] We experienced a case of GPA that flared up with massive bleeding, perforated the gastrointestinal tract, and went into remission.

## P3-224

**A case of polyarteritis nodosa with Raynaud phenomenon as the initial manifestation**

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Conflict of interest: None

Case: 56-year-old male. Since January of X year, Raynaud's phenomenon appeared on the left fifth finger and right third finger about 4-5 times a month. In May of the same year, Raynaud's phenomenon also appeared

in the left first toe, and the left fifth finger and left first toe remained cyanotic and did not return. At the same time, fever in the 37°C range, livedo reticularis and partially infiltrated purpura appeared on the lower extremities. a blood test showed a high CRP level of 10.22 mg/dL, Antinuclear antibody negative, ANCA negative. Dorsal, plantar, and toe sensory insensitivity predominantly to the left, and nerve conduction studies showed distal latency prolongation of the left ulnar nerve. Skin biopsy from livedo reticularis of the left thigh and left lower leg revealed necrotizing vasculitis. Angiography showed microaneurysms in the left shallow femoral artery and branches, and a diagnosis of polyarteritis nodosa was made. The patient was started on 60 mg/day of prednisolone as remission induction therapy, and fever, leg pain, and CRP level improved. Discussion: Polyarteritis nodosa is also an important differential diagnosis in cases showing Raynaud's phenomenon.

## P3-225

**A case of eosinophilic colitis (EoC) that was difficult to differentiate from eosinophilic polyangiitis granulomatosa (EGPA)**

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Conflict of interest: None

Case: A 65-year-old woman was diagnosed with Crohn's disease at the age of 28 and had 4 small bowel resections. At 59 years old, she was diagnosed with ANCA-negative granulomatosis with polyangiitis. At 65 years old, she had abdominal pain and diarrhea, and lower gastrointestinal endoscopy revealed numerous mottled erythema on the mucosa. Histopathology showed numerous eosinophil infiltrates were observed, and eosinophilic granulomatous with polyangiitis (EGPA) was suspected. The diarrhea did not improve with PSL 30 mg/day and improved with PSL 60 mg/day. Intrahepatic cholangiocarcinoma was detected after 7 months, and she died 9 months later. Discussion: We considered it was atypical for EGPA, and diagnosed eosinophilic colitis (EoC). The pathological findings of infiltration of the submucosa and crypt abscess are helpful in the diagnosis. 20% of EoC are refractory to systemic corticosteroid therapy and it was reported that treatment-resistant EoC coexisting with malignancy. We should keep in mind the possibility of EoC when the disease is atypical.

## P3-226

**A study of two cases of ANCA-associated vasculitis associated with scleroderma**

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Conflict of interest: None

ANCA-related vasculitis with scleroderma features anti-Scl-70 and MPO-ANCA positivity, kidney lesions, and onset around 10 years after scleroderma. We report two cases from our hospital. In Case 1, a patient diagnosed with systemic scleroderma and anti-Scl-70 positivity 12 years prior developed pulmonary alveolar hemorrhage and ANCA-related vasculitis. Despite treatment, urine protein, urine occult blood persisted. Labs showed sCr at 0.63 mg/dL, urinary protein at 0.5g/gCr, and MPO-ANCA at 27.3 IU/mL. Kidney pathology revealed fibrocellular crescents, indicating a renal lesion. Case 2 involved a patient diagnosed with limited cutaneous systemic sclerosis due to skin changes and anti-centromere positivity 8 years prior. They later showed kidney dysfunction, with labs revealing serum Cr at 1.6 mg/dL, urinary protein at 1.6g/day, and MPO-ANCA at 130 IU/mL. Kidney pathology showed fibrinoid necrosis, leading to a vasculitis diagnosis. ANCA positivity occurs in about 5% of scleroderma cases, but vasculitis symptoms are rare. Both cases developed vasculitis around 10 years post-scleroderma diagnosis, highlighting the need for awareness of ANCA-related vasculitis as a potential long-term complication in scleroderma.

## P3-227

**Exploratory cluster analysis of patients with ANCA-associated vasculitis: a historical cohort study using J-CANVAS data**

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Conflict of interest: None

[Purpose] In order to achieve stratified treatment for patients with ANCA-associated vasculitis (AAV), we aimed to discover new entities based on the organ lesions at the initial presentation of MPA and GPA. [Method] We enrolled patients with new-onset or severe relapsing AAV between Jan 2017 and Jun 2020 at 24 Japanese centers. Patients were classfied by cluster analysis using the presence or absence of BVAS items, interstitial lung disease (ILD), and hypertrophic pachymeningitis at enrollment. [Results] The 461 patients were classified into 6 clusters. Cluster2 showed the lowest survival rate, whereas cluster6 exhibited the highest, and the other clusters were intermediate in survival rate. The same trend was observed even when restricting to five factor score of two or higher. Cluster2 was characterized by fewer systemic symptoms with progressive nephritis and lung involvements. Cluster6 was characterized by localization to otorhinolaryngological involvements. [Conclusion] Our findings reveal unique disease clusters for which prognosis cannot be predicted using existing indices, emphasizing the need for precise stratified medicine. [COI] no conflicts of interest.

## P3-228

**A case of microscopic polyangitis (MPA) suspected complication with segmental arterial mediolysis (SAM)**

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Conflict of interest: None

[Case] A 57-year-old man suffered from sensory abnormality in lower limb and muscle weakness in four extremities since October, 202X visited the neurology department after a month. While laboratory tests showed high titer of MPO-ANCA, elevated CRP, severe renal insufficiency, he had no history of allergic diseases thus was diagnosed as MPA. Steroid pulse therapy was immediately administered, and he was transferred to the rheumatology department. On the 6th hospital day, he had developed severe abdominal pain. Contrast-enhanced CT showed bleeding from a branch of the superior mesenteric artery. Angiography revealed microaneurysms in multiple lesions and a bleeding site in the branch then interventional embolization was successfully applied. Owing to a multidisciplinary treatment, the patient survived to discharge. [Discussion] Only one case of MPA with multiple microaneurysms by segmental arterial mediolysis (SAM) in arterial branches had been reported. SAM is to be diagnosed histologically, however, number of the cases without pathologically diagnostic specimen due to emerging transcatheter treatments is increasing. Since diagnostic criteria of SAM excludes inflammatory and sclerotic change in arterial wall, we may provide an argument to pathological and diagnostic aspects of SAM.

## P3-229

**A case of cryoglobulin vasculitis due to rheumatoid arthritis and multiple myeloma**

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Conflict of interest: None

Case: A 50-year-old woman was being followed up for rheumatoid arthritis and monoclonal gammopathy of undetermined significance (MGUS) with no symptoms. She presented with generalized purpura and visual field defects (right nasal hemianopsia), and was diagnosed with multiple myeloma and associated retinopathy. A skin biopsy revealed vasculitis and cryoglobulin was positive, so she was diagnosed with cryoglobulin vasculitis. Because of no CRAB symptoms, rheumatoid arthritis was suspected as the primary disease. The patient was treated with plasma exchange, cyclophosphamide, and prednisolone, and showed improvement. However, immunoelectrophoresis of the cryoglobulin itself revealed IgG-type λ-type M protein, she was diagnosed with Type-I cryoglobulin vasculitis. Chemotherapy was initiated. Discussion: Cryoglobulin vasculitis is classified as type I-III. Type I is mainly blood diseases such as multiple myeloma and macroglobulinemia. Types II-III are mainly collagen diseases. In this case, multiple myeloma and rheumatoid arthritis were combined, and the problem was to differentiate between type I and type II. She was eventually diagnosed with multiple myeloma.

## P3-230

**A case of microscopic polyangiitis with tubulointerstitial nephritis**

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Conflict of interest: None

85-year-old woman was referred to our hospital because of livedo reticularis of both lower limbs, numbness in both lower limbs and elevated inflammatory markers. Laboratory findings showed C-reactive protein was 1.57 mg/dL, creatine was 0.75 mg/dL, myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) was positive, proteinase3-ANCA and anti-SS-A antibody was negative. Urinalysis showed the spot urine protein to creatinine ratio was 0.45 g/gCr, β-2-microglobulin and NAG was elevated. Chest CT showed interstitial pneumonia. Nerve conduction study showed mononeuropathy multiplex of the lower limbs. Microscopic polyangiitis (MPA) was diagnosed based on EULAR/ACR 2022 classification criteria for MPA. A kidney biopsy revealed tubulointerstitial nephritis without glomerulonephritis. She received prednisolone 0.5 mg/kg/day, rituximab, high-dose intravenous immunoglobulin, and avacopan. After 5 weeks of treatment, livedo reticularis disappeared, MPO-ANCA turned negative, and proteinuria improved. The typical nephrological presentation of MPA is rapidly progressive glomerulonephritis. ANCA-associated vasculitis (AAV)-associated interstitial nephritis without glomerular lesions was rare. We report the clinical features of AAV-associated interstitial nephritis and literature review.

## P3-231

**orbital apex syndrome during the course of treatment for ANCA-associated vasculitis**

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Conflict of interest: None

[Case] A 75-year-old man diagnosed as ANCA-associated vasculitis (AAV) due to episcleritis and high MPO-ANCA was treated with PSL40 mg. When the dose was reduced to PSL 17.5 mg+MTX4 mg/W, severe pain appeared behind the right eye, and eyesight became light perception. Paralysis of the right II and VI nerves and insufficiency of the III and IV nerves were present. MRI scan showed a contrast-enhanced mass at the tip of the right orbit, and the patient was transferred to another hospital with a diagnosis of orbital apex syndrome (OAS). Biopsy from the right ethmoid sinus was performed. Pathology showed inflammatory cell infiltration in the vessel wall, with no fibrinoid necrosis or obvious fungal bodies. He was diagnosed with OAS associated with AAV and treated with steroid pulse therapy. Pain and cranial nerve palsy improved, but there was no improvement in eyesight. he received RTX 500 mg as maintenance therapy followed by the same dose of RTX every six months. PSL could be tapered without relapse. [Clinical Significance] The causes of OAS are diverse, including inflammatory diseases, infections, and tumors. If the patient develops OAS during the course of treatment for AAV, it is necessary to carefully determine whether exacerbation of the primary disease is the cause of it.

## P3-232

**Characteristics of IgG4-Related Disease with Low Levels of Serum Cholinesterase**

Hiroki Ozaki[1], Risa Wakiya[2], Mao Mizusaki[2], Shusaku Nakashima[2], Taichi Miyagi[2], Yusuke Ushio[2], Koichi Sugihara[2], Ryoko Kagawa[2], Hayamasa Yamaguchi[2], Hiromi Shimada[2], Hiroaki Dobashi[2]
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Conflict of interest: None

[Object] We often experience low levels of serum cholinesterase (ChE) in IgG4-related disease (IgG4-RD). In this study, we examined the characteristics of IgG4-RD with low levels of serum ChE. [Method] We analyzed 50 patients diagnosed IgG4-RD from 2008 in our facility. The diagnosis for IgG4-RD was based on the 2020 revised comprehensive diagnostic criteria for IgG4-RD. We compared patients who decreased serum ChE (low group) with the others (normal group). Laboratory data and clinical course were analyzed from their medical records retrospectively. [Results] Low levels of serum ChE was observed in 16 patients. The low group was older than the normal group. Compared to the normal group, the low group had more lesions in kidney and retroperitoneum. The low group showed higher CRP, serum IgG, IgA and IgE. Hypocomplementemia was more common in the low group. In the low group 14 out of 16 patients required treatment, while 20 out of 34 patients in the normal group. There is no significant difference in relapse rate between two groups. [Conclusion] We showed the characteristics of organ lesions and laboratory findings for IgG4-RD with low levels of serum ChE. Although many cases with low serum ChE required therapeutic intervention, no difference in prognosis was observed.

## P3-233

**Differences in clinical features and treatment between patients with IgG4-related retroperitoneal fibrosis and/or aortitis and patients with other IgG4-related diseases**

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Conflict of interest: None

[Objective] This study elucidated the difference in baseline characteristics and clinical courses in IgG4-related disease (IgG4-RD) between patients with or without retroperitoneal fibrosis (RPF) and/or aortitis. [Methods] Forty-eight patients who visited the Department of Hematology and Rheumatology at Kagoshima University Hospital between January 1, 2013, and May 31, 2023, were diagnosed with IgG4-RD were included in this study. We divided the subjects into the RPF and/or aortitis (R/A+) group and the non-RPF and/or aortitis (R/A-) group and analyzed them. [Results] The R/A+ group had significantly higher serum CRP (0.15 vs. 0.07 mg/dL) and sIL2-R (1244 vs. 528 U/mL) levels, lower rate of complication of allergic conditions (9.5 vs. 48.1%), higher initial (37.6±9.0 vs. 24.7±11.8 mg) and maintenance (6.2±1.8 vs. 3.8±2.0 mg) doses of prednisolone in the R/A+ group. The R/A+ group had fewer complications of lacrimal gland lesions (28.6% vs. 55.6%). Complete response rates after 6 months of treatment tended to be lower in the R/A+ group (53.8% vs. 72.7%). The relapse and reoccurrence rate was significantly higher in the

R/A+ group (HR 4.9, 95%CI 1.0-23.6). [Conclusions] IgG4-RD patients with RPF and/or aortitis may have a higher relapse and reoccurrence rate despite higher PSL dosage.

## P3-234

**A case of IgG4-related sclerosing mesenteritis accompanied by renal pelvis and ureteral lesions**

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Conflict of interest: None

[Case] A 67-year-old woman was diagnosed with central diabetes insipidus two years ago. IgG4 titer was high, but a lip biopsy did not reveal the diagnosis. Since then, a CT scan detected abdominal panniculitis. One year later, CT findings progressed, and serum soluble IL-2 receptor (sIL2R) titer went high. Malignant lymphoma was considered, but there was no lymphadenopathy. In July this year, CT and MRI scans detected soft tissue abnormalities of the renal pelvis and ureter on both sides. At the end of July, she was admitted to our hospital because of fever and nausea. CT scan detected progressing panniculitis, and PET-CT scan detected FDG accumulations at the mesentery, kidney, pancreas, and spleen. Serum IgG4 and sIL2R titers were still high, so a laparoscopic biopsy of the mesentery and great omentum was performed. Pathological findings showed infiltration of inflammatory cells, IgG4-positive plasma cells (IgG4/IgG = 84%), and no evidence of malignancy. She was diagnosed with IgG4-related sclerosing mesenteritis and treated with prednisolone. [Clinical Implications] IgG4-related sclerosing mesenteritis is rare. Almost existing cases did not have other organ involvement nor many IgG4-positive cells. This case reveals renal urinary lesions and compatible pathological findings.

## P3-235

**Two cases of IgG4-related disease affecting both parent and child**

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Conflict of interest: None

[Objective] The pathogenesis of IgG4-related disease (IgG4-RD) is still unclear. Although genetic factors may be involved, family cases are extremely rare. In this report, we described two cases of IgG4-RD, involving the parent and child. [Case 1] A 61-year-old woman visited due to bilateral swelling of the submandibular glands, dry mouth, dry eye and high serum IgG4 377 mg/dL (IgG1540). A biopsy of the submandibular gland confirmed IgG4-RD. The patient responded well to treatment using prednisolone. [Case 2] A 41-year-old male, the son of Case 1, was diagnosed with autoimmune pancr eatitis at another hospital, then he was referred to our hospital He had submandibular gland swelling, and high serum IgG4 540 mg/dL (IgG 1890). The patient responded well to treatment using prednisolone. [Discussion] Many factors may be involved in the development of IgG4-RD A retrospective study in China reported that, of the 628 cases of IgG4-RD, IgG4-RD within a family was reported in 16 cases. Genetic polymorphisms, such as HLA and FCRL3, have also been implicated in the development of IgG4-RD. [Conclusion] We experienced a case of IgG4-RD occurring within the same family. The genetic predisposition of IgG4-RD warrants further studies.

## P3-236

**2 cases of IgG4-related disease with pleuritis**

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Conflict of interest: None

We describe 2 cases of IgG4-related disease with pleuritis in middle-aged men. Patient 1 presented with cough, pleural and pericardial effusions. He was treated for hyperthyroidism and cardiac insufficiency. One year later, pleural effusion increased without worsening heart failure. He tested positive for anti-SS-A antibodies, and his serum IgG4 level was 1239 mg/dl. The gum test and Schirmer test were negative, Pleural and lymph node biopsies showed lymphocytic and plasma cell infiltration, IgG4/IgG positive cell ratio >50%, and positive cell count >100 cells/HPF, which were not shown in the lip biopsy. The pleural effusion responded to prednisolone 30 mg/day. Patient 2 presented with dyspnea on exertion for the past 2 months with bilateral pleural and pericardial effusions. His serum IgG4 level was 491 mg/dl. MPO-ANCA and PR3-ANCA were negative. Lymphadenopathy was too mild to undergo a biopsy. Lip, pericardial, and pleural biopsies showed lymphocytic and plasmacytic infiltrates, IgG4/IgG positive cell ratio >40%, and positive cell count > 10 cells/HPF. Pleural effusion decreased with the prednisolone 60 mg/day. Our cases had good steroid responsiveness, but they had diastolic dysfunction due to pericarditis. We should consider biopsy promptly for early diagnosis.

## P3-237

**A case of IgG4-related disease diagnosed several years after onset of warthin's tumor**

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Conflict of interest: None

[Case] A man in his 70s [Chief complaint] Bilateral neck swelling [Present medical history] He developed a left-sided Warthin's tumor 3 years ago. He was referred to our department because bilateral neck swelling appeared a few months ago and his IgG and IgG4 levels were high (IgG 7229 mg/dL and IgG4 4920 mg/dL). Imaging showed bilateral parotid soft-tissue shadows, pancreatic swelling, thickening of the common bile duct wall, and soft-tissue shadows around the renal pelvis and ureter. Right parotid biopsy showed a lesion suggestive of a Warthin's tumor and confirmed the diagnosis of IgG4-related disease based on comprehensive diagnostic criteria. Prednisolone (PSL) 1.0 mg/kg/day was started and after 3 weeks, IgG and IgG4 were decreased (IgG 1678 mg/dL and IgG4 919 mg/dL). The bilateral parotid swelling and each organ lesions were improved on imaging. In addition, the left parotid Warthin's tumor was also reduced. [Discussion] Recently, it has been reported that some patients with Warthin's tumor have high serum IgG4 levels and high infiltration of IgG4-positive cells. Although serological details of this case are unknown at the time of diagnosis of Warthin's tumor, we suggest that the two diseases may be related.

## P3-238

**A case of pyloric stenosis associated with IgG4-related disease**

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Conflict of interest: None

We present a case of pyloric stenosis associated with IgG4-related disease in a 51-year-old male patient. The individual exhibited symptoms such as anorexia, weight loss, hypoalbuminemia, hypergammaglobulinemia, and anemia. Differential diagnoses considered included Castleman's disease, malignant lymphoma, and multiple myeloma, but lymph node biopsy and bone marrow examination yielded negative results. The patient experienced upper abdominal discomfort following meals, leading to a repeat upper gastrointestinal endoscopy that revealed multiple ulcers and edematous narrowing adjacent to the pyloric ring. Serum IgG4 levels were elevated, and immunostaining demonstrated the presence of IgG4-positive plasma cells in the duodenum, indicating pyloric stenosis due to IgG4-related gastrointestinal disease. Treatment with prednisolone (PSL) was initiated, resulting in the alleviation of symptoms. However, the patient experienced relapses upon PSL tapering, accompanied by progressive anemia, an increased inflammatory response, and elevated serum IgG4 levels. Consequently, the PSL dosage was augmented due to the recurrence of

multiple gastrointestinal ulcers. Given the success of steroid therapy, methotrexate was introduced, and the patient is currently under outpatient observation.

## P3-239

**Clinical characteristics of relapsed IgG4-related disease patients**

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Conflict of interest: None

[Objective] Most patients with Immunoglobulin G4-related disease (IgG4-RD) respond well to glucocorticoids, but relapses occur frequently. We investigated the clinical features of relapsed IgG4-RD patients. [Methods] We retrospectively investigated the clinical records of IgG4-RD patients who was diagnosed at our hospital. Relapse was defined as worsening of clinical symptoms or imaging findings, or treatment intensification. We compared relapse group and non-relapse group about affected organs, laboratory findings at onset (eosinophil count, IgG4, IgG4/IgG, CRP, complement), and treatment. [Results] Twenty-seven IgG4-RD patients were treated with prednisolone (PSL). And 14 patients were classified into the relapse group. There were no significant differences in clinical findings between two groups. Median duration from start of treatment to relapse was 280 days and median PSL dose at relapse was 7 mg/day. Six patients in the relapse group were added azathioprine. And seven patients were reduced PSL dose compared to the time of relapse. The PSL doses at last observation of both groups were 5 mg/day. [Conclusions] In this study, it was difficult to find predictors of relapse before treatment. Further study is required to establish appropriate maintenance therapy for IgG4-RD.

## P3-240

**"Serum IgG4 + IgG" may be useful for inferring the presence of autoimmune pancreatitis/periaortitis/retroperitoneal fibrosis in IgG4-related disease**

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Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: None

[Objective] IgG4-related disease (IgG4RD) could lead to deep organ lesions such as autoimmune pancreatitis (AIP) and periaortitis/retroperitoneal fibrosis (PA/RF), whose diagnosis needs imaging. This study is to clarify whether the presence of AIP and PA/RF can be inferred from serum IgG4/IgG. [Methods] We reviewed the medical records of 58 cases of IgG4RD treated at our department from Apr 2015 to Aug 2022. In 53 patients with no missing data (67.9% male, mean age at diagnosis 65.6 years), pre-treatment serum IgG4, IgG, IgG4/IgG ratio, and IgG4+IgG were compared between two groups with or without AIP/PA/RF (U test). [Results] Median of serum IgG4, IgG, IgG4/IgG ratio, and IgG4+IgG of 31 cases with AIP and/or PA/RF were 784.0 mg/dl, 2235.0 mg/dl, 0.35, and 2819 mg/dl, respectively. These tended to be higher than those of 22 cases without AIP or PA/RF: 436.5 mg/dl, 1722.0 mg/dl, 0.22, and 2054 mg/dl, serum IgG4+IgG values being significantly higher ($p = 0.035$). ROC analysis on serum IgG4+IgG revealed AUC was 0.672, and the cut-off value of 2191 mg/dl for detecting AIP or PA/RF had a sensitivity of 87.1% and specificity of 54.5%. [Conclusion] In IgG4RD, serum IgG4, IgG, IgG4/IgG ratio, and IgG4+IgG, especially serum IgG4+IgG, may be useful in estimating the presence of AIP and PA/RF.

## P3-241

**A case of a child with a refractory IgG4-related disease accompanied by eosinophilia whose symptoms improved with the introduction of mepolizumab**

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Conflict of interest: None

[Introduction] IgG4-related disease (IgG4RD) is a refractory disorder characterized by hypertrophic lesions in various organs with high serum IgG4 levels and infiltration of IgG4-positive plasma cells in the lesions. We report a pediatric case of refractory IgG4RD with recurrent parotiditis and eosinophilia treated with mepolizumab. [Case] A 10-year-old girl with a history of bronchial asthma, allergic rhinitis, atopic dermatitis, and sinusitis had repeated parotiditis and her blood tests revealed eosinophilia, a high level of IgG4 and negative autoantibodies. At age 7, she was diagnosed with IgG4RD by a parotid gland biopsy. Prednisolone (PSL) was started, but the symptoms flared up as the dose of PSL was reduced. The combination of various immunosuppressants to reduce PSL dose did not work. She also developed sclerosing sialadenitis, to which the addition of rituximab was ineffective. So, she was started on mepolizumab, which gradually improved her symptoms. [Discussion] IgG4RD responds well to steroids but is prone to relapse with dose reduction and childhood onset is rare. There are scattered reports of adult cases treated with duplimab for IgG4RD, but few reports of mepolizumab. We discuss effectiveness of biologics for a refractory IgG4RD based on a literature review.

## P3-242

**Usefulness of FDG PET/CT in IgG4-related diseases (IgG4-RD)**

Rina Okita[1], Tefi Shin[1], Keiju Yamada[1], Mai Nakano[1], Kaori Seki[1], Satoko Nozato[1], Hiroko Uesugi[2], Masayasu Kitano[1], Shinichiro Tsunoda[1]
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Conflict of interest: None

[Objective] Since early diagnosis of $IgG_4$-RD is closely related to clinical outcome, FDG PET/CT has been applied in recent years. The usefulness of FDG PET/CT in $IgG_4$-RD was studied. [Methods] Patients with $IgG_4$-RD diagnosed at our hospital who underwent FDG PET/CT were identified and examined for discrepancies in the number of accumulated organs, test data, and conventional radiology (CT). [Results] Of the 45 patients with $IgG_4$-RD diagnosed at our hospital (32 males, 13 females), 9 patients (20%, 7 males, 2 females) underwent FDG PET/CT. The average number of organs involved was 3.89 (2-8), of which salivary glands, lymph nodes, and urinary system were all involved in 4 patients (44.4%). Compared to conventional radiology, FDG PET/CT was superior in depicting pituitary, vascular, and renal lesions. Especially for vascular lesions, the combination of FDG PET/CT with contrast-enhanced CT was useful for diagnosis even when tissue biopsy was difficult. There were no obvious features in the laboratory data in patients who underwent FDG PET/CT. [Conclusions] $IgG_4$-related diseases are systemic diseases, and FDG PET/CT is excellent for detecting multiorgan involvement and evaluating activity. It is particularly useful for intracranial and vascular lesions where tissue biopsy is not possible.

## P3-243

**Secretion of mitochondrial DNA via exosomes promotes inflammation in Behçet's syndrome**

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Conflict of interest: None

Mitochondrial DNA (mtDNA) leakage can occur when cells are exposed to noxious stimuli. Specific sensors recognize the leaked cytoplasmic mtDNA to promote cytokine production, and extracellular mtDNA released due to extensive cell damage induces sterile inflammation. However, the mode of secretion of mtDNA out of the cells upon noxious stimuli and its relevance to human disease remain unclear. Here, we showed that pyroptotic cells secrete mtDNA encapsulated within exosomes. Activation of caspase-1 induced mtDNA leakage from the mitochondria into the cytoplasm via gasdermin-D. Caspase-1 also induced intraluminal

membrane vesicle formation, allowing leaked mtDNA to be taken up and secreted as exosomes. Encapsulation of mtDNA within exosomes promoted a strong inflammatory response, and exosome biosynthesis inhibition ameliorated the inflammasome-mediated inflammation in vivo. We further showed that monocytes derived from Behçet's syndrome (BS) patients exhibited caspase-1 overactivation, leading to excessive mtDNA secretion via exosomes, causing the pathophysiology of BS. Collectively, mtDNA-containing exosome-mediated inflammation provides new insights into the propagation and exacerbation of inflammation in human inflammatory diseases.

## P3-244

**A Case of Behcet's Disease (BD) Switching from Infliximab (IFX) to Adalimumab (ADA) Against Uveitis developed Neural and Intestinal BD**

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Division of Rheumatology, Department of 1st Comprehensive Medicine, Saitama Medical Center, Jichi Medical University

Conflict of interest: None

[Clinical Significance] We experienced a suffering case of BD who treated with IFX for her uveitis; however, her BD developed neurointestinal lesions and switching to ADA. [Case] 40-year-old female occurred uveitis with oral aphthous ulcer when she was 34-year-old (y/o). She referred to another hospital and was diagnosed having BD; thus, she was started to treatment for her uveitis with IFX at 35 y/o. Moving to our hospital at 37 y/o and continuing the therapy; however, her genital ulcer and her headache were occurred at 38 and 39 y/o, respectively. Her colchicine was stopped to her anorexia. Nine days before, her left uveitis attack was occurred; thus, a local steroid injection was performed; however, her condition worsened. At the day when she was taking periodic IFX injection, she came to our hospital accompanied by her father and had impaired consciousness, her left eye was index valve, and her various pathological reflexes were observed; thus, she was rushed to the emergency division in our hospital. Using a maximum dose of IFX against neuro-BD, trying different types steroid and using IVCY, there was no effect at all. Then, we switched to ADA, her condition improved.

## P3-245

**A case of HLA-A26-positive CNS Behcet's disease with irreversible personality devastation, which was diagnosed from a diary kept at the onset of the disease**

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Conflict of interest: None

[Case] 48-yr-old female [CC] Personality deterioration [HPI] At X-22 mos, she had fever and headache, followed by inability to stand due to vertigo, bilateral hearing loss. At X-21 mos, she sought care, revealing increased CSF cells and pelvic MRI indicated superior sacroiliitis. Brain MRI showed no abnormalities. From X-15 mos, she displayed bizarre behavior and utterance. Gradually, her condition worsened to incomprehensible speech and violent outbursts. Due to prolonged hospitalization, she was transferred to our department. Peripheral blood analysis: WBC 7300, ESR 58 mm/h, CRP 0.53 mg/dL, HLA-A26 (+) & B51 (-). CSF: cells 28/mm$^3$, IL-6 195 pg/mL. Though direct interviews were impossible, a diary from onset time revealed symptoms. At X-23 mos, painful erythema appeared on her left lower leg, and repeated urinary pain and oral aphthous ulcers since X-22 mos. Diagnosis: CNS Behcet's disease. Colchicine, methotrexate, infliximab halted progression and resolved inflammation, normalizing CSF. Severe personality deterioration persisted. [Discussion] HLA-B51 association is strong in this disease; but Japan has HLA-A26+ & B51- in 30% of cases. Untreated CNS symptoms result in irreversible personality deterioration. Accordingly, thorough medical history collection is pivotal for prognosis.

## P3-246

**A case report of chronic progressive neuro-Behcet's disease with long-term follow-up**

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Conflict of interest: None

Chronic progressive neuro-Behcet's disease (CPNBD) is a debilitating disorder characterized by progressive neurological deterioration, including cognitive impairment and ataxia. The case is a 64-year-old man. At age 37, with uveitis, recurrent oral aphthous ulcers and folliculitis, he was diagnosed with Behcet's disease (BD) and treated with colchicine. At age 41, he developed fever and dysarthria. Magnetic resonance imaging (MRI) revealed high signal intensity lesions in the midbrain, consistent with neuro-Behcet's disease. He was treated with prednisolone (PSL) 60 mg, which was then tapered to 10 mg for maintenance. Fever and fatigue continued, and methotrexate (MTX) 5 mg /week was added. He became apathetic and was unable to work by age 46. MRI revealed atrophy of the pons, and cerebrospinal fluid IL-6 was elevated to 46 pg/mL, consistent with CPNBD. He developed recurrent cytomegalovirus (CMV) enteritis. Therefore, infliximab was not initiated. He developed gait difficulty due to truncal ataxia and was transferred to a nursing home. He has been completely dependent on care since age 50, but his condition has not worsened since then. This case suggests that even with severe cerebral atrophy, CPNBD patients may maintain vital functions if they avoid secondary infections.

## P3-247

**A case of recurrent epiglottitis in Behçet's disease: Evaluation of the temporal changes in epiglottic findings**

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Conflict of interest: None

[Case] A 22-year-old, female patient was referred to our hospital 5 years ago with a chief complaint of sore throat for 2 weeks. The pharynx was unremarkable, and laryngoscopy revealed edema of epiglottis with ulceration and left aryepiglottic fold edema. She was treated with antibiotics and glucocorticoids (GCs) for epiglottitis. She had a history of genital ulcers, oral aphthous ulcers, and acneiform skin lesion and was positive for HLA-A26. She was diagnosed with incomplete type of Behcet's disease (BD). 5 years later, she complained of a sore throat and presented to our hospital. Laryngoscopy revealed epiglottic edema with a white lesion suggestive of ulceration. GCs and colchicine were started for recurrent epiglottitis due to BD. Follow-up laryngoscopy showed rapid improvement of her epiglottic edema. GCs were tapered and discontinued, and she has remained in remission. [Clinical Significance] Epiglottitis is a rare organ manifestation of BD. In this case, we were able to observe the temporal changes in the appearance of the epiglottis and follow up the response to treatment. This is the first report to provide a detailed longitudinal observation of the epiglottis in patients with BD. This case provides new insights into the understanding of the disease pathophysiology.

## P3-248

**Renal Function in Rheumatoid arthritis and Scleroderma**

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Conflict of interest: None

[Objective] To clarify whether renal function declines over time in rheumatoid arthritis (RA) and scleroderma (SSc). [Methods] Laboratory results of patients with RA or SSc attending Shinonoi General Hospital and Kitasato University Medical Center were analyzed retrospectively. Patients who had been attending the hospital for at least 10 years after the onset of the disease were included. The oldest and most recent serum creatinine (Cr) values on the electronic medical record were tabulated and analyzed. [Results] There were 107 patients with RA, 41 patients with SSc, and 12 patients with combined RA and SSc, with mean ages of 72.7±12.8, 71.7±11.8, and 68.1±8.3 years, respectively, and mean disease duration of 21.0±11.2, 18.8±7.7, and 21.3±6.9 years, respectively. The oldest mean Cr values (O-Cr) were 0.61±0.17, 0.65±0.12, and 0.61±0.12 mg/dL, respectively, and the latest mean Cr values (L-Cr) were 0.83±0.57 mg/dL, 0.78±0.24 mg/dL, and 0.74±0.16 mg/dL, respectively, showing no significant differences among the disease groups. However, there was a significant difference between O-Cr and L-Cr values for each disease group. There was no correlation between L-Cr and the history of steroid administration in each disease group. [Conclusions] RA and SSc showed renal dysfunction over time.

## P3-249

**A case of secondary pulmonary alveolar proteinosis during treatment of refractory adult Still's disease**

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Conflict of interest: None

A 63-year-old woman was diagnosed with adult Still's disease (ASD) and was treated with methylprednisolone (mPSL) pulse therapy, PSL 120 mg/day, IVIg, cyclosporine and tocilizumab in 20XX. However, she developed macrophage activation syndrome, which was successfully treated with baricitinib. In Feb 20XX+3, her ASD relapsed on PSL 3 mg/day and she received treatment with mPSL pulse therapy, dexamethasone 8 mg/day, cyclosporine, IVIg and baricitinib. In Jun, she had high KL-6 levels and bilateral ground-glass opacity on lung CT. mPSL pulse therapy and dexamethasone 6 mg/day were given, followed by mycophenolic acid mofetil and nintedanib. In Oct, bronchoscopy was performed for hypoxemia. Bronchoalveolar lavage fluid was opaque and biopsy showed PAS-positive intra-alveolar granular material. Since anti-GM-CSF antibody was negative, the patient was diagnosed with secondary PAP which developed under immunosuppressive therapy. After discontinuation of immunosuppressive drugs, PSL tapering and the whole lung lavage, her PAP improved, and she was discharged from the hospital in Dec. PSL dose was reduced to 7 mg/day without recurrence. Our case suggests that the possibility of PAP should be considered in ASD patients when a lung ground-glass shadow appears during immunosuppressive therapy.

## P3-250

**Two cases diagnosed with Hodgkin lymphoma through repeated biopsies during the treatment of sarcoidosis**

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Conflict of interest: None

[Case] In Case 1, a 58-year-old male presented with persistent bilateral shoulder joints pain for one month. Multiple enlarged lymph nodes (LNs) were found in the left neck. Ultrasound depicted a benign blood flow pattern from the LN hilum with serum sIL-2R at 773 U/mL. A biopsy (BPY) of the left neck LN revealed non-caseating granulomas (NCG) led to the robust diagnosis of sarcoidosis (SA). Treatment with prednisolone (PSL) at 40 mg/day was initiated. Left neck LN re-enlargement and serum sIL-2R 3030 U/mL were clarified under the treatment of PSL 15 mg/day. A re-BPY made it possible to confirm Hodgkin lymphoma (HL). In Case 2, a 63-year-old male had para-aortic LN swelling for 5 years. NCG were pathologically demonstrated in para-aortic LN before 1 year. A cerebrospinal fluid analysis revealed increased monocytes and protein with sIL-2R at 3990 U/mL. MethylPSL pulse was initiated for neuroSA. Exacerbation of para-aortic LN swelling and serum sIL-2R 6230 U/mL were found nevertheless the therapy of PSL 20 mg/day. A re-BPY revealed HL. [Discussion] SA-lymphoma syndrome, malignant lymphoma develops during the treatment of SA, has been sporadically reported. Acknowledgement of co-existence of malignancy is crucial for the SA-patient care under the consideration of re-BPY.

## P3-251

**Study on 23 cases with pulmonary hypertension associated with connective tissue diseases**

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Conflict of interest: Yes

[Objective] Patients with connective tissue disease (CTD) can develop pulmonary hypertension (PH), often associated with interstitial lung disease (ILD). This study explores clinical features and treatment course of CTD-PH patients at our institution. [Methods] We retrospectively studied 23 PH patients with mean pulmonary arterial pressure (mPAP) >20mmHg by right heart catheterization. [Results] The average age was 63.3 years, with 15 females and 8 males. The underlying diseases was as follows: systemic sclerosis (SSc) 11 cases, mixed connective tissue disease 4 cases, Takayasu arteritis 3 cases, systemic lupus erythematosus 2 cases, and other 3 cases. 14 cases showed mPAP within the range of 25 to 35 mmHg. ILD was observed in 7 cases, all associated with SSc. Immunosuppressive therapy was performed in 8 cases. Vasodilators were used in almost all cases except one, with macitentan used most frequently in 10 cases. Among ILD cases, tadalafil was the predominant monotherapy in 6 cases. Combination therapy was more common in cases without ILD. [Conclusions] This study on CTD-PH predominantly included SSc patients diagnosed at a relatively early stage with lower mPAP. Vasodilators were often used as monotherapy for patients with ILD.

## P3-252

**Rapid development of AA amyloidosis in patient with giant cell arteritis; Consideration from clinical and genetic characteristics**

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Conflict of interest: None

[Objective] To clarify the clinical and genetic characteristics of a GCA patient complicated by rapid progressive AA amyloidosis. [Case] An 80-year-old man was admitted to our hospital with fever, headache, and diarrhea for 2 weeks. Ultrasonography showed wall thickening of his right shallow temporal artery. He was diagnosed as giant cell arteritis (GCA) based on 2022 ACR/EULAR classification criteria for GCA. He was treated with PSL 40 mg/day, but diarrhea was not improved. Histopathology of the duodenal mucosa revealed amyloid deposits by Congo red staining, and AA amyloidosis was diagnosed. Therefore, Subcutaneous tocilizumab 162 mg/week was added. The diarrhea improved, but the patient developed perforation of the sigmoid colon and died. [Method] SAA1 gene genotype was analyzed by PCR-RFLP method [Result] The patient had *SAA* 1.3 allele. [Discussion] The case of AA amyloidosis immediately after the onset of vasculitis are rare. The *SAA*1.3 allele and aging are a high-risk factor for AA amyloidosis. Rheumatic diseases other than rheumatoid arthritis can also develop AA amyloidosis when factors such as genetic background and aging combine. This case suggests the importance of intestinal mucosal biopsy in patients with gastrointestinal symptoms resistant to treatment.

## P3-253

**A case of concomitant IgG4-related disease during the treatment of rheumatoid arthritis**

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Conflict of interest: None

[Case] A 78-year-old male with a five-year history of rheumatoid arthritis was initially managed with anti-rheumatic drugs, followed by biologics due to progressive disease activity. Subsequent exacerbation prompted a switch in biologic agents. He presented with anorexia, jaundice, and suspected cholecystitis. Magnetic resonance imaging (MRI) revealed cholelithiasis and bile duct dilation, while endoscopy indicated stenosis of the lower bile duct. Histological analysis from the biopsy site confirmed fibrosis and IgG4-related disease. Initiation of prednisolone therapy demonstrated favorable improvement, resulting in resolution of the bile duct stricture within a year. [Clinical Significance] IgG4-related disease is a systemic autoimmune disorder that affects multiple organs. While its co-occurrence with rheumatoid arthritis is reported as exceptionally rare, heightened disease activity in rheumatoid arthritis has been documented to stimulate the production of IgG4 through autoimmune stimulation. Regular follow-up of IgG levels through blood tests may hold potential utility in predicting the onset, as supported by the literature.

## P3-254

**A case of mixed connective tissue disease with posterior reversible leukoencephalopathy syndrome**

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Conflict of interest: None

A 56-year-old female had diagnosed with RA, MCTD and started treatment with tacrolimus in X-1. In July X, she was hospitalized because of pancytopenia. and discharged after withdrawal of tacrolimus and treatment with blood transfusion. She continued to have fever and pancytopenia, and was referred to our departmen, and admitted for treatment. On the first day of admission, mPSL pulse therapy was started for pancytopenia. Headache and difficulty walking began on the 4th day. On the 6th day, marked visual loss and impaired consciousness appeared. Head CT scan revealed extensive hypoabsorption areas in the bilateral occipital and parietal lobes, and suggesting a posterior reversible encephalopathy syndrome (PRES). Glycerin was started for cerebral edema. On the 7th day, she was admitted to the ICU due to temporary CPA. On the 8th day, the patient was transferred to a higher medical institution due to complications of cardiomyopathy. (Discussion) PLES is a syndrome characterized by seizures, impaired consciousness and visual abnormalities as main symptoms, with brain edema mainly in the posterior white matter, and abnormal clinical and imaging findings that are reversible and disappear with treatment. It should always be kept in mind when differentiating disorders of consciousness.

## P3-255

**A case of idiopathic multicentric Castleman's disease diagnosed by lymph node biopsy during treatment of seronegative rheumatoid arthritis**

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Conflict of interest: None

The diagnosis of idiopathic multicentric Castleman's disease (iMCD) requires differentiation from autoimmune diseases, malignant tumors, and infectious diseases that present similar histopathological features. The patient is a 63-year-old man. He complained of polyarthralgia and was referred to our department. He showed severe right knee joint pain and persistent inflammatory reaction, but no specific antibodies related to major collagen diseases were found. The results of Ga scintigraphy and contrast-enhanced CT showed Ga accumulation in the right knee joint, multiple lymphadenopathy. He underwent right knee surgery, and the pathology of the synovial tissue obtained was consistent with RA synovitis. He was judged to have seronegative rheumatoid arthritis (SNRA), and salazosulfapyridine was started. 2 years later, a follow-up CT scan showed a tendency of lymph node enlargement, and a lymph node biopsy was performed. The patient was diagnosed as having a plasmacytoid iMCD and started treatment with TCZ. One of the exclusion criteria for iMCD is autoimmune diseases including RA. While there were several findings consistent with iMCD, including lymph node pathology, it was difficult to determine whether prior SNRA should be treated as exclusion criteria or not.

## P3-256

**Two cases of connective tissue disease with hemorrhagic macules during wintertime**

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Conflict of interest: None

[Objective] Hemorrhagic macula is a common form of connective tissue disease. Although hemorrhagic maculas are generally innocuous, in some cases they may cause patients distress, and there is a need to exclude drug-induced or malignancy. [Methods] We represented a 49-year-old female and 77-year-old male who were diagnosed connective tissue diseases and presented with hemorrhagic maculas on upper and forearms during wintertime. [Results] 49-year-old female visited our clinic because of Raynaud phenomena. Further examine showed that she had reflux esophagitis. We couldn't find other significant abnormalities. 77-year -old male visited our clinic because of arthralgia. He hadanti-CCP antibody and arthritis in hands, was diagnosed Rheumatoid arthritis and used Methotrexate. He said he had hemorrhagic macules since he was young during the wintertime. Both had any significant abnormalities on clotting function. [Conclusion] This is reported case regarding the hemorrhagic maculas during wintertime of two connective diseases patients. They are no abnormalities in coagulation exams. The cause was possibility that they had autoimmune diseases and/or overuse.

## P3-257

**Retrospective observational study to determine longitudinal changes in renal function among Japanese patients with rheumatoid arthritis (RA)**

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Conflict of interest: Yes

**Objective:** To determine the longitudinal changes in renal function and associated risk factors among Japanese patients with RA. **Method:** Utilizing a nationwide electronic medical record database, patients with and without RA (RA and non-RA patients, respectively) who had at least two serum creatinine results from January 2012 to December 2017 were analyzed. The propensity score matching was applied with patient demographics, including sex, age, and baseline eGFR, to construct RA and non-RA patient groups. The longitudinal change in eGFR was assessed using a linear mixed effect model. **Result:** Overall, 14,531 patients were included for both groups. The proportion of women was 68.5%, and mean age was 67 years in both groups. The mean difference of eGFR slope (mL/min/1.73m$^2$/year) between RA and non-RA patients, which was the primary endpoint, was -0.05 (95% CI: -0.22, 0.11), and no specific trend was observed in subgroup analyses based on patient demographics. Post-hoc analysis exhibited that RA patients treated with MTX had a larger decline in eGFR compared to overall RA patients (-1.38 vs -1.08). **Conclusion:** The eGFR slope was similar between RA and non-RA patient groups. Renal function was suggested to be more strongly impaired in RA patients treated with MTX than in overall RA patients.

## P3-258

**Atypical femur fractures in patients with rheumatic diseases -from the YamaCAFe extension study**

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Conflict of interest: None

[Objective] Non-traumatic atypical femur fractures (AFF) have been reported to be associated with rheumatic diseases and abnormal femur morphology. In this study, we examined the characteristics of AFF occurred in patients with rheumatic diseases. [Methods] AFF cases associated with rheumatic diseases that developed in Yamagata Prefecture from 2009 to 2018 were included in the study. Simple radiographs were analyzed retrospectively in a blinded fashion to examine fracture site, femoral neck angle, and femoral lateral bowing angle. [Results] During the study period, 12 AFF patients with rheumatic diseases were gathered. These included 8 cases of sub-trochanteric fractures (ST) and 4 cases of diaphyseal fractures (DP). All patients were female. The mean age was 60.0 year-old in the ST group and 80.3 year-old in the DP group, the femoral lateral bowing angle 1.1°and 11.4°, the femoral neck angle 129.3°and 124.3°, respectively. There were significant differences in age and femoral bowing angle ($p$<0.05). [Conclusions] ST AFF was more common in patients with rheumatic diseases compared to DF AFF. For the diagnosis and treatment of AFF in patients with rheumatic diseases, it is important to understand the characteristics of each type.

## P3-259

**Hereditary angioedema associated with autoimmune diseases**

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Conflict of interest: None

Background: Hereditary angioedema (HAE) has been pointed out to often be associated with autoimmune diseases, but its actual status is not known. In hereditary angioedema, a decrease in complement is observed along with a decrease in C1 inhibitors. On the other hand, since complement is one of the indicators of activity in autoimmune diseases, the presence or absence of complications between the two may affect diagnosis and treatment. Methods: We retrospectively surveyed 195 HAE patients who visited our hospital between October 2004 and July 2019 who had reduced C1INH. As observation items, the type of autoimmune disease, the values of C3, C4, CH50, and factor XII were examined. Results: There were 51 men and 144 women, with an average age of 42.9 years. Twenty-three patients (11.8%) had autoimmune diseases, of which rheumatoid arthritis (12) (52.1%) and systemic lupus erythematosus (9) were common, including Behcet's disease and 1 scleroderma. In both cases, complement tended to be lower. Conclusion: Although complement is important as an indicator of activity in autoimmune diseases, in cases with HAE, complement is reduced regardless of disease activity, and differentiation may be required.

## P3-260

**A case of TNF receptor-associated periodic syndrome with interstitial pneumonia**

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Conflict of interest: None

A 64-year-old male had experienced febrile attack that lasted about 2 weeks with abdominal pain since childhood. The attacks occurred once every three months. At the age of 51, he was diagnosed with proteinuria. The following year, he began suffering from chronic diarrhea. After pathological examination of the intestinal tract and kidneys, he was diagnosed with amyloidosis. Based on the clinical course, familial Mediterranean fever was diagnosed, however, treatment with colchicine, infliximab, and tocilizumab was not effective. At age 60, his granddaughter was diagnosed with TNF receptor-associated periodic syndrome (TRAPS), and a pathogenic variant in the *TNFRSF1A* gene (p. Cys72Arg) was also confirmed in him. Treatment with canakinumab was started, and the febrile attacks resolved. At age 61, the patient was confirmed to have increased KL-6 serum levels. A lung CT scan revealed interstitial lesions, mainly in the lower lobes of both lungs. Although tests were performed for collagen-induced lung disease, drug-induced interstitial pneumonia, infection, and neoplastic lesions, the cause of these interstitial lesions was not yet identified. Symptoms of TRAPS are diverse, however, interstitial pneumonia is rarely reported as a complication of TRAPS.

## P3-261

**A case of an elderly SLE patient with central nervous system lymphomatoid granulomatosis**

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Conflict of interest: None

[Background] Lymphomatoid granulomatosis (LYG) is an EBV-associated lymphoproliferative disease that primarily affects the lungs. Isolated cases in the central nervous system are very rare, and no case has been reported in a patient with SLE. We report here a case of CNS LYG in an elderly SLE patient whose disease had been stable for a long time. [Case] 85 years old, female [Chief complaint] dysarthria, abnormal behavior [Current medical history] She was diagnosed with SLE in X-26. In February of X year, she developed dysarthria and abnormal behavior. Contrast-enhanced MRI of the head showed multiple nodular and ring-like staining, suggesting CNS SLE or infection, and treatment was started with mPSL 40 mg/day, meropenem, and ST combination drug. A cerebral biopsy was performed from the right frontal lobe. EBER-ISH-positive cells were more than 100 in the high magnification view, and a diagnosis of LYG Grade 3 was made. After starting tirabrutinib, her dysarthria and abnormal behavior disappeared, and MRI of the head showed shrinkage of the lesion. [Conclusion] In patients with SLE, when multiple nodular or ring-like lesions are seen on head MRI, it is important to make a histological diagnosis by brain biopsy, with CNS LYG, an EBV-associated lymphoproliferative disease in mind.

## P3-262

**Two cases of inflammatory arthritis preceding the diagnosis of myelodysplastic syndrome**

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Conflict of interest: None

Myelodysplastic syndrome (MDS) is known as a disease complicated with various autoimmune disorders. We report two rare cases of MDS preceded by inflammatory arthritis within a year before the diagnosis. [Case 1] A 78-year-old male was referred to our department due to polyarthralgia with bilateral pitting edema on his hands and feet. Glucocorticoid (GC) therapy was performed under the diagnosis of RS3PE syndrome after screening of malignancy. Despite of its initial good response, the arthritis was flared accompanied with neutropenia on GC tapering. Multiple times of bone marrow examination for G-CSF-resistant progressive neutropenia

revealed the findings of MDS. [Case 2] A 75-year-old female visited to our department with polyarthralgia with remarkable tenosynovitis on hands and leg edema. As it Implyed RS3PE with low titer of CRP, we carefully excluded paraneoplastic syndrome by cancer screening. According to the patient's will avoiding GC therapy, methotrexate, salazosulfapyridine and TNF inhibitor were used but ineffective. While these treatments, thrombocytopenia was observed, followed by pancytopenia and detection of blast cells in peripheral blood. Evaluation of bone marrow led to the diagnosis of MDS.

## P3-263

**Serum polysorbate-specific IgE in rheumatic disease patients with a history of allergy to polysorbate-containing drugs**

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Conflict of interest: None

[Objective] We reported that serum polyethylene glycol-and polysorbate (PS)-specific IgE was significantly higher in the allergy group than in the control group in patients with suspected allergy to COVID-19 mRNA vaccine. PS has been identified as a possible allergen in drug allergies of unknown origin. We investigated PS-specific IgE in the serum of patients with a history of allergy to injectable preparations containing PS. Also, we observed whether PS-containing medications could be continued in patients with rheumatic diseases. [Methods] Serum PS-specific IgE was measured by ELISA and compared between 12 patients and 19 controls. Skin tests were performed on several patients and serum PS-specific IgE levels were compared. [Results] Of the 12 patients in the allergy group, 8 had rheumatic diseases. In the allergy group, PS-specific IgE was significantly higher than in the control group. In the allergy group, there was no difference in PS-specific IgE between patients with rheumatic diseases and those with other diseases. Some patients with high serum PS-specific IgE, and positive skin tests were able to safely continue taking oral PS. [Conclusions] In patients with suspected PS allergy, including patients with rheumatic diseases, PS-specific IgE may aid in the diagnosis.

## P3-264

**Hospital network to late elderly aged collagen vascular disease patients**

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Conflict of interest: None

[Background] The prevalence of collagen vascular diseases in late onset of elderly people is increasing in recently an aging society. While considering with immunosuppressive therapy for the elderly patients, they should be also considered the aging phenomenon including frailty/sarcopenia. In such situation, we might be strength the medical corporation between hospitals (hospital network). Thus, we examined the effectiveness for collaboration with our two facilities of rheumatologists. [Objective/Methods] The aim is to evaluate clinical aspect for 11 cases. [Results] 11 cases were 4 males and 7 females, and average age was 84.3±4.0 [77-90] years. The category of rheumatological disease were 7 ANCA, 3 Dermatomyositis and 1 IgG4RD. Because of the severe frailty was showed in all of patients after initial treatment, thus they cannot discharge from hospital immediately. The main reasons for the poor ADL were occurred with the late treatment after initial symptoms. [Discussion/Conclusions] Construction of hospital-hospital network in addition with early diagnosis/treatment might be necessary for the treatment with the late onset of elderly aged collagen vascular disease patients.

## P3-265

**Two Cases of Sjögren syndrome and systemic sclerosis with pulmonary multiple cystic lesions**

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Conflict of interest: None

Case 1: A 43-year-old woman. Positive for Both anti-SSA and anti-SSB antibodies, decreased secretion ability of lachrymal fluid ability by ophthalmological examination, and She was diagnosed as Sjögren syndrome. Her plane CT of chest revealed multiple thin-walled cystic shadows of a few millimeters to 2 cm in size in bilateral lung field. A small amount of macrolides is administered. The shadows are not getting worse. Case 2: A 76-year-old woman. Raynaud phenomenon, dermatosclerosis findings were observed, anti-centromere antibodies were positive. She was diagnosed as limited cutaneous systemic sclerosis. Her chest plain CT revealed multiple thin-walled cystic shadows of several a few millimeters to 1 cm in size in bilateral lung field. Sjögren syndrome and systemic sclerosis are often accompanied by lung lesions, but cystic lesions are rare and are known to be resistant to treatment. The mechanism of cyst formation is not clear, but it is speculated that bronchiolitis contributes to cyst formation. Although the efficacy of small-dose macrolide therapy for chronic airway inflammation has been established, administration of a small amount of macrolide in this case did not detect the progression of cystic lesions and suggested that it may act suppressively.

## P3-266

**Analysis of collagen disease patients who developed pneumomediastinum**

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Conflict of interest: None

[Objective] In the medical treatment of collagen diseases, the complication of pneumomediastinum has been reported. However, the number of reports is extremely rare. In this study, we aggregated the incidence of pneumomediastinum in patients with collagen disease in past clinical practice, and analyzed trends based on each patient's profile. The purpose is to analyze and use it in future clinical practice. [Methods] Among patients with collagen disease who visited Gifu Red Cross Hospital, Gifu Prefectural General Medical Center, Gifu Municipal Hospital, and Gifu University Hospital during the past 10 years from April 1, 2013 to March 31, 2023, patients with pneumomediastinum Patients who developed this were included in the observational study. Evaluation items included gender, age of onset, BMI, smoking history, LDH, CRP, CPK, HbA1c, presence or absence of steroid administration, and presence or absence of interstitial pneumonia. The above evaluation items were statistically analyzed. [Results] A one-group t-test was performed and significant differences were found in LDH and CRP values. All cases were complicated by interstitial pneumonia. [Conclusions] LDH, CRP, and interstitial pneumonia were estimated to be correlated with the occurrence of pneumomediastinum.

## P3-267

**Decreased SAFE-Q is a risk factor for falls in RA patients with or without subjective foot symptoms**

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Conflict of interest: None

[Objective] To determine the risk factors related to falls in patients with rheumatoid arthritis. [Methods] A total of 94 adult with seropositive

RA who responded to the "Questionnaire on the Impact of Foot Problems on Daily Life" and the "SAFE-Q", a patient-reported evaluation specific to the foot, were recruited in the study. Twelve months after the survey, the presence or absence of falls was confirmed, and the risk factors for falls were analyzed. [Results] Thirteen patients experienced falls during the 12-month period. Univariate analysis showed that fallers had significantly low walking level, baseline fall history over the preceding 12 months and low SAFE-Q score. In logistic regression analysis, low score on SAFEQ items related to physical function and daily living conditions and history of falls in the past 12 months were independent predictors of prospective falls in the next 12-month. [Conclusions] Regardless of the patient's subjective perception of foot problems, there are cases of reduced foot function. Since decreased foot function is a risk factor for falls, it is essential for physicians to proactively check for foot pain as well as foot function in daily life and identify problems.

## P3-268

**A case of chance fracture of the ankylosing spine associated with alkaptonuria**

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Conflict of interest: None

[Objective] Alkaptonuria (AKU) is an autosomal recessive congenital metabolic disorder characterized by the accumulation of homogentisic acid due to homogentisic acid oxidase deficiency, which is manifested by ochronosis, melanuria, and arthropathy. We report a rare case of spinal fusion surgery for a chance fracture of the ankylosing spine caused by AKU. [Case] A 58-year-old man with a history of bilateral total knee arthroplasty for arthropathy caused by AKU. He fell down at home, and back pain appeared. An X-ray of the lumbar spine showed a vertebral fracture at L1, and the patient was transferred to our hospital. Spinal CT showed an ankylosing spine from T11 to L3, and the fracture extended horizontally from the L1 vertebral body to the spinous process. Posterior spinal fusion from T9 to L4 and local bone graft were performed. Intraoperative findings showed melanosis of the supraspinous ligament and facet joints. At the final follow-up, the fracture was fused, and there were no adverse events with the spinal implants. [Discussion] In case of a chance fracture, surgical treatment is recommended to prevent pseudarthrosis and neurological symptoms due to the instability. In this case, a multilevel posterior fusion was performed to stabilize the fracture site.

## P3-269

**Operative management for intraosseous ganglion of the talus; a case report**

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Conflict of interest: None

[Backgrounds] The intraosseous ganglion of the talus is rare. We report a case of a symptomatic ganglion of the talus. Curettage and debridement had a good result. [Case] A 21-year-old woman had ankle pain and instability. She had no history of injury or autoimmune disease. CT and MRI showed chronic injury of the ankle ligament with bone fragment and subtalar soft tissue tumour. The homogenously T2WI hyperintense lesion indicated ganglion, but it also involved the posterolateral side of the talus. Anterior talofibular ligament repair and curettage were performed. The lesion was filled with jelly-like fluid. The posterior talofibular ligament was lost and replaced by synovium and the ganglion penetrated the subtalar joint and the talar cartilage. The subchondral lesion was removed by curate. 1-year postoperatively, the patient was pain-free and the Japanese Society for Surgery of the Food scale was improved. [Clinical Significance] The Scottish Bone Tumour Registry reported only two cases of intraosseous ganglion of the talus over fifty-six years and other existing literature is limited. Differential diagnosis includes subchondral cysts related to rheumatoid arthritis and osteoarthritis, pigmented villonodular synovitis and other malignant tumours.

## P3-270

**Development of rheumatoid arthritis in the early postoperative period after CM arthroplasty of the thumb: a case report**

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Conflict of interest: None

Background: Osteoarthritis and bone destruction due to rheumatoid arthritis often coexist. We report a case in which arthroplasty was performed for bilateral thumb CM arthropathy, and joint erosion occurred in the wrist, which was initially affected only by osteoarthritis, leading to the diagnosis of rheumatoid arthritis. Case: The patient was a 48-year-old woman at the initial examination. She had pain in the bilateral thumb CM joints, and X-rays and CT images showed osteoarthritic changes. Arthroplasty was performed for the left thumb CM joint. Four months later, arthroplasty was performed for the right thumb CM joint. Four months after the right surgery, she developed bilateral shoulder pain, and various examinations led to the diagnosis of rheumatoid arthritis. Preoperative CT images of the left thumb CM joint showed osteophyte formation, narrowing of the joint gap, and subluxation of the joint, and the diagnosis of osteoarthritis was confirmed. However, a review of the preoperative CT images of the CM joint of the right thumb revealed that, in addition to the findings of osteoarthritis, there was bone destruction in part of the carpal bones. Conclusion: During the treatment of arthropathy, it is necessary always to consider the possibility of developing rheumatoid arthritis.

## P3-271

**Outcomes of Total Hip Arthroplasty (THA) for patients with Rheumatoid Arthritis (RA) in the past 10 years**

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Conflict of interest: None

[Objective] To analyze THA outcomes for patients with RA in the past 10 years. [Methods] The study included 16 patients with 18 hips who underwent THA for patients with RA at our hospital from April 2013 to March 2023 and were followed for at least one year. We examined patient background, surgical procedure, postoperative complications, and the number of THAs in RA patients as a percentage of total THAs for the first five years from 2013-18 and the second five years from 2019-23. [Results] The patients included 11 patients with 12 hips in the first half and five patients with six hips in the second half. There were no significant differences in patient background and surgical procedure between the two groups. Postoperative JOA scores were significantly improved in the two groups respectively. Postoperative complications included one case of dislocation in the first half. The rate of THA for patients with RA decreased 1.4% (6/420) in the second half compared to 3.9% (12/304) in the first half. [Conclusions] The rate of THA for patients with RA at our hospital in the past decade showed a trend to decline, like the results of previous reports. There were no significant differences in patient backgrounds or postoperative outcomes between the first and second halves of the past 10 years.

## P3-272

**Musculoskeletal ultrasonography (MSK) by Nurses to Improve Shared Decision Making**

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Conflict of interest: None

[Objective] Musculoskeletal ultrasonography (MSK) is an effective test in the treatment of rheumatic diseases. To examine whether nurse-performed MSK is an adjunctive means of diagnosing and initiating treatment at the initial visit and contributes to improved shared decision making (SDM). [Methods] From September 2022 to August 2023, 78 first-time patients with suspected rheumatic disease were included. The attending physician gave instructions to the nurse during the consultation, and the nurse performed the MSK. The findings of the MSK were compared with the disease activity status and treatment introduction status. [Results] 71.8% of the first-time patients were diagnosed with rheumatoid arthritis (RA) and 23.1% with psoriatic arthritis (PsA). Within one month, 75.4% were started on anti-rheumatic drugs or biologic agents (BIO). There was a significant difference (P=0.021) between the presence of PD findings and the number of joint swellings. There were also significant differences in DAS28-ESR, SDAI, etc., with and without PD findings and disease activity status. [Conclusions] MSK performed by nurses have led to early initiation of treatment and introduction of BIO for patients with high disease activity. In summary, MSK performed by nurses contributes to improving SDM.

## P3-273

**Long-term safety of rheumatoid arthritis patients receiving JAK inhibitors under our multi-disciplinary collaborative care**

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Conflict of interest: None

[Purpose] We previously presented lower incidence of severe infection among rheumatoid arthritis (RA) patients receiving JAK inhibitors under our multidisciplinary collaborative care. We further investigated their long-term safety. [Methods] We retrospectively reviewed RA patients treated with JAK inhibitors at our department by June 2023. [Results] Of 50 patients (mean age of 68, 20% men), 9 was treated with TOF, 15 with BAR, 11 with UPA, and 15 with FIL. Twenty patients (40%) had two or more risk factors for infection (age >65, lung lesions, diabetes, corticosteroid use, history of cerebrovascular disease). The mean observation period was 25 months. The treatment retention rate, the cumulative discontinuation rate for adverse events and that for inadequate response were 57.6%, 23.9%, and 22.2%, respectively. Two elderly patients with multiple risk factors for infections hospitalized by pneumonia and mandibular osteitis/abscess, respectively. Three patients developed herpes zoster without any sequelae. [Conclusion] Severe infections were not completely abolished under our multidisciplinary collaborative care. It is important to provide more extensive guidance to elderly patients having multiple risk factors.

## P3-274

**Current Situations of Rheumatology Nursing Outpatient Clinic in Japanese Red Cross Narita Hospital**

Kaori Mori, Miyuki Tanaka
Japanese Red Cross Narita Hospital

Conflict of interest: None

[Purpose] Currently, our hospital has over 800 patients with rheumatoid arthritis (RA) and they are cared for by 5 physicians. The consultation time for each patient was short and there was no time to listen to each patient's concerns. To alleviate this burden not enough the physicians and to provide patients with the opportunity to express issues they might not typically discuss, we initiated the nursing outpatient clinic in 2022. [Method] We have analyzed the patients' concerns and evaluated the trends in consultation content, as well as the degree of our understanding of RA. [Results] As of September 2023, 28 patients have visited the nursing outpatient clinic. The most frequent consultation topic was foot-related concerns, with many patients expressing issues related to calluses due to deformities and problems with footwear. The next most common topic was rehabilitation. Additionally, there were consultations regarding cost and techniques related to biologics. [Conclusion] Many patient consultations were time-consuming during regular medical appointments, and they often involved topics that patients were hesitant to discuss with physicians. This analysis of patient concerns has provided valuable insights into the trends that patients are looking for.

## P3-275

**The Role of Multidisciplinary Team and Care for the Patients with Rheumatic Diseases**

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Conflict of interest: None

[Objective] The needs of patients with rheumatic diseases are diverse and unique. To achieve the goal allowing patients to work and live as good as possible, a systemic support of health professionals is needed. [Methods] In October 2020, the multidisciplinary team for the care of the patients with rheumatic diseases was established. The team held the meetings every other months and carried out activities to support the patients with rheumatic diseases. [Results] First, a team survey was conducted and clarified the role, activities and challenges of each health professional. Second, we issued a pamphlet for patients and families to provide information on rheumatic diseases and support. Third, a patient survey revealed that 62% used internet for information, 82% have already read the pamphlet, 10 to 38% would like to consult for each health professional. [Conclusions] With the multidisciplinary team for the care of the patients with rheumatic diseases, we can conduct and expect a better support for patients.

## P3-276

**currents situations and future challenges of rheumatology nursing outpatient clinic-from perspectives of a certified dermatology and excretion care nurse**

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Japanese Red Cross Narita Hosupital

Conflict of interest: None

[Objective] in april 2022, a rheumatology nursing outpatient clinic (referred to as "the outpatient") has been established. over a year has passed, and the purpose is to assess the current situations and future challenges clearly. [Methods] patient assessments were based on nursing records, including the content of consultations, provided guidance, and the number of visits of patients who attended the outpatient clinic. [Results] the study included 28 participants with an average age of 62.3 years. the primary consultation topics were foot care and skincare. patients seeking advice on foot care often had foot deformities or calluses. recommendations were made regarding footwear selection, insole usage, and dermatologist visits. few patients practiced daily skin care, and implementing preventive skin care was encouraged. [discussion] among the 28 patients who sought medical attention, 62% had only one visit. many ra patients have a history of steroid use. therefore, preventative skincare becomes essential. however, many patients are not implementing skincare practices, making the guidance provided in the nursing outpatient clinic valuable. [Conclusions] it has become evident that many ra patients lack skincare knowledge and face various foot-related concerns.

## P3-277

**Challenges Nurses faced in Caring for Elderly Patients with Rheumatoid Arthritis in Japan**

Mie Fusama[1], Hideko Nakaahra[2], Yukitomo Urata[3], Kimito Kawahata[4], Yutaka Kawahito[5], Masayo Kojima[6], Takahiko Sugihara[7], Motomu Hashimoto[8], Takako Miyamae[9], Atsuko Murashima[10], Masaaki Mori[11], Nobuyuki Yajima[12], Toshihiro Matsui[13]
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Conflict of interest: None

Objective: To identify the challenge rheumatology nurses faced when caring for elderly RA patients. Methods: The participants were rheumatology care nurses. A qualitative content analysis was conducted using free-text descriptions in a self-administered questionnaire survey regarding the difficulties they experienced when caring for elderly RA patients. Results: 133 nurses participated. A total of 167 codes were identified and classified into the following 8 categories: (1) Patients have poor comprehension skills, (2) Patients have difficulty in self-management, (3) Patients have challenges with their treatments due to complications and comorbidities, (4) Patients have challenges other than the disease and treatment, (5) Patients do not have enough support from their family members, (6) Patient's support requires substantial time, (7) nurses lack knowledge and skills, and (8) Insufficient cooperation among multidisciplinary healthcare professions Conclusion: Elderly RA patients experience a variety of medical and non-medical challenges. Assessment of the comprehension and self-management of patients and understanding of the patient's situation at home are necessary. Moreover, the importance of multidisciplinary team care, including collaboration with family members, is recognized.

## P3-278

**A study of the persistence of educational effects after pharmacist outpatient clinic for rheumatoid arthritis patients**

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Conflict of interest: None

[Objective] To evaluate the effectiveness of pharmacist outpatient clinic for the patients with RA. [Methods] RA Patients who were able to receive the questionnaire between 11/1/2019 to 9/30/2023 were included. The same questionnaire was administered before and after the clinic. The interval was divided into two groups: less than 1 year and more than 1 year. The Fisher test was used to see if there was a difference in answers after the intervention; the McNemar test was used to assess the effect before and after the clinic. [Results] Of the 161 patients who visited the clinic, 60 were able to survey the questionnaires before and after the clinic, with a median questionnaire interval is 7 months. There was no significant difference in understanding of sick day respons after the clinic between less than 1 year and more than 1 year groups (P=1). Before and after the clinic, (i), (ii), (iii) are increased (P<0.05). In cases with a questionnaire interval of more than one year, there was no change in responses to (1) (P=0.13), while the number of respondents to (2) and (3) increased (P<0.05). [Conclusions] The effect of pharmacist outpatient clinic was observed and didn't differ between questionnaire intervals.

## P3-279

**Investigation of pharmacological management of home self-injection instruction in an outpatient immunopharmacist clinic (Report 2)**

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Conflict of interest: None

[Objective] Although pharmacists' pharmacological management involves joint decision-making on drug selection, dispensing and follow-up, they also provide instruction on self-injection technique and administration assistance as part of their pharmacological management in task shift/sharing with physicians in 2022. Therefore, we investigated the self-injection continuation rate and prescribing suggestions by pharmacists when the guidance was provided by an outpatient immunopharmacist in the office and by a nurse. [Methods] The endpoints were the rate of continuation of self-injection in the Pre and Post groups, the number of adverse drug reactions reported by pharmacists or nurses, and the number of prescribing suggestions made by pharmacists to physicians. [Results] The retention rate at 24 weeks was 111 (86%) in the pre group and 115 (97%) in the post group (p<0.01). There was a statistically significant difference in the number of prescriptions proposed: 0 in the pre group and 62 in the post group (p<0.01). [Conclusions] The collaboration between the physician and pharmacist in the examination room to provide self-injection instruction enabled the acceptance of the patient and prescription suggestions regarding side effects, which led to a high early self-injection continuation rate.

## P3-280

**Involvement of a woman who refused glucocorticoids and biologic dmard in the treatment of takayasu arteritis. -clinical practices and difficulties in shared decision making-**

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Meiyo Immunology and Rheumatology Clinic

Conflict of interest: None

[Purpose] Shared decision making (SDM) has been proposed, in which patients and health care providers work together to make the best treatment choice. We will examine whether SDM can be practiced and whether the best treatment choice can be made while eliciting a patient's thoughts through the patient who refuses to receive glucocorticoid (GC). [Case] 25-year-old woman was diagnosed with Takayasu arteritis. She was explained GC treatment at a hospital but did not receive it and visited our clinic. The doctor explained that GC was necessary for her condition and that GC could be reduced or discontinued early with the combination of immunosuppressants (IS). After several consultations, she agreed to GC treatment and then was treated with two other ISs as well. After repeated explanations, she consented to bDMARD. Further GC reduction was achieved. [Clinical Significance] The physician and nurse explained and interviewed her about the values she held, her treatment choices and the risks involved. As a result, she was able to make a choice each time despite her conflicts. However, it is believed that overcoming this process is what SDM is itself. It is thought that human resource development to deal with the patient with connective tissue diseases (CTD) is the future challenges.

## P3-281

**An example of improvement of skin sequelae of psoriasis using Alexandrite laser**

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Conflict of interest: None

[Objective] A 16-year-old female. She had skin symptoms, but her local doctor diagnosed her with atopic dermatitis. Along with pain and dactylitis in her toes, exfoliative erythema appeared on the back of her head, on the extensors of her joints, and on her extremities, and she was diagnosed with psoriatic arthritis. As topical therapy and Iguratimod didn't provide sufficient improvement, Guselkumab was started, there was marked improvement in both the skin and joints, patchy pigmentation remained on the extremities and back. [Methods] Irradiation of the Alexandrite laser to pigmented areas such as extremities was started at the minimum output. The output was gradually increased once every six months, and performed four times. [Results] Pigmentation throughout the body was clearly improved by alexandrite laser irradiation. And hair removal and skin beautification effects were achieved, so patient satisfaction and motivation for treatment improved. [Conclusions] Alexandrite laser irradiation is often used to treat pigmentation due to atopic dermatitis, but there are few reports on psoriasis. Even if the disease can be controlled, psoriasis can leave behind skin problems such as pigmentation. Laser treatment

was considered to be highly useful in resolving these residual symptoms.

## P3-282

**Considering psychological support for rheumatoid arthritis patients~Reflecting on a Case Using Crisis Theory~**

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Conflict of interest: None

Purpose: Rheumatoid arthritis (RA) patients should adjust their living background according to the number of patients. Here, we use crisis theory to introduce cases from outpatient and inpatient treatment. Case: 80-year-old woman, chief complaint: joint pain. Occupation: Head of tea ceremony Personality: Active, serious, Family composition: Divorced, living alone, Key person: Eldest son, Primary caregiver: Apprentice, Living separately: Eldest son and his wife, Eldest daughter Progress: In early April 20XX, neck pain appeared. Although the patient visited a nearby doctor, the patient did not improve and was referred to our department. In June of the same year, she was diagnosed with rheumatoid arthritis and began treatment, but his symptoms did not improve, and he was hospitalized in July for the introduction of a biological agent. She was transferred to another hospital due to depression. Results: After being diagnosed with rheumatoid arthritis, the patient entered a crisis state and was unable to overcome the stages of (1) shock and hope for recovery, (2) sadness, and (3) defense and efforts to recover. [Conclusion] Through this case, the nurses who provide support during regular outpatient visits after discharge from the hospital.

## P3-283

**A case of pregnancy complicated by SLE with placental infarction despite serologically stable term phospholipid antibody syndrome not suggested**

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Conflict of interest: None

A 36-year-old woman with SLE. She was in remission with PSL 5 mg/day, TAC+, HCQ. After two miscarriages (less than 5 weeks), she deliverd a healthy baby at 39 weeks with biaspirin and subcutaneous heparin injection In X year, she became pregnant outside Japan and was treated with Lonavex from 10 weeks' gestation, then returned to Japan and was switched to subcutaneous heparin injection at 15 weeks' gestation. At 19 weeks' gestation, ddimer increased to 11 μg/ml, and at 24 weeks' gestation, she was sent to our hospital due to impending preterm delivery. Serologically, there was no worsening of SLE, and ddimer rose to 38 μg/ml. No venous thrombosis was found in the mother, and the baby was delivered by Cesarean section at 25 weeks' gestation. Three days postpartum, ddimer decreased to 2.4 μg/ml. Placental histopathology showed that trophoblastic maturation was equivalent to late gestation, and extensive infarcts were observed in the placental bed dehiscence membrane. The details of the vascular lesions are pending the results of the histopathological examination. The child was admitted to the NICU with no evidence of disability. We herein report a rare presentation of pregnancy with placental infarction who suffered from SLE with remission without APS.

## P3-284

**Postpartum Depression Scale in Patients with rheumatic diseases**

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Conflict of interest: None

[Objective] Postpartum depression occurs in 10-15% women, and a history of psychiatric disorders as well as illness during pregnancy and poor postpartum health have been reported as risk factors. There have been few reports on the association between RA or SLE complicated pregnancies and the development of postpartum depression. [Methods] We included 16 RA patients, 18 pregnancies, and 14 SLE patients who attended our maternal outpatient clinic and gave birth in our obstetrics and gynecology department between April 1, 2018, and August 31, 2023. Clinical data and the Edinburgh Postpartum Depression Scale (EPDS) at 1 month postpartum were examined using descriptive statistics and the Wilcoxon test. [Results] Median age at delivery was 36 years, 21 of the 30 women were primipara. The median duration of RA was 4 years and 4.5 years for SLE. The median EPDS score for RA was 0.5 (0-3) and 1 (0-5) for SLE, with no significant difference in EPDS scores by disease (p=0.43). 41% of all pregnancies were scored on the parenting anxiety component of the EPDS. Only one patient with SLE (3% of all pregnancies) had a positive score of 9 or higher on the EPDS. [Conclusions] EPDS positivity rates in RA and SLE patients were lower than general data from Japan.

## P3-285

**Pregnancy outcomes and significance of Ro52 in anti-SS-A antibody positive rheumatic disease patients**

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Conflict of interest: None

[Objective] We clarify the association between Ro52 and pregnancy outcomes, including congenital heart block (CHB), in anti-SS-A antibody positive patients. [Methods] We selected the anti-SS-A antibody positive patients from our registry. We analyzed pregnancy outcomes such as CHB, preterm birth (PB) and low birth weight (LBW), anti-SS-A antibody titers and therapeutic agents was extracted from medical records. Ro52 was measured by ELISA. [Results] The subjects were 92 cases. Mean anti-SS-A antibodies titer was 519.4±1368.3 IU/ml, and 28 cases were positive for anti-SS-B antibodies. Glucocorticoids (GCs) was administered in 56 cases, and hydroxychloroquine (HCQ) was in 12 cases. Of the 40 cases in which Ro52 could be measured, 19 cases were positive, and mean titer was 131.4±148.8 IU/ml. Anti-SS-A antibodies titer was significantly higher in Ro52 positive cases (P=0.02). CHB was observed in 2 cases, both of whom were positive for Ro52, neither GCs nor HCQ were administered. 14 PB cases and 25 LBW cases was not associated with anti-SS-A antibody titer or the positivity for anti-SS-B or Ro52. LBW was significantly associated with GCs. [Conclusions] In anti-SS-A antibody positive pregnancies, it is important to assess and manage risks by Ro52 positivity and therapeutic agents.

## P3-286

**Experience of transferring patients with childhood-onset rheumatic diseases from pediatric to adult care: a multiple-case study design**

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Conflict of interest: Yes

[Objective] This study aims to explore the experiences of patients with rheumatic diseases in the transition period. [Methods] Semi-structured interviews were conducted with participants who were at least 18 years old, had a history of childhood rheumatic disease. [Results] The study conducted with two female participants in their 30s, both diagnosed with SLE. For the first participant, the factors that facilitated her transition included the suggestion that she should move on from pediatrics, the need to balance her work, and recommendations from peers. The second participant was influenced by changes in the social framework, such as Covid-19 related restrictions on medical institution acceptance, and parental involvement to foster independence appropriate to her development and age. However, a

lack of knowledge about treatment was a barrier to the transition. [Conclusions] Life events, such as starting higher education or employment, and the discomfort of continuing with a pediatrician into adulthood, were insufficient to facilitate the transition from pediatric to adult care. Therefore, this study suggests the necessity for the transfer of medical information between healthcare institutions, with patients taking a central role, to promote the shift from pediatric to adult care.

## P3-287

**Assessment of pregnancy complications and pregnancy outcomes in SLE complicated pregnancies: A multi-center cohort study**

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Conflict of interest: None

(Objective) This study examined clinical data including outcomes of pregnancies complicated by SLE as part of a study to elucidate the mechanism of pregnancy complications and to identify risks using peripheral blood single cell information of SLE patients registered in the JNIH. (Methods) We conducted a prospective observational study on the clinical data of 43 patients with SLE-complicated pregnancies registered at 16 facilities from February 2022 to August 2023. (Results) In 43 cases of SLE patients during pregnancy, the median age at pregnancy was 33 years (IQR 31-37), and the median duration of the disease was 7 years (4-13.3). Planned pregnancies were observed in 28 cases (63.8%). Among the 33 cases (excluding one twin pregnancy) that resulted in live births during the study period, 26 cases (78.8%) were full-term deliveries, 7 cases (12.2%) were preterm, 2 cases (6%) had fetal growth restriction, 5 cases (15.1%) had pregnancy-induced hypertension, and 13 cases (39.3%) underwent cesarean section. (Conclusions) In this study, the incidence of pregnancy-induced hypertension and the cesarean section rate were higher compared to healthy individuals. Education on appropriate contraceptive methods as part of preconception care is one of the future challenges.

# Morning Seminar

## MS1

**Potentials of IL-17 Inhibition in the treatment of spondyloarthritis**

Akira Hashiramoto
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Conflict of interest: Yes

After years of changes to diagnostic criteria and disease typing, spondyloarthritis (SpA) has been classified into 7 diseases types: ankylosing spondylitis, psoriatic arthritis, SpA associated with inflammatory bowel disease, reactive arthritis, juvenile onset SpA, unclassified SpA and non-radiographic axial SpA. Clinical practice guidelines in Japan, as well as ASAS/EULAR recommendations, state that IL-17 inhibitors show both initial and long-term therapeutic efficacy comparable to TNF inhibitors. Also, it is mentioned that IL-17 inhibitors may have some efficacy in cases of inadequate response to TNF inhibitors, and that IL-17 inhibitor administration may worsen enterocolitis in patients with inflammatory bowel disease. Immune system cells activated by IL-23 secrete a variety of cytokines, including IL-17, IL-22, and TNFa. Among them, IL-17A, which is important for the pathogenesis of SpA, binds to the IL-17 receptor A/C heterodimer in the form of a homodimer or a heterodimer with IL-17F. This presentation will outline the fundamentals of IL17 inhibition on axial SpA and psoriatic arthritis, to achieve early diagnosis and appropriate treatment.

## MS2

**Potential of IL-23 Inhibitors in PsA and PPP~Evidence from Clinical Trials of Risankizumab~**

Mitsumasa Kishimoto
Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

Psoriatic arthritis (PsA) and palmoplantar pustulosis (PPP) are both inflammatory diseases with cutaneous and musculoskeletal manifestations. According to the study among three tertiary care centers in Japan, prevalence of PsA among psoriasis is 14.3%, which is similar to those in western countries. The inflammation in enthesis is thought to be triggered by mechanical stress, which activates various types of immune cells through the overproduction of inflammatory cytokines such as IL-23. On the other hand, PPP is a chronic skin disease consisting of aseptic blisters and pustules on the palms and soles, and is associated with nail deformities and extra-dermatological manifestation. Prevalence of pustulotic arthro-osteitis (PAO) among PPP was also reported to be about 10~30%. As with PsA, IL-23 is involved in the pathogenesis of PPP. As in other rheumatic diseases, biologic agents have made remarkable progress in the treatment of PsA/PPP, and are now considered important treatment options in GRAPPA/EULAR recommendations for PsA and in the Clinical Practice Guides for PPP, respectively. PsA/PPP has various complications and extra-articular symptoms due to the nature of the disease, and therefore, it is necessary to establish a cross-disciplinary treatment system involving not only rheumatologists and dermatologists but also multiple professions and departments. Risankizumab, an IL-23p19 monoclonal antibody, was approved for PsA in May 2019 and PPP in May 2023 in Japan, and is widely used in daily practice. In this seminar, we would like to discuss the characteristic pathophysiology of PsA/PPP and the importance of caution and collaboration with other departments in differential diagnosis with other rheumatic diseases, as well as with treatment strategies using biologic agents, mainly IL-23 inhibitors, with a focus on Risankizumab.

## MS3

**Long-Term Strategies to Prevent Joint Destruction: Achieving Both Efficacy and Safety of TNF Inhibitor Therapy**

Yuji Nozaki
Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: None

The treatment landscape for rheumatoid arthritis (RA) has undergone significant advancements in recent years, leading to noticeable therapeutic benefits in routine clinical practice. These experiences serve as a source of support for both patients and healthcare providers. However, the necessity for long-term treatment strategies prompts a further exploration of treatment effectiveness and safety. In cases of RA diagnosis, methotrexate (MTX) is typically the initial consideration, serving as a foundational treatment across various scenarios. Nevertheless, instances where MTX becomes challenging to administer or escalate are increasing with age, often due to reasons such as liver, kidney, lung impairments, or upper gastrointestinal issues. The emergence of subcutaneous MTX formulations has been a welcomed development, offering expanded therapeutic options from Phase 1 to 3, especially for cases that have abandoned MTX escalation or oral administration due to gastrointestinal issues. In situations where treatment goals are not met in Phase 1, Phase 2-3 considerations may involve biological agents or Janus kinase (JAK) inhibitors, with MTX co-administration being crucial for treatment effectiveness. While TNF inhibitors may exhibit a synergistic effect when used in conjunction with MTX, determining effective treatment strategies for cases where sufficient oral MTX is challenging remains a key question. Regarding safety, there is currently no consensus on an increased risk of malignancy, cardiovascular events, or infection rates with TNF inhibitors based on abundant use and numerous reports. However, the optimal treatment strategy from this perspective remains an open question. This presentation aims to evaluate the evidence up to the present day regarding TNF inhibitors as a treatment for RA, focusing on long-term strategies for joint destruction prevention. The goal is to maximize treatment effectiveness and safety while minimizing side effects, providing insights into the future of rheumatoid arthritis treatment.

## MS4

**The positioning of Rituximab in the treatment strategy for Lupus Nephritis**

Yoshiya Tanaka
First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

Lupus nephritis (LN) is one of the most serious complications of systemic lupus erythematosus (SLE) and develops in 50-60% of SLE patients within the first 10 years of disease onset. LN is one of the main causes of morbidity and mortality in SLE patients. Although advances have been made in effective therapeutic approaches for SLE and LN, unmet medical needs remain for treatment options, particularly among patients with refractory disease. B-cell depletion therapy with an anti-CD20 antibody Rituximab has been reported to be effective in treating SLE, including LN, in many preliminary observational non-blind trials since we first reported a SLE patient successfully treated with rituximab in 2003. We reported that recovered peripheral B cells after B cell-depletion by rituximab were mainly naive B cells in patients on long-term remission, suggesting the reconstitution of the B cell compartment by rituximab. However, in two large-scale double-blind placebo-controlled Phase III clinical trials examining the efficacy and safety of Rituximab in patients with active SLE (EXPLORER) or SLE patients with active proliferative LN (LUNAR), Rituximab did not demonstrate superiority over placebo. Nevertheless, led by the Rituximab Use Survey Subcommittee of the Japan Rheumatism Association, a usage survey was conducted jointly by four academic societies to aim for insurance reimbursement of Rituximab in Japan. The efficacy was recognized with a renal response of 48.6% (375 mg/m2 usage), and the main safety issues included 11 cases of infusion reactions and 15 cases of infection. As such, a certain level of effectiveness was recognized in the Rituximab usage survey, and after about 10 years, Rituximab was approved for additional use in lupus nephritis refractory to conventional treatments on August 23, 2023. In this seminar, we will introduce the current treatment of Lupus Nephritis and how Rituximab, given its effectiveness and safety, can be positioned. We will also deliver a lecture on the future prospects of Lupus Nephritis treatment strategies.

## MS5-1

**ERAS for Arthroplasty and Work Style Reform for Doctors**

Norikazu Yokoyama
Omuro Orthopedic Clinic

Conflict of interest: None

In a super-aging society, the demand for arthroplasty surgery is increasing, raising concerns about a global rise in medical costs. This trend is also observed in rheumatoid arthritis (RA) patients. Japan faces a unique situation where the duration of hospital stays after joint replacement is longer compared to other countries, resembling a “Galapagos” phenomenon. While satisfaction post-total hip arthroplasty (THA) is relatively high, patient needs are becoming more diverse. It is essential to explore strategies to enhance individual patient satisfaction and ensure a safe discharge. In response to these challenges, the concept of Enhanced Recovery After Surgery (ERAS) has gained global recognition. Within the field of orthopedics, ERAS for hip and knee arthroplasty (THA, TKA) is gaining prominence. The ERAS consensus statement has already been presented overseas and is currently under further consideration. While acknowledging the high hurdle of implementing the overseas concept of outpatient surgery (same-day discharge surgery) in Japan, there is a need to identify changes that align with the Japanese mentality. Furthermore, starting from April 2024, significant reforms to doctors’ work styles will commence. The focus will be on improving not only actual surgical time but also overall efficiency. Even in THA and TKA surgical techniques, to facilitate early recovery, methods respecting soft tissues in the procedures themselves should be introduced. Additionally, a multidisciplinary team approach should be considered to provide early recovery to patients with high satisfaction. At our hospital, we are currently working towards enabling patients to independently return home one week after TKA surgery and four days after THA surgery. I invite you to collaborate in exploring the optimal form of ERAS for joint replacement surgery in Japan in the future.

## MS5-2

**Total Knee Replacement in the era of ‘diversity’**

Yoshinori Soda
Midorii Orthopaedics, Joint Reconstruction &Arthroscopy Center

Conflict of interest: Yes

There are numerous causes of harassment that hinder the spread of ‘diversity’. The same may be true for Total Knee Arthroplasty (TKA). We have been performing TKA using the mechanical alignment method proposed by Freeman, Insall, and colleagues, which aims for neutral alignment. This is the current golden standard technique with emphasis on durability. The postoperative results of TKA have improved due to advances in surgical techniques and the development of evaluation instruments to achieve this neutral alignment. However, patient satisfaction with TKA has not reached the level of that with hip replacement. Some say, “We should not talk about TKA together because the anatomical structures are different.” However, we should not be complacent. We should not be complacent, because the patients have no such feelings. In recent years, a lot of ‘diversity’ has been spreading, and in TKA, the concept of constitutional varus has been touted. In other words, it can be interpreted as ‘diversity’ of lower limb alignment. The percentage of humans with neutral lower limb alignment is only 70-80%, even with a range of 3 degrees, and the remainder are considered outliers. Therefore, if we continue to aim for neutral alignment, which is only captured in two dimensions, this outlier will be disregarded, and further improvement in patient satisfaction with TKA may never be expected. TKA based on the kinematic alignment method proposed by Howell et al., a technique that predicts native or pre-arthritic joint morphology and performs resurfacing, is advantageous in terms of postoperative pain and functional recovery because it does not involve unnecessary soft-tissue procedures. For what cannot be compensated by the surgical technique alone, we rely on implant characteristics, but the constraint in the coronal plane (especially medial) is key. Our group started TKA using the kinematic alignment method in 2019, and to date, over 3000 cases have been performed, with no implant loosening or sinking, and good postoperative results have been obtained, albeit in the short term. In order to avoid “alignment harassment,” which is the practice of applying a one-fits-all alignment to all patients in TKA, it is important to break free from stereotypes and to fully understand the ‘diversity’ of the patients. and be flexible to individual patients with a full understanding of their ‘diversity’.

## MS6

**The advanced application of subcutaneous MTX for RA in clinical setting ~Novel treatment strategy of RA phase I in this new era~**

Kenta Misaki
Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

Recently, many biologics (Bio) and JAK inhibitors (JAKi) have been approved for the treatment of rheumatoid arthritis (RA), methotrexate (MTX) has been positioned as the first-line and anchor drug for RA therapy in Japan and overseas. MTX is focused as the anchor drug because MTX demonstrated the highest efficacy, safety, and tolerability among csDMARDs in many clinical trials also such as the combination therapy with Bio or JAKi. MTX is also approved for juvenile idiopathic arthritis, psoriatic arthritis, and other indications. In Europe, subcutaneous administration of MTX has been the mainstream of RA treatment. In Japan, MTX guidelines allow dosage escalation up to 16 mg/week under the treatment of oral MTX in 2011, however it is rare to increase the dosage of MTX successfully up to 16 mg due to adverse events in actual clinical setting. It is suggested many Japanese RA patients cannot be treated with sufficient doses of MTX. Finally, the subcutaneous MTX treatment was approved for the first time in Japan on September 26, 2022. In this seminar, I'm going to talk about the latest evidence and prospects for the treatment of RA focused on the efficacy and safety of MTX subcutaneous therapy based on clinical trials in Japan with some own experiences and pitfalls from the point of view of Rheumatologist.

## MS7

**2022 Updated EULAR RA Management Recommendations in a Global Perspective**

Josef S Smolen
Division of Rheumatology Department of Medicine 3, Medical University of Vienna, Austria

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic inflammatory disease which can cause cartilage and bone damage and lead to irreversible disability. Treatment algorithms involve evaluating signs and symptoms, applying a treat-to-target strategy, and use of conventional synthetic and biological disease-modifying antirheumatic drugs. Since the information of these drug is not always sufficient for rheumatologists to decide which path to follow when initiating or changing therapy in RA patients, the treatment strategy may differ among them. Taking this into consideration, the EULAR has developed recommendations for the management of rheumatoid arthritis (RA) with disease-modifying antirheumatic drugs (DMARDs) in 2010 and, thereafter, updates of these recommendations have been produced every 3 years, as insights have evolved, and new classification criteria, new definitions of remission, new treatment strategies and many new drugs have emerged. The last update of the recommendations was in 2022. In the 2022 update, The Overarching principles and the original Treat to Target recommendations were unchanged, but the recommendations regarding glucocorticoids were clarified and changed to incorporate newly emerging data. This seminar will highlight the future of RA treatment, focusing on IL-6 inhibitor therapy in line with EULAR Recommendations. We will also discuss emerging challenges like personalized approaches to therapy, Pre-RA and Difficult to treat RA - cases resistant to conventional therapies. The remaining unmet needs underscore the necessity for continued research and innovative solutions in RA treatment.

## MS8-1

**Pathology and treatment strategies of psoriatic arthritis and the potential of bimekizumab, an IL17A/F inhibitor**

Tadashi Okano
Center for Senile Degenerative Disorders (CSDD), Osaka Metropolitan University Graduate School of Medicine

Conflict of interest: Yes

The majority (70 to 80%) of psoriatic arthritis (PsA) patients have skin psoriasis before their PsA diagnosis. Various symptoms such as peripheral arthritis, axial lesions, enthesitis, nail lesions, and digitactylitis might occur in PsA patients. The treatment goals for PsA are to improve the patient's QOL and prevent joint destruction and deformities, and T2T targeting MDA/LDA has been proposed. In recent years, PsA treatment has made great progress with biological DMARDs and JAK inhibitors, and it has become possible to aim for PASI 90 or PASI clear for skin lesions, and MDA (minimal disease activity) for arthritis. The pathological conditions may be slightly different for each patient, and it is extremely important to consider a treatment strategy based on the pathological conditions and the domain of PsA patients. Among these drugs, bimekizumab, which has been newly indicated for PsA and axSpA, is the only drug that inhibits IL-17A and F, and is expected to be effective for various domains including skin lesions. In this session, we will introduce treatment strategies and the usefulness of bimekizumab for PsA based on clinical results.

## MS8-2

**Efficacy of Bimekizumab for axial spondyloarthritis and its potential in therapeutic management**

Kurisu Tada
Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine

Conflict of interest: Yes

Axial spondyloarthritis (axSpA) is a group of diseases that cause inflammation mainly in the axial joints and is known to be strongly associated with HLA-B27. It often develops in the 10 ~ 20 s, and the progression of spinal ankylosis may interfere with activities of daily living. Although axSpA is classified into ankylosing spondylitis (AS) and nonradiographic axial SpA (nr-axSpA) according to the degree of plain x-ray changes in the sacroiliac joints, and is considered to be a spectrum of conditions that progress from nr-axSpA to AS, not all patients with nr-axSpA progress to AS, and some may spontaneously resolve. However, nr-axSpA, like AS, has a high burden of disease in patients, and early intervention is important, especially in patients at risk of progression to AS. Treatment for axSpA may include TNF inhibitors, IL-17 inhibitors, or JAK inhibitors for axial disease uncontrolled with NSAIDs. Bimekizumab, newly approved for axSpA in Japan, is the only drug that inhibits both IL-17A and F, and is expected to be effective and safe. In this lecture, we will introduce the treatment strategy of axSpA and the potential of Bimekizumab discussed from the clinical trials.

## MS9-1

**Up to date of pathology in interstitial lung diseases with connective tissue diseases**

Junya Fukuoka
Department of Pathology Informatics, Nagasaki University Graduate School of Biomedical Sciences

Conflict of interest: Yes

In connective tissue disease, accurate diagnosis of interstitial lung lesions that affect prognosis is important. Pathological diagnosis often does not play a key role in pulmonary collagen disease. Many diseases are diagnosed clinically or by their disease progression over the follow up, and depending on their progression, the patients will likely be treated. Treatment varies depending on the situation, involving either pulmonologists or rheumatologists. Either way, the understanding of background pathology along with its clinical benefits will help improve the practice. In this session, I first provide a basic knowledge of the pathology in idiopathic interstitial pneumonia, followed by a discussion on the pathological features observed in pulmonary lesions associated with collagen disease. Additionally, as an update, we will explain 1) how to understand and apply the pathological findings of collagen diseases related to recently defined PPF in clinical practice, 2) points to note in pathological diagnosis in cryobiopsy, and 3) the application of pathology AI in the treatment of interstitial pneumonia, incorporating publicly reported data from our own experiences.

## MS9-2

**Daily practice management of connective tissue disease-associated interstitial lung disease ~in view of the importance of early diagnosis and therapeutic intervention~**

Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: Yes

The prognosis of rheumatic disorders has seen significant improvements due to the utilization of immunosuppressive and biological agents. Nevertheless, pulmonary fibrosis remains a leading cause of mortality, resulting from organ damage due to the primary disease including renal and pulmonary damage. Connective tissue disease-associated interstitial lung disease (CTD-ILD) is a frequent and crucial prognostic factor. Its etiology is a complex interplay of genetic, environmental, and immunological factors, many of which are yet to be identified. Moreover, the pattern of pulmonary involvement, including the distribution of lesions in the lungs and the pathological features, varies among collagen diseases, and even within the same disease, the clinical features differ from one case to another, contributing to the disease's diversity. Of particular concern is progressive fibrosing interstitial lung disease (PF-ILD), a form of CTD-ILD characterized by lung fibrosis, declining respiratory function, and worsening respiratory symptoms. The prognosis of PF-ILD is poor, with progressive lung fibrosis, declining respiratory function, and worsening respiratory symptoms. The incidence of PF-ILD varies depending on the underlying disease, but it is most common in ILD associated with scleroderma and rheumatoid arthritis. Early detection and diagnosis using screenings such as auscultation and image examination, as well as early and adequate immunosuppressive treatment based on the underlying disease, are expected to be effective with antifibrotic agents. With regard to poor prognostic factors, monitoring, and timing of treatment initiation, a consensus statement on CTD-ILD has been presented from Japan, and the key points on how to understand and manage disease progression of this disease in daily clinical practice are becoming clear. In this lecture, I would like to address the timing of early diagnosis, monitoring, and treatment of CTD-ILD and treatment options.

## MS10-1

**Optimization of rheumatoid arthritis treatment from the perspective of immune abnormalities**

Shingo Nakayamada
First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), clinical, structural and functional remission has become a realistic goal with appropriate early therapeutic intervention with conventional synthetic anti-rheumatic drugs such as methotrexate (MTX), biological DMARDs, and targeted synthetic DMARDs. However, only about 60% of patients achieve these goals, and the existence of difficult-to-treat RA (D2TRA), a group of patients who do not achieve remission with current pharmacological therapies, is becoming increasingly clear. Since the response to each targeted therapy often differs markedly among patients due to the heterogeneities in the pathogenesis of this disease, the establishment of precision medicine is considered particularly important. Abatacept strongly suppresses the activation of follicular helper T (Tfh) cells, which control the maturation and activation of B cells, and suppresses the production of autoantibodies from B cells. Previous studies reported a difference in the predictors of the response to treatment; patients who had higher titers of RF or anti-CCP antibody were shown to respond well to abatacept. Thus, patients with active Tfh cell-B cell-autoantibody axis are expected as good responder for abatacept. Immunophenotypic analysis of 533 RA patients conducted by our department showed that T-cell abnormalities in RA patients were characterised by elevated levels of terminally differentiated effector cells (TEMRA), suggesting that these are predictive of the therapeutic effect of abatacept. Further, abatacept has little effect on the innate immune system and seems to be safe as regards the risk of serious infections for elderly patients. In this seminar, we would like to highlight recent advances the pertain to basic and clinical significance of T cell targeting in the treatment of RA based on the results of our clinical registry and immunophenotyping analysis.

## MS10-2

**Treatment strategy for RA with lung comorbidities**

Motomu Hashimoto
Department of Clinical Immunology, Graduate School of Medicine, Osaka Metropolitan University

Conflict of interest: Yes

Rheumatoid arthritis is accompanied by a variety of lung comorbidities. They include interstitial pneumonia (ILD) with UIP/NSIP/OP pattern, or airway diseases such as chronic bronchitis or bronchiolitis. Further, immunosuppressive treatment for RA can facilitate the colonization of pseudomonas or non-tuberculous mycobacteria in RA lung. Thus, lung comorbidities in RA are a major cause of treatment resistance in RA (difficult to treat RA; D2TRA). RA lung comorbidities can be caused by the immunological abnormalities inherent in RA. ACPA is a characteristic autoantibody in RA, and RA with lung comorbidities are associated with high titer of ACPA. Inhalation of environmental substances such as smoking causes airway inflammation, that leads to citrullination and immune reaction against citrullinated proteins in the lung. Ectopic lymphoid follicles are developed in RA lung tissues, where T cells and B cells locally interact to produce ACPA. Considering these mechanisms, it is important to suppress the overactivated acquired immune system including T and B cells to treat RA lung. On the other hand, it is desirable not to suppress innate immunity excessively because it is an important arm for the protection against infection. In this regard, CTLA4-Ig, which specifically target T cells and do not suppress innate immunity, can be a good treatment option for RA with lung comorbidities. TNF inhibitors (TNFi), IL-6 receptor inhibitors (IL-6Ri), and JAK inhibitors (JAKi) can also be the options for immunosuppression. However, TNFi can sometimes cause paradoxical reaction that leads to exacerbation of ILD. Also, IL-6 inhibitors (IL-6Ri and JAKi) have a characteristic to delay the detection of infection because CRP can be masked. If the fibrosis progress even after immunosuppression, anti-fibrotic treatments can also be considered. In this seminar, the mechanism and treatment strategy for RA with lung comorbidities will be discussed.

## MS11-1

**Medical care support for rheumatoid arthritis patients to continue treatment with relief**

Makiko Matsuda
Meiyo Immunology & Rheumatology Clinic

Conflict of interest: Yes

How do patients think about their disease and confront treatment when they develop rheumatoid arthritis (RA)? At each point of onset of RA, the treatment, the remission, and thinking about the patient's own future, the patient's thoughts will differ according to their medical condition and environment at each time. Patients face their illnesses and continue treatment while living their lives. Treatment previously provided in hospitalization is increasingly being provided in the outpatient setting due to the increase in the number of patients with a chronic disease and the shortening of hospital durations, and thus the importance of "medical care support " is being called for. In providing medical care support, we will assess the patient's medical treatment life at home and provide direct care and guidance as needed. We believe that this will enable us to respond to changes in circumstances and ensure that treatment and recuperation at home can continue safely and smoothly. In order for patients to live a safe life under their care, it is necessary to understand their difficulties and needs related to their illness and life, and to provide support for disease management and medical treatment, support for continuing medical care, support for decision making, and utilization of social resources.

## MS11-2

**Importance of Inhibition of Joint Destruction in the Treatment of Rheumatoid Arthritis and Significance of TNF Inhibitory Therapy**

Asami Abe
Niigata Rheumatic Center

Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has changed significantly with advances in therapeutic drugs. By providing powerful treatment at an early stage of onset, it is possible to create a state in which there is almost no joint destruction, and the patients were possible to live as before the onset of the disease. However, there are still cases in which the timing of treatment is delayed and the treatment does not proceed well due to complications, resulting in bone destruction. Recently, it may be difficult to treat with difficult to treat RA (D2TRA). According to the Paper on Japan Rheumatology Friendship Association, what patients expect most from treatment is that the progression of joint destruction will be stopped and joint pain and swelling will disappear. It is important to control disease activity at an early stage of onset. If the anchor drug methotrexate is not controlled even with sufficient doses, treatment with anti-TNF preparations is often used, depending on age, kidney function, and complications. If the addition of csDMARDs does not suppress synovial growth, it is not possible to stop the progression of bone destruction. The addition of oral steroids only produces D2T, which is not a good idea. It is important to prevent D2TRA by suppressing disease activity, reducing joint swelling and tenderness, and preventing bone destruction. In addition, the treatment of patients requires the cooperation of medical staff with advanced knowledge and experience. With nurses as guides, doctors, pharmacists, physical therapists, occupational therapists, laboratory technicians, nutritionists, MSWs, etc. can combine their abilities to provide the best treatment for patients. I will explain the collaboration at our hospital.

## MS12-1

**ANCA-associated vasculitis treatment UP to date 2024**

Hiroaki Dobashi
Division of Hematology, Rheumatology and Respiratory Medicine, Department of Internal Medicine, Faculty of Medicine, kagawa University, Kagawa, Japan

Conflict of interest: Yes

Microscopic polyangiitis (MPA) and granulomatosis polyangiitis (GPA) are systemic necrotizing vasculitis mainly involving small vessels (small arteries, microvessels, capillaries, and small veins), and are associated with antineutrophil cytoplasmic antibodies (ANCA) in their pathogenesis and included in ANCA-associated vasculitis (AAV). Treatment consists mainly of corticosteroids (GCs) and immunosuppressive drugs, however relapse rate is a high. Furthermore, treatment-related adverse events, including infection, are problematic. In recent years, biologics and other novel agents have been introduced, which are expected to improve therapeutic efficacy and reduce adverse events. Avacopan, a complement C5a receptor inhibitor, is attracting attention as an alternative to GC, which has been the mainstay of treatment medicine. This seminar will provide an overview of the treatment of AAV, focusing on avacopan. The updated the European Alliance of Associations for Rheumatology (EULAR) recommendation 2022 for AAV therapy suggests that avacopan may be considered as remission induction therapy for MPA and GPA in combination with RTX and CY as a strategy to significantly reduce GC exposure. Furthermore, the “ANCA-associated vasculitis practice guideline 2023” developed in Japan also suggests the use of avacopan rather than high-dose GC when CY or RTX is used as remission induction therapy. The efficacy and safety of the drug as well as how to use in actual clinical practice will be verified in the future. This presentation will give an overview of the latest information on efficacy and safety.

## MS12-2

**Positioning of Abacopan based on experience in use**

Hajime Kono
Department of Internal Medicine, Teikyo University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

Avacopan, a C5a receptor inhibitor, is a small molecule with anti-inflammatory properties, indicated for the treatment of microscopic polyangiitis (MPA) and granulomatous polyangiitis (GPA). The ADVOCATE study, a double-blind, comparative trial of 331 patients with active MPA and GPA at induction of remission, provides representative evidence. Compared to the current standard of care, corticosteroids, the avacopan treatment arm demonstrated non-inferiority in the Birmingham Vasculitis Activity Score (BVAS) at 26 weeks and statistically significant superiority at 52 weeks. Although the use of corticosteroids in ANCA-associated vasculitis has been substantially reduced following the PEXIVAS and LoVAS trials, the ADVOCATE trial has further minimized corticosteroid use. In some instances, corticosteroid-free oral treatment of vasculitis is now achievable. The ADVOCATE trial did not include severe cases such as those with alveolar hemorrhage or patients with low disease activity. Consequently, there is limited evidence of the benefit of avacopan in these populations. We aim to share our experiences using avacopan in these severe cases and during the maintenance phase of remission, which clinical trials have not yet addressed. While avacopan is proposed as a treatment option for various types of vasculitis, additional studies are required to solidify the evidence base and further assess its long-term efficacy and safety.

## MS13

**Upadacitinib 2024: Thoughts on Long Term Safety/Efficacy in RA and Appropriate Use**

Roy Fleischmann
Metroplex Clinical Research Center, University of Texas Southwestern Medical Center at Dallas, USA

Conflict of interest: Yes

## MS14-1

**New paradigm in the treatment of RA: Evolution from monoclonal antibodies to JAK-inhibitors -The new era**

Gerd R Burmester
Department of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin, Berlin, Germany

Conflict of interest: Yes

This presentation will focus on a transformative shift in treating rheumatoid arthritis (RA), highlighting the evolution from monoclonal antibodies to the novel approach of Janus Kinase (JAK) inhibitors. This new era emphasizes the significant advancements in understanding and managing RA, proposing JAK inhibitors as a promising alternative with a distinct mechanism of action compared to conventional therapies. It underscores the role of JAK inhibitors in addressing unmet needs in RA treatment, offering insights into their efficacy, application, and potential to improve patient outcomes.

## MS14-2

**Psoriatic and Rheumatoid Arthritis: Distinctive and Overlapping Features**

Christopher Ritchlin
Allergy, Immunology and Rheumatology Division, University of Rochester Medical Center, Rochester, USA

Conflict of interest: Yes

For many years, psoriatic arthritis (PsA) was considered a sub-type of rheumatoid arthritis (RA). A seminal paper published in 1973 by Moll & Wright in 1973, however, outlined distinguishing characteristics of PsA including family history, clinical features, laboratory abnormalities and radiographic findings not observed in RA. RA is generally a symmetric polyarthritis, more common in post-menopausal women, associated with a positive rheumatoid factor and/or positive anti-cyclic citrullinated protein antibody. The disease is considered autoimmune given tight association with DR alleles and activated B and plasma cells that produce autoantibodies driven, in part, by interleukin (IL)-6. Current biologic treatments include anti-TNF agents, B-cell depleting agents, abatacept, anti-IL-6 agents along with conventional DMARDs (methotrexate) and Jak-STAT inhibitors. In contrast, PsA is often oligoarticular or asymmetric polyarticular at presentation and is observed in younger patients with psoriasis in a 1:1 male to female ratio. Both enthesitis and dactylitis are prevalent but not observed in RA. Unlike RA, it is not considered autoimmune in etiol-

ogy. The strongest genetic associations are with HLA B alleles. Moreover, definable biomarkers have not been identified. About 40% of patients demonstrate axial involvement that is not observed in RA and the bone phenotype may be erosive, as seen in RA, but also proliferative, with new bone formation in the spine and peripheral joints. The primary effectors in psoriasis and PsA are CD8+ TH17 cells, activated by IL-23 to produce iL-17, IL-22, GM-CSF and like RA, TNFa. Effective treatments include methotrexate and apremilast, TNF inhibitors, Jak-STAT inhibitors and agents that block IL-17 and IL-23. Both disorders are associated with flares and remissions and contrasting extra-articular manifestations. In RA, these include extensor nodules, Felty's Syndrome, vasculitis and scleritis compared to PsA where psoriasis, uveitis and inflammatory bowel disease are more commonly observed.

# Luncheon Seminar

## LS1

**Modern management strategies for RA: achieving clinical and structural remission with filgotinib**

Peter C Taylor
Norman Collisson Professor of Musculoskeletal Sciences, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, UK, University of Oxford, Oxford, UK

Conflict of interest: Yes

On behalf of Gilead Sciences K.K. and Eisai Co., Ltd, please join us for a dynamic, live presentation by Prof Peter Taylor. This presentation will focus on the importance of early intervention for rheumatoid arthritis (RA) to prevent joint damage and cover the latest clinical data for filgotinib, a once-daily oral Janus kinase inhibitor approved for the treatment of RA, in patients who have had an inadequate response to conventional therapies. Prof Taylor will review recent topics and emerging data in RA, EULAR recommendations that emphasize patient education and active patient involvement in the selection of treatment options, and the importance of early intervention in mitigating consequences of difficult-to-treat RA. He will also discuss pain as an RA symptom of particular importance to patients and a key target for treatment, as well as the role JAK inhibitors can play in managing pain in RA. Finally, he will speak about the importance of specific, stringent clinical trial remission end points for evaluating RA disease activity. Prof Taylor will summarize recent clinical evidence for the efficacy of 200 mg of filgotinib in combination with methotrexate (MTX) in reducing radiographic progression of joint damage and achieving clinical remission in the presence of poor prognostic factors. Data from clinical trials and ongoing long-term safety studies regarding the safety of filgotinib will also be presented. The presentation will also provide an understanding of patient groups who may be good candidates for receiving filgotinib therapy, particularly patients who have experienced an inadequate response to MTX.

## LS2-1

**Precision medicine of rheumatoid arthritis based on the understanding of T cell immunity**

Keishi Fujio
Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a destructive joint disease associated with autoimmunity. The most important disease susceptibility gene for RA is HLA-DRB1. Abatacept, which inhibits T-cell co-stimulation, is believed to act on the function of HLA-DRB1, suppressing excessive activation of CD4-positive T cells. Clinical evidence suggests that abatacept is as effective as anti-cytokine therapy, without increasing the risk of infections, indicating that T-cell co-stimulation inhibition is consistent with the pathophysiology of RA. Recent single-cell analyses of RA synovium have elucidated the composition of immune cells present. Synovial CD4+ T cells include central memory T cells, regulatory T cells, and TFH/TPH cells that support B cells. In synovial CD8+ T cells, there are two types of cytotoxic T cells and effector CD8-positive T cells. IFN-γ is a potent cytokine that enhances IL-6 and HLA-DR expression in synovial fibroblasts (SF), and effector CD8+ T cells are a major source of IFN-γ production. Traditionally, the synovium has been classified pathologically into lymphoid types with strong T and B cell infiltration, myeloid types with T cell and myeloid cell infiltration, and fibroid types dominated by fibroblasts. Recent single-cell analyses classify RA synovium into six types, three of which are rich in T cell infiltration. These analyses suggest that treatments targeting particularly abundant cell types in individual cases could be more effective. There are increasing reports of immune cells in peripheral blood and their responsiveness to abatacept treatment. We have found that treatment-resistant cases have a high number of preDC, a precursor to dendritic cells, while treatment-responsive cases have a high number of CD8+CD25+ T cells. Overseas reports suggest that cases with a high number of follicular helper T cells are more responsive to abatacept but less responsive to TNF inhibitors, and cases with a high number of Age-associated B cells and high serum CXCL13 concentrations are more likely to

respond to abatacept. Combining these findings, it can be concluded that abatacept is highly effective in RA with specific heightened adaptive immune pathways. Furthermore, as the assessment of immune status advances, the optimization of targeted molecular drugs, including abatacept, is expected.

## LS2-2

**Therapeutic strategies for rheumatoid arthritis utilizing Anti-Citrullinated Protein Antibodies (ACPA)**

Masato Okada
Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: Yes

The management of rheumatoid arthritis (RA) begins with a pernonalized treatment plan that includes factors like the time from onset to treatment, joint health, disease activity, comorbidities, and personal life goals such as pregnancy. Oral Disease-Modifying Anti-Rheumatic Drugs (DMARDs) are often chosen for monotherapy, with the selection and dosing crucial for both immediate remission and the effectiveness of future therapies like biological agents or JAK inhibitors. Early treatment strategies also incorporate NSAIDs and steroids to control acute inflammation alongside long-term DMARDs, biologicals, and JAK inhibitors. The American College of Rheumatology (ACR) and The European League Against Rheumatism (EULAR) suggest starting with DMARD monotherapy, followed by combination therapy if necessary. The goal is early remission, personalized to each patient's situation, and maintained with minimal medication. This approach weighs the patient's social and medical context, medication costs, and the need for additional therapies. Immunological considerations, such as T-cell activation and the response to ACPA immune complexes, are fundamental, with the Shared Epitope implicated in antigen presentation to T-cells. The Shared Epitope is recognized as a genetic factor in ACPA-positive rheumatoid arthritis, associated with the presentation of citrullinated peptides to T-cells. The pathological and clinical importance of abatacept, which acts on co-stimulatory molecules of T-cells, is garnering attention. Shared decision making underpins RA treatment, accounting for drug-specific risks, sustained effects, and the potential impact on other conditions like interstitial lung disease. Ongoing research informs the positioning of each drug, aiming to optimize patient-specific treatment outcomes in RA management.

## LS3

**The Role of Interleukin-6 in Rheumatoid Arthritis**

Gerd R Burmester
Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, Berlin, Germany

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic autoimmune disease causing articular and extra-articular damage due to tissue and organ infiltration by leukocytes resulting in a prolonged systemic inflammation driven also by additional proinflammatory cytokines. In this regard, interleukin-6 (IL-6), which is an important cytokine in the control of the acute-phase reaction as signified by CRP elevation has a key position. IL-6 is crucial for both the innate and adaptive immune systems. It is a pleotropic cytokine that is involved in hematopoietic, metabolic, and hormonal regulation. It can mediate its biological activities only by binding to its specific IL-6 receptor (IL-6R), and this cytokine-receptor complex associates with the gp130 IL-6R β-subunit leading to intracellular signalling (1,2). In recent years, the success of the IL-6R inhibitors tocilizumab (TCZ) and sarilumab (SAR) in the treatment of RA has further highlighted the important role of this cytokine. SAR, like TCZ, also binds to both the mIL-6R and sIL-6R. However, SAR differs from TCZ in structure and affinity. SAR as the first fully human mAb against IL-6Rα showed 10- to 40-fold greater affinity to recombinant monomeric human and monkey IL-6R compared with TCZ in a preclinical study (1). AS initially shown with TCZ, the conducted phase II and phase III trials demonstrated efficacy of SAR both in MTX-IR and tumor necrosis factor inadequate responder (TNF-IR)- active RA patients [1]. In addition, SAR monotherapy demonstrated superiority over adalimumab monotherapy in patients with intolerance or inadequate response to MTX. Moreover, although displaying a significantly higher affinity and longer half-life, SAR showed a similar safety profile compared with TCZ. In summary, recent advances in the treatment of RA have made significant breakthroughs, with IL-6 inhibition playing an important role alongside other biologics in both combination therapy with MTX and as monotherapy. The combination of acceptable safety data with high efficacy has led to long-term drug survival rates in treatment with IL-6R inhibitors clearly showing the important role of this class of biologic DMARDs in the treatment of rheumatic diseases.

## LS4-1

**Pathological Continuity and Clinical Challenges of Still's Disease from the Perspective of Pediatrician**

Nami Okamoto
Department of Pediatrics, Osaka Rosai Hospital

Conflict of interest: None

In 1896, Sir George Still of the United Kingdom reported "'On a form of chronic joint disease in children" and described that the pediatric rheumatic condition was different from that of adults. Of the several types, the one with fever, skin rash, and hepatosplenomegaly as the main symptoms has come to be called Still's disease. Dr. Bywaters, who has worked in the pediatric rheumatology unit, noticed that there are patients with the same type of disease in adults, and in 1971, he summarized it as Adult onset Still's disease (AOSD). Still's disease in children is now called systemic juvenile idiopathic arthritis (sJIA), but two diseases were originally one piece and are still regarded as such in Europe. However, it is somewhat complicated to handle in clinical practice due to different classification criteria, different indications of drugs, and different medical subsidy systems. Although epidemiological data and pathological findings suggest subtle differences between sJIA and AOSD, much remains unclear. The prevalence of sJIA is higher than that of AOSD, and is one of the rare areas of pediatric disease research that is more advanced, but both are based on innate immune activation. Starting from the release of endogenous innate immune activators such as pathogen-associated molecular pattern and damage-associated molecular pattern, TLR activation → inflammasome production → caspase activation → IL -1 and IL -18 production on the phagocyte occurs in the individual prone to innate immune activation/resistant to inflammatory inhibitory system. Inactivation by IL -18 binding protein, production of IL -10, activation of regulatory macrophages, and dysfunction of NK cells are insufficient, and repeated positive feedback of inflammation results in a cytokine storm, resulting in the production of large amounts of various inflammatory cytokines such as IL -6, TNF, and IFN-γ. This results in a very severe secondary hemophagocytic lymphohistiocytosis called macrophage activation syndrome (MAS) in about 10 ~ 15% of patients. In recent years, it has also been shown that, if innate immune activation continues for a long period of time, the activation of innate adaptive immunity such as NKT cells and γδ T cells can lead to the production of IL -17 and the transition to chronic arthritis. Clinical issues in sJIA include (1) biomarkers for early diagnosis, (2) effects of early treatment on natural history, (3) changes in treatment algorithms, (4) early diagnosis and treatment of MAS, and (5) prediction and prevention of recurrence and MAS transition.

## LS4-2

**Pathological spectrum and clinical implications of Still's disease from the department of adult medicine**

Tomohiro Koga
Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Conflict of interest: Yes

Adult-onset Still's disease (AOSD) and systemic-onset juvenile idiopathic arthritis (sJIA) share many clinical features, including hepatosplenomegaly, lymphadenopathy, elevated white blood cell count, elevated CRP, hyperferritinemia, and macrophage activation syndrome (MAS), in addition to spike-like fever, arthritis, and skin rash. These diseases are classified as autoinflammatory diseases and show excessive production of inflammatory cytokines (IL-1, IL-6, IL-18), with neutrophils and macrophages, the cells responsible for innate immunity, playing a central role.

Thus, continuity has been suggested in the pathogenesis of both diseases, particularly the overexpression of IL-1 and IL-6 and similar responses to their suppression, highlighting the possibility that they are complex, multifactorial autoinflammatory syndromes. However, because Still's disease is rare and AOSD is primarily treated in adult medicine and sJIA in pediatrics, the pathogenesis of these diseases and their continuum is still poorly understood. In addition, since the diagnostic and classification criteria for both diseases are different, and different insurance-approved drugs are used for treatment, there are a wide range of clinical issues common to both departments, such as transitional care, the significance of autoinflammatory disease genetic testing for difficult-to-diagnose cases, and the selection of appropriate therapeutic agents for difficult-to-treat cases. Therefore, this lecture will focus on AOSD from the viewpoint of a rheumatologist, providing a detailed clinical overview (epidemiology/clinical picture/diagnosis/treatment) and pathomechanisms of AOSD. It will also focus on current clinical issues, with a particular emphasis on the commonalities and differences between AOSD and sJIA, with the aim of promoting a deeper understanding of these issues.

## LS5

**Usefulness of Apremilast in the patient with early psoriatic arthritis**

Mitsumasa Kishimoto
Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

Psoriatic arthritis (PsA) is associated with decreased quality of life. As delayed diagnosis may lead to progressive joint destruction and long-term disability, the key clinical features of PsA should be recognizable to a wide range of clinicians to facilitate early diagnosis. In addition to assessment and identification of skin and nail lesions, clinicians should be aware of both the joint manifestations and co-morbidity/related conditions (multi-domains) reviewed here. T2T treatment strategy should be decided after a thorough discussion between the physician and the patient, taking into account the progress of therapeutic agents, the disease activity of the individual patient, and the patient's background. The GRAPPA treatment recommendations and the EULAR treatment recommendations have recently been updated, and both recommendations promote the use of oral synthetic DMARDs, including methotrexate, before the initiation of biologic agents. However, many patients are obese or have abnormal liver function, which may contraindicate the use of methotrexate. Furthermore, relatively few patients in clinical practice have polyarthritis with swelling and tender joints exceeding 10-20 joints, as seen in clinical trials (RCTs) of biologic agents, and probably more than half of patients have oligoarthritis. There was an urgent need to build evidence showing the efficacy of drugs for patients with oligoarthritic PsA. The FOREMOST study evaluating the efficacy and safety of apremilast in patients with PsA with oligoarthritis was presented at the ACR meeting in November 2023. This was a randomized, double-blind, placebo-controlled study of apremilast in the patients with PsA (n=308, mean duration of disease 9.9 months, SJC 2.6, TJC 3.2), evaluating the efficacy and safety of apremilast in 203 patients in the apremilast group and 105 in the placebo group. The primary endpoint, MDA at 16 weeks, was significantly higher in the apremilast group, as was the secondary endpoint, cDAPSA REM/LDA at 16 weeks. Based on these results, we would like to discuss with you how to use apremilast in daily practice.

## LS6

**Overview of drug treatment for rheumatoid arthritis - Focusing on the positioning of biosimilars -**

Shintaro Hirata
Department of Clinical Immunology and Rheumatology, Hiroshima University Hospital, Hiroshima, Japan

Conflict of interest: Yes

Molecular targeted therapy for rheumatoid arthritis (RA) has been one of the most advanced areas of medicine in the past two decades. Currently, twelve biological disease modifying anti-rheumatic drugs (bDMARDs) (including 3 biosimilars) and five targeted synthetic DMARDs (tsDMARDs) have been approved for RA in Japan. While the abundant options are available, it often requires to take confusingly numerous factors into account for choosing a single drug fitting with the individual patient's characteristics and their preference. Of course, Shared Decision Making (SDM) between patients and physicians is important in medical practice, however it is difficult to provide full picture of whole options in detail to patients due to constraints including limited time and patients' various cognitive level. Therefore, the pragmatic practice for physicians may be to provide several recommended options with reviewing various factors (formulation properties, efficacy, safety, convenience, economics, patient's preference, etc.). In this lecture, I would like to take a bird's-eye view of the current state of treatment for RA in Japan, where medical costs are tight, and discuss the usefulness and challenges of biosimilar DMARDs (bsDMARDs), which have economic advantages.

## LS7-1

**Pitfall of osteoporosis diagnosis**

Taku Saito[1,2]
[1]Orthopedics, The University of Tokyo Graduate School of Medicine, [2]Osteoporosis Center, The University of Tokyo Hospital

Conflict of interest: None

In recent years, there have been advancements in osteoporosis treatments that show a substantial increase in bone mass. We have entered an era where even severe cases of osteoporosis can be managed. However, among patients exhibiting severe reduction in bone mass and fragility, there are conditions other than primary osteoporosis, such as osteomalacia and endocrine disorders, which require careful diagnosis. This presentation will introduce key points for assessing osteoporosis and for distinguishing conditions that should be differentiated, such as osteomalacia and endocrine disorders.

## LS7-2

**Don't miss a tip of chance to diagnose adult hypophosphatasia with non-specific symptoms**

Takamasa Ichijo
The Department of Diabetes and Endocrinology, Imperial Founded Saiseikai Yokohamashi Tobu Hospital

Conflict of interest: None

Hypophosphatasia (HPP) is an inherited systemic disorder with autosomal recessive inherited type in most cases which affects mineralization in bone, caused by loss-of-function mutations of alkaline phosphatase (*ALPL*) gene. This gene encodes tissue non-specific alkaline phosphatase (TNSALP), and reduction of this enzyme activity impairs systemic bone mineralization. HPP is classified in 6 major forms, perinatal lethal, prenatal benign, infantile, childhood, adult and dental localized type, odonto-hypophosphatasia. In generally, early onset type shows more severity. TNSALP is abundant in whole body and patients often complain some non-specific symptoms, such as muscle pain, muscle weakness, bone pain, joint stiffness, etc., and this often makes us hard to diagnose. Some cases were reported HPP were misdiagnosed as osteoporosis and inappropriate therapy resulted in recurrence of non-traumatic bone fractures. In this session, based on our experience of an adult HPP patient with non-specific complications, we introduce our case diagnosed as adult HPP triggered by low serum ALP, subsequently underwent genetic testing for *ALPL* mutation. We review adult HPP and hope this session helps you to make adequate diagnosis and pick adult HPP up among non-specific symptoms complaint patients. A 40-year-old female visited our hospital because of malaise. She had no history of early loss of primary teeth nor family history of skeletal dysplasia. Laboratory examination showed low serum alkaline phosphatase levels of 18 U/L. In addition, hypozincemia was also observed, but alkaline phosphatase level did not increase after zinc replacement. Mediators, including calcium and phosphorus metabolism, were within normal range. X-ray examination showed no evidence of osteomalacia, but mineral bone density was slightly decreased compared with the young adult mean. Urine phosphoethanolamine level was increased, and we then suspected hypophosphatasia. Genetic tests detected *ALPL* gene heterozygous missense mutation (c. 529G>A p. Ala177Thr and c. 670A>G p. Lys224Glu) and adult-onset hypophosphatasia was finally diagnosed. It is important to evaluate alkaline phosphatase levels in

the screening of patients with non-specific symptoms.

## LS8-1

**Pitfalls in Managing Renal Impairment with JAK Inhibitors: Perspectives from Rheumatology and Nephrology Specialists on Addressing Chronic Kidney Disease Patients**

Yuji Nozaki
Department of Hematology and Rheumatology, Kindai University Faculty of Medicine

Conflict of interest: Yes

The efficacy of JAK inhibitors in treating rheumatoid arthritis (RA) is on the rise, particularly in challenging cases like Difficult-to-treat RA, MTX-resistant cases, and those managed with JAK monotherapy. Consequently, their use is increasingly prevalent in routine clinical practice. However, as JAK inhibitors are low-molecular-weight compounds metabolized through renal and hepatic excretion, careful consideration of potential organ complications is essential. The aging of RA patients and the emergence of late-onset RA have brought about issues related to declining renal, hepatic, and respiratory functions, alongside a heightened prevalence of comorbidities. Notably, chronic kidney disease demonstrates a higher incidence in RA cases compared to non-RA cases, underscoring the importance of regular renal function assessments. In evaluating renal function, it is crucial to measure both the estimated glomerular filtration rate (eGFRcrea) and eGFRcys using cystatin C, as eGFRcrea may overestimate in cases with reduced muscle mass. Additionally, to assess hepatic function impairment, the FIB4 index, based on factors such as age, AST, ALT, and platelet count, aids in evaluating the risk of liver fibrosis progression. Moreover, in elderly patients at high risk of malignancy and thrombosis, a thorough Risk and Benefit analysis is imperative before JAK inhibitor use, alongside obtaining patient consent. This presentation will explore the response to and precautions for organ complications, especially renal impairments, in JAK inhibitor therapy, from the perspectives of rheumatology and nephrology specialists.

## LS8-2

**The role of JAK inhibitor for personalized care for elderly patients with rheumatoid arthritis**

Sae Ochi
Department of Laboratory Medicine, The Jikei University School of Medicine

Conflict of interest: Yes

With the advancement in the treatment of rheumatoid arthritis (RA), its treatment target has changed from survival or pain control to clinical remission, functional remission, and even more, better life. In addition, extended life expectancy of RA patients, in combination with the increase in elderly-onset RA patients, have caused significant increase in the number of elderly RA patients. Now it becomes essential for rheumatologists to eye personalized care especially for elderly patients. As elderly RA patients in general have risks of physical, mental, and social frailties, reducing total lifetime cost including costs for disuse syndrome and fracture is important. Therefore, treatment should be deliberately designed depending on the demographic, social, and economic background of the patients and their caregivers. The framework of such care is called '5M' -Medication, Mobility, Multi-complexity, Mind, Matters-most. JAK inhibitor is a targeted-synthetic disease modifying anti-rheumatic drugs. As it is oral medication, it has some advantages such as simple medication protocol and short half-life, fast-acting property, effectiveness on patients with residual pain and possible effectiveness on difficult-to-treat RA. On the other hand, JAK inhibitor has several disadvantages such as increased risk in herpes-zoster infection. In addition, too quick improvement in physical activity may increase among elderly patients may increase fracture risk. There also exist several pros and cons in a longer-term prescription. This presentation will discuss broadness of personalized care for elderly RA patients - from tailor-made treatment to advanced care planning.

## LS9-1

**Development of software as a medical device (SaMD) for psychiatric diseases using digital phenotyping**

Taishiro Kishimoto
Hills Joint Research Laboratory for Future Preventive Medicine and Wellness, School of Medicine, Keio University

Conflict of interest: Yes

Rheumatic diseases including rheumatoid arthritis and Sjögren's syndrome have been reported to have a higher incidence of psychiatric disorders such as depression compared to healthy individuals. The absence of biomarkers and difficulty in quantifying symptoms in psychiatric disorders have led to problems such as diagnostic discrepancies, difficulties in treatment evaluation, and difficulties in new drug development. We have been working on the development of several software medical devices (SaMDs) in the hope of solving such problems by utilizing various devices and artificial intelligence technology. During the course of depression, symptoms such as decreased activity and sleep disturbances appear. In addition to these, by utilizing data on autonomic nervous system activity reflected in heart rate variability it may be possible to screen for depression and assess its severity. We are developing a software medical device with the aforementioned functions using a wristband-type wearable device. Amnesic aphasia is one of the typical symptoms observed in Alzheimer's disease. But it is possible that changes in the use of parts of speech and changes in the structure of sentences occur even before these aphasic symptoms are manifested. We have developed software to screen for dementia using natural language processing. With the progress of medical digital transformation, there is a need to develop technologies originating in Japan. The prospects and challenges for the development of programmed medical devices in Japan will be discussed.

## LS9-2

**Can we estimate the disease activity of RA with watch-type wearable devices, weather sensors, etc.? -Practical approaches to digital biomarker development (AMED Rheumatology IoT research)**

Keisuke Izumi[1,2,3]
[1]TechDoctor, Inc., [2]Division of Rheumatology, Department of Internal Medicine, School of Medicine, Keio University, [3]Division of Rheumatology, NHO Tokyo Medical Center

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a disease that causes persistent symptoms such as generalized joint swelling, pain, and general fatigue, as well as irreversible joint destruction and impairment of physical functions. While joint exercise and muscle strength maintenance are necessary to maintain physical condition, physical exertion is an aggravating factor for arthritis, making it difficult to determine the appropriate amount of physical exertion. In addition, joint symptoms are known to be related to weather conditions such as changes in air pressure and temperature, depression, anxiety, and sleep disorders. Therefore, we investigated whether wristwatch wearable devices and environmental sensors are associated with RA symptoms and disease status. We used data such as daily physical activity, sleep status, and heart rate variability obtained by a wristwatch wearable device; data such as temperature, atmospheric pressure, illuminance, UV index, and noise from environmental sensors; weather information near home obtained from a public API; and PRO records developed by the research team. The data is anonymized and stored in the cloud platform SelfBase®, including patients' own symptom records obtained through the "Today's Kansetsu" smartphone application, consultations at medical institutions, and EDC information such as blood sampling data. Focusing also on systems that handle the large amount of medical-related information that is updated daily, the issues and solutions in conducting research and development will be discussed, introducing examples of practical efforts to develop digital biomarkers using wearable devices and IoT devices.

## LS10

**Current issues in the management of rheumatoid arthritis and their solutions**

Yutaka Kawahito

Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a disease decreasing a reduction in disease activity and an improvement in long-term prognosis and life expectancy due to treatment strategies based on the T2T (treat to target) concept and advances in the development of biologic agents and molecular targeted drugs such as Janus kinase (JAK) inhibitors. The development of newer molecular-targeted agents has made it possible to not only reduce disease activity, but also improve long-term and life outcomes. What is important in the current treatment of RA is the methodology of drug selection and intensification of therapy, taking into consideration the patient's background. The major challenges for the future treatment of RA are the treatment of elderly RA patients, refractory conditions such as "difficult-to-treat RA (D2TRA)," and health economic aspects. Elderly patients have multiple diseases, long-term use of medications and multiple medications due to chronic diseases, decreased organ reserve, and regular drug dosing leads to overdose, decreased adherence due to cognitive ability and hearing loss (decreased comprehension), and misuse of medications. In addition, RA carries a high risk of developing malignant lymphoma, and the use of MTX, an immunosuppressive agent, increases the risk, especially in the elderly. Biologics and JAK inhibitors tend to increase the risk of infections, cardiovascular events, and malignancies. The factors that contribute to D2TRA include not only the biological aspects of the disease, but also psychological and socioeconomic aspects, in addition to comorbidities such as fibromyalgia-like pain and other medical conditions. The treatment and total care of elderly RA patients and D2TRA patients is still insufficient, and the medical costs associated with these patients are significant. In this lecture, these issues and their countermeasures will be outlined in light of the latest guidelines.

## LS11

**Update on the management of ILD in rheumatic diseases**

Anna Maria Hoffmann-Vold
Department of Rheumatology, Oslo University Hospital, Oslo, Norway

Conflict of interest: Yes

The prevalence of both the underlying rheumatic diseases (RMDs) and interstitial lung diseases (ILD) in RMDs vary widely which make unified management approaches challenging. Importantly, the impact on morbidity and mortality of ILD on patients with RMD is devastating, with ILD being the major cause of death in these patients. Optimized management, including screening, early detection, treatment and monitoring is therefore of utmost importance. Management recommendations have been very recently proposed, which include recommendations for screening, monitoring and treatment approaches for ILD across different RMDs. In this lecture, the used methodology will be discussed. We will then review the official American Thoracic Society clinical practice guideline the treatment of systemic sclerosis-associated ILD (SSc-ILD) and the American College of Rheumatology 2023 ILD guideline on screening, monitoring and treatment of ILD in RMDs. We will discuss the underlying evidence and lastly, how these guidelines can be applied in clinical practice.

## LS12-1

**The future of RA treatment - no more guesswork?**

Iain B McInnes
University of Glasgow, UK

Conflict of interest: Yes

The last two decades have witnessed remarkable progress in the management of rheumatoid arthritis (RA). This has been driven in part by the advent of several new modes of action of therapeutics which have delivered improvements in clinical disease activity, reduction in articular damage and preservation of long term function. These include biologic agents targeting cytokines, immune cells, and recently small molecular inhibitors targeting JAK dependent cytokine signalling. In parallel key strategic advances included the introduction of early intervention and adoption of treat to target paradigms embodied in several international recommendations, e.g. EULAR. However unmet clinical needs remain including low levels of sustained remission and continuing concerns about adverse events. Individualised decision making for patients is elusive. This lecture will describe new approaches to unravel pathogenesis, and thereby deconstruct disease at the molecular level. The use of artificial intelligence will further play a role in optimising clinical decision making. In future, this will together facilitate novel approaches to clinical decision making based on active cellular and molecular pathways, that complement clinical disease activity measure and their surrogates. Such studies will eventually enable precision medicine in the management of RA.

## LS12-2

**Optimization Strategy for Rheumatoid Arthritis Treatment Based on the Latest Recommendations and Evidence**

Kosuke Ebina
Department of Orthopaedic, Osaka University Graduate School of Medicine

Conflict of interest: Yes

In the EULAR Recommendation 2022, for phase II treatment, it is recommended to add biological agents or JAK inhibitors to csDMARDs in cases with poor prognostic factors (RF/ACPA positivity, high disease activity, existing joint damage, failure of two or more csDMARDs). It is emphasized that, when using JAK inhibitors, a thorough risk assessment for cardiovascular events and malignancies should precede administration. Conversely, despite reported advantages of JAK inhibitors over biological agents in improving disease activity, patient-reported outcomes, and inhibiting joint damage, careful consideration of risk-benefit balance is warranted. Therefore, updating information on RA treatment, sharing appropriate information with patients, and engaging in Shared Decision Making are crucial. This presentation provides insights into understanding the EULAR Recommendation 2022 and discusses the optimization of RA treatment, drawing on data from the Kansai multi-center ANSWER cohort regarding the current status of JAK inhibitor therapy in Japan.

## LS12-3

**Management of adverse events associated with JAK inhibitors**

Satoshi Kubo
Department of Molecular Targeted Therapies, School of Medicine, University of Occupational and Environment Health

Conflict of interest: Yes

Rheumatoid arthritis is a systemic autoimmune disease characterized by polyarthritis, irreversible joint destruction, and organ involvement including the lungs. In Japan, an estimated one million people grapple with this condition, posing a significant societal impact. Currently, four classes of molecular targeted therapies-JAK inhibitors, CTLA4-Ig, anti-IL-6 receptor antibodies, and TNF inhibitors-are available for rheumatoid arthritis treatment in Japan, achieving remission induction in approximately half of the patients. However, non-responsive cases necessitate frequent medication changes, and some individuals experience persistent high disease activity despite these therapies. Optimizing the balance between effectiveness and adverse effects is crucial for minimizing the societal and economic impact of the disease. Notably, JAK inhibitors have demonstrated superior efficacy in various clinical trials, but concerns about malignancies, major adverse cardiovascular events (MACE), and shingles have been raised. This presentation will delve into strategies for managing adverse events associated with JAK inhibitors.

## LS13

**Targeting the BAFF in the treatment of systemic lupus erythematosus**

Shingo Nakayamada
First Department of Internal Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is an autoimmune disease caused by the breakdown of immune tolerance that originates from genetic predis-

position and environmental factors. For more than a half-century, the mainstay of SLE treatment was glucocorticoids (GCs) and immunosuppressants. However, treatment with these drugs is not specific to the pathology of SLE. The development of drugs aiming to control specific abnormal immune network is anticipated for the treatment of SLE. The EULAR recommendations for the management of SLE updated in 2023 stated that GCs should be used for short-term to control active disease; taper to ≦ 5 mg/day as quickly as possible and discontinue, if possible. B cells play a pivotal role in autoimmunity not only by producing pathogenic autoantibodies but also by modulating immune responses via the production of cytokines and chemokines. The B cell-activating factor (BAFF) promotes not only B cell survival and differentiation but IFN-γ production by Tfh cells and thus plays a prominent role in the pathogenesis of autoimmune diseases. Belimumab (BEL) is a fully human monoclonal antibody against BAFF, which was the first biologic approved for SLE treatment. BEL is reported to be effective in reducing GC, preventing relapse of disease activity and preventing the progression of organ damage in patients with SLE. Recently, its efficacy in lupus nephritis has been reported. Our clinical data showed that the use of belimumab during the maintenance phase reduced GCs and GC discontinuation was achieved in almost 40% of patients. The safety profile of the drug in real-world clinical practice is also being confirmed, but attention should be paid to the adverse events of depression and suicide. In this seminar, we would like to highlight recent advances the pertain to basic and clinical significance of the BAFF targeting in the treatment of SLE based on the results of our clinical registry and immunophenotyping analysis.

## LS14

**Clinical significance of IL-23 in the treatment of Psoriatic arthritis**

Paul Bird
St George Clinical School, University of New Souht Wales, Australia

Conflict of interest: Yes

Psoriatic arthritis (PsA) affects up to 25% of patients with psoriasis. Incidence varies among different populations - 22.7% in European psoriasis patients, 21.5% in South American patients, 19.5% in North American patients, 15.5% in African patients, and 14.0% in Asian patients with psoriasis. In Japan, a recent study showed a 10.5% occurrence of PsA in patients with psoriasis. A heterogeneous disease with varied presentations, early diagnosis can be a challenge. Regrettably, delayed diagnosis of PsA has been associated with poor physical function and quality of life, with increasing evidence supporting the premise that early treatment using a treat to target approach results in more favourable outcomes. The principal cytokine in the pathogenesis of PsA is IL23. IL-23 is a heterodimer composed of two subunits p19 and p40 subunits, which bind to IL23R. The binding of IL-23 to IL23R leads to the recruitment of JAK2 and TYK2 kinases, to promote the differentiation, survival, and expansion of Th-17 cells. Downstream, recruitment of TNF@ and IL-17 augment this inflammatory response with manifestations in skin, joints and in extra-articular tissues. This lecture will explore the importance of early diagnosis in managing patients with psoriatic arthritis, the central role of IL-23 in the pathogenesis of the clinical manifestations, the role of imaging in diagnosis and monitoring, and the importance of the treat to target approach in achieving the optimal outcome.

## LS15-1

**Rheumatoid Arthritis Treatment from the Perspective of Clinical Practice Guidelines ~Positioning of tocilizumab and its evidence~**

Yutaka Kawahito
Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: Yes

The 2024 edition, an update of the Rheumatoid Arthritis Clinical Practice Guidelines 2020, has been published. These guidelines incorporate the T2T (treat to target) concept and the introduction of new anti-rheumatic drugs, which have significantly improved the prognosis of RA. The current practice of RA aims for higher goals beyond clinical remission. Achieving clinical remission within the first six months of treatment is the first hurdle, but many challenges remain. One of these is the aging of RA patients, reflecting improved prognosis and older age of onset. In Phase I of the RA drug treatment algorithm, the use of MTX is first considered, and if not possible, other csDMARDs are used. In addition to contraindications, age, renal function, pulmonary complications, etc., are considered for MTX use. This is a major issue in the treatment of RA in Japan, where there are many elderly patients. Even in Phase II and III, the drug of choice depends on whether MTX can be used. In the elderly, the dose of MTX should be reduced if renal function is impaired, and attention should also be paid to malignant lymphoma in terms of age. Biologics are safer in that liver and kidney function are not metabolized, but the probability of infection is higher; with JAK inhibitors, further complications of malignancy and cardiovascular events are also in the spotlight. Considering each individual patient's comorbidities, complications from treatment, and compliance, it is important for physicians to fully understand the characteristics of each drug and how to select the safest drug from a variety of therapeutic agents and how to treat patients. In this presentation, I would like to outline the usefulness of tocilizumab in the treatment of rheumatoid arthritis and points to be considered in its use, based on clinical guidelines, with the positioning of tocilizumab in the treatment algorithm in mind.

## LS15-2

**Challenges in RA Practice: Difficult-to-treat (D2T) RA and Health Economic Issues**

Eiichi Tanaka
Division of Rheumatology, Department of Internal Medicine, Tokyo Women's Medical University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

The sufficient use of methotrexate and the introduction of biological DMARDs (bDMARDs) and/or tsDMARDs (JAK inhibitors) have resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). In the IORRA cohort, the proportion of the patients who achieved DAS28 remission increased from 8.4% in 2000 to 64.3% in 2022, and approximately 80% of the patients with RA were well-controlled. However, despite these advances in RA treatment, some patients still experience moderate or high disease activity. Therefore, appropriate treatment should be considered an unmet need of these patients including difficult-to-treat (D2T) RA. At this seminar, I would like to explain various issues that may contribute to D2T RA, including (1) treatment for RA when methotrexate cannot be prescribed, (2) treatment for multidrug-resistant RA, especially for inadequate response to bDMARDs, and treatment for RA with various types of complications using data from clinical trials and registries such as the IORRA cohort. In addition, rising RA care costs have caused concern, placing a heavy burden on society as well as patients with RA. Health economic issues in patients with RA will be discussed.

## LS16

**Modernizing the clinical approach to RA management by preventing structural joint damage: the JAK inhibitor filgotinib**

Peter C Taylor
Norman Collisson Professor of Musculoskeletal Sciences, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

Conflict of interest: Yes

On behalf of Gilead Sciences K.K. and Eisai Co., Ltd, please join us for an interactive, discussion-based session chaired by Prof Tatsuya Atsumi. This session will include a short presentation by Prof Peter Taylor followed by a panel discussion with Japanese experts Prof Ikeda and Drs Asai and Koga. Key topics in the session will include the evolution of rheumatoid arthritis (RA) therapy, the importance of early intervention for RA to prevent structural damage, and how a treat-to-target strategy and shared decision-making can help achieve optimal patient outcomes. Prof Atsumi will also discuss the importance of specific, stringent clinical trial remission endpoints for evaluating RA disease activity. The session will highlight the utility of filgotinib, a once-daily oral Janus kinase (JAK) inhibitor approved for the treatment of RA, and will include a review of the latest clinical data for filgotinib in patients who have had an inadequate response to conventional therapies. The program will begin with a short presentation by Prof Taylor that will summarize recent clinical evidence

for the efficacy of 200 mg of filgotinib in combination with methotrexate (MTX) in reducing radiographic progression of joint damage and achieving clinical remission in the presence of poor prognostic factors. Data from clinical trials and ongoing long-term safety studies regarding the safety of filgotinib will also be presented. He will also discuss pain as an RA symptom of particular importance to patients and a key target for treatment, as well as the role JAK inhibitors can play in managing pain in RA. The presentation will also provide an understanding of patient groups who may be good candidates for receiving filgotinib therapy, particularly patients who have experienced an inadequate response to MTX. Following the presentation there will be an interactive panel discussion featuring Japanese experts discussing the key topics identified above and sharing their clinical perspectives on the use, efficacy, and safety of filgotinib, as well as its position in the RA treatment landscape.

## LS17-1

**Optimal Drug Selection in the Phase II - The Potential of Sarilumab as a First Biologics-**

Ryu Watanabe
Department of Clinical Immunology, Osaka Metropolitan University Graduate School of Medicine

Conflict of interest: Yes

Remission has become a feasible treatment goal for rheumatoid arthritis (RA) with the advent of biologics and JAK inhibitors. The EULAR recommendations 2019 update stated that biologics or JAK inhibitors should be added in cases with inadequate response to MTX (Phase II). However, as older age and smoking were found to be risk factors for adverse events associated with JAK inhibitors, the EULAR recommendations 2022 update changed the statement that appropriate risk assessment should be performed when JAK inhibitors are administered in the Phase II. Thus, drug selection tailored to the patient's clinical profile, risk assessment prior to initiation of therapy, and an in-depth understanding of drug characteristics are crucial in optimizing RA treatment. IL-6 inhibitors inhibit osteoclast differentiation via suppression of RANKL expression by synovial fibroblasts. In addition, recent studies have shown that IL-6 inhibitors may not only suppress joint destruction but also improve the pathophysiology of RA through quantitative and qualitative improvement of regulatory T cells and suppression of follicular helper T cell function. Sarilumab is the second IL-6 inhibitor launched in Japan. Evidence for efficacy and safety has been accumulating both in Japan and overseas, and it has been shown to suppress joint destruction for a long period of time. Its efficacy has been reported not only in Phase II patients (inadequate response to MTX) but also in Phase III patients and patients with difficult-to-treat RA. In this seminar, I will introduce the latest information on sarilumab, including our experience and the data from the ANSWER cohort. The potential of sarilumab as a first biologics in the Phase II will be discussed.

## LS17-2

**Prediction of Efficacy in IL6R inhibitor**

Hirofumi Shoda
Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: None

The effectiveness of IL6R inhibitors in the treatment of rheumatoid arthritis is well-established through clinical trials and post-marketing observational studies. However, there remains some patients with unresponsiveness to IL-6 inhibition, presenting an unmet need in this field. To address this issue, achieving more precise rheumatoid arthritis treatment is imperative, and efforts to predict effectiveness are actively under investigation. In addition to utilizing clinical parameters, exploratory research on new biomarkers is actively pursued to predict the effectiveness of biological drugs for rheumatoid arthritis. Regarding Sarilumab, a post-hoc analysis of clinical trial data has suggested that factors such as higher serum IL-6 concentration may contribute to efficacy prediction. Additionally, high CRP levels and ACPA positivity have been employed as factors in machine learning prediction models. Moreover, by directly assessing the inflammatory state of local joints through synovial biopsies, valuable information regarding cell groups and pathways associated with the effectiveness and treatment resistance of biological drugs has been discovered. These findings will be applied to the clinical practice in near future. In this presentation, I aim to provide an overview of the current state of efficacy prediction for IL6R inhibitors, with a specific focus on Sarilumab.

## LS18-1

**Treatment Strategies for Elderly RA Patients to Extend Healthy Life Expectancy**

Masahiro Tada
Orthopaedic Surgery, Osaka City General Hospital

Conflict of interest: None

The aging is coming without exception to rheumatoid arthritis (RA) patients, and elderly RA patients is expected to increase further in the future. Increased comorbidity leads to polypharmacy, and declining renal function causes increased adverse events. Attention should also be paid to mistaken medicine due to cognitive decline. On the other hand, early diagnosis, early treatment, T2T, and bs/ts-DMARDS have made quality of life (QOL) comparable to that of healthy individuals. Considering both phenomenon, rheumatologists need to balance effective and safe treatment of elderly RA patients in the extended term. According to the National Survey, falls and fractures account for 12% of the causes of nursing care needs. While there have been approaches to prevent these from bone research, including bone density, metabolic markers, and quality, falls and fractures prevention from muscle-focused research has been less than adequate. Sarcopenia is a risk factor for falls and fractures. Our prospective study (CHIKARA study) found that the prevalence of sarcopenia in RA patients was 28%, higher than the prevalence in the healthy individuals (10%). Disease activity control and glucocorticoid reduction/stop are minimal sarcopenia prevention. However, there are no drugs that increase muscle mass, and recovery from sarcopenia is not easy. Early diagnosis and intervention are important to prevent sarcopenia. Treatment must be initiated before joint destruction and exercise and nutritional interventions must be actively incorporated. The importance of these is also emphasized in the EULAR 2021 recommendations on lifestyle and work participation. Guidance by the rheumatologist regarding the patient's lifestyle is essential to maximize the QOL. In this presentation, we will discuss optimal treatment methods to maximize QOL, avoiding nursing care and cognitive decline. We will also share what rheumatologists should be guiding patient lifestyle in order to promote healthy life expectancy.

## LS18-2

**Treatment of rheumatoid arthritis using anti-TNF inhibitor -Feature of etanercept-**

Nobunori Takahashi
Department of Orthopedic Surgery, Aichi Medical University

Conflict of interest: Yes

Drug therapy for rheumatoid arthritis (RA) has changed dramatically with methotrexate (MTX) in 1999 and molecular targeted therapies since 2003. Both are true game changers in the RA treatment, and we can say that they are completely different from the RA treatments available until the 1990s. Whereas in the past, each individual physician had their own treatment strategy based on so-called expert opinion, now a standard treatment strategy has been established based on the evidence, and basically the same initial treatment is given to anyone receiving medical care anywhere. The first-line drug is MTX, with the use of molecularly targeted therapies if efficacy is inadequate, but no class is specified in the guidelines. However, recently, TNF inhibitors have been avoided in some cases due to concerns about the long-term safety of MTX and the fact that non-TNF agents or JAK inhibitors are often used in the absence of MTX. However, the current treatment strategy is based on initial therapy centered on MTX, and considering that MTX suppresses IL-6, the therapeutic strategy of directly inhibiting TNF as the next step when a sufficient dose of MTX is used and response is inadequate is considered reasonable. Once therapeutic goals are achieved and stabilized with MTX and molecularly targeted agents, drug dose reductions are common; whether to reduce MTX or molecularly targeted agents depends on the economic and safety situation, and etanercept (ETN) is a drug for which evidence is building in both di-

rections. The administration of the drug to elderly patients has also been studied through an all-patient survey, and data on its use in young women have been accumulated based on data on placental passage and other factors. Thus, the greatest feature of ETN is that it has multiple evidence for young to elderly patients within the MTX-centered standard of care as a TNF inhibitor. Also important is the emergence of clickwise as an electronic device for self-injection. The large contact area with the skin eliminates the need to pinch the skin during self-injection, and in some cases, the device can be operated with both hands, which is good news for patients with advanced hand deformities. The fact that the chemicals are in cartridges to save space during storage, compared to the Embrel-Pen type is also an important feature when sufficient storage space in the refrigerator is not available. We will reconsider ETN, which has accumulated 19 years of history since its adaptation in 2005.

## LS19

**Title of Presentation: Unsolved Issues in Treatment of Rheumatoid Arthritis- Role of the Next Generation Antibody Ozoralizumab -**

Kosuke Ebina
Orthopedic Surgery, Osaka University Graduate School of Medicine

Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has evolved significantly over the past two decades. The advent of biologics and JAK inhibitors with innovative therapeutic effects has greatly expanded options for drug therapy. The tumor necrosis factor (TNF) inhibitor first launched is positioned as a first-line drug for standard treatment with biological drugs based on abundant and high-quality evidence supporting it. Recent studies have shown that TNF plays a major role in bone and cartilage destruction and the importance of its control has been re-recognized. Under these circumstances, ozoralizumab (OZR), the first Nanobody® drug in Japan, was launched as a new TNF inhibitor. Nanobody® molecule is a low-molecular-weight antibody produced via fragmentation and humanization of the antibody variable region called the heavy chain antibody (composed only of heavy chains) which is naturally produced by camelids. This molecule specifically binds to antigens in a single domain. OZR, a type of low-molecular-weight antibody, has a trimeric structure composed of two anti-human TNF-α Nanobody® molecules and one anti-human serum albumin Nanobody® molecule. It does not have an Fc region and its molecular weight is approximately 1/4 that of a typical IgG antibody. In nonclinical studies of OZR immune complexes, it is assumed to bivalently bind to TNF-α trimer; OZR has also been reported to not form an immune complex with a molecular size of 2,000 kDa or higher, activate neutrophils via the Fcγ receptor, or induce acute inflammation via subcutaneous injection in mice. In this seminar, I state the significance of and issues concerning TNF inhibition in RA treatment based on recent research. In the latter half of the seminar, I will outline the pharmacokinetics, safety, potential, and expectations of OZR in RA treatment based on nonclinical research, a phase II/III clinical study and a phase III clinical study of OZR.

## LS20

**Prevention, diagnosis, and treatment for Periprosthetic Joint Infection: Practice of daily medical treatment and novel evidences**

Naomi Kobayashi
Department of Orthopaedic Surgery, Yokohama City University Medical Center

Conflict of interest: Yes

Periprosthetic joint infection (PJI) is a complication that occurs in approximately 1% of patients following arthroplasty surgery, and is one of the urgent postoperative complications in the treatment of rheumatoid arthritis. Many studies and guidelines have been presented to date regarding various issues related to the prevention, diagnosis, and treatment of PJI. For prevention, by bundling together each measure that is considered effective, it is possible to achieve a more reliable effect. It is important to be aware of taking all possible measures in cases where the risk is high. Antibacterial surface technology (AG-PROTEX) is one such technology for implant selection, and the broad antibacterial spectrum of silver ions is expected to play a certain role in the prevention and treatment of PJI. Despite thorough preventive measures, PJI occurs unexpectedly in actual clinical settings, and many factors such as the site of infection, systemic condition, local condition, causative bacteria, and onset pattern/timing are heterogeneous. There are many points to consider in each individual case. For example, if wound exudate is confirmed about two weeks after the initial THA and an increase in the CRP value is observed, how should we diagnose and respond? What antibiotic should be selected at the stage where culture results are not yet available, and how should a combination of multiple drugs be used once the causative bacteria have been identified? What about second-stage revisions after multiple surgeries or in difficult cases due to atypical bacterial species? In this lecture, based on cases that the speakers have actually experienced, we will introduce how we deal with prevention, diagnosis, and treatment, and we will also present evidence based on the latest knowledge based on a systematic review and meta-analysis that we recently conducted.

## LS21-1

**Echocardiography and AI for Early Screening of PAH**

Kenya Kusunose
Department of Cardiovascular Medicine, Nephrology, and Neurology, Faculty of Medicine, University of the Ryukyus

Conflict of interest: Yes

Pulmonary hypertension was once perceived as a disease with difficult treatment options and poor prognosis. However, the advent of pulmonary vasodilators targeting the improvement of pulmonary arterial hypertension has raised hopes for life prognosis improvement through early diagnosis and accurate treatment. In this context, the diagnosis of pulmonary hypertension via echocardiography holds an extremely important position. Various methods exist for assessing pulmonary hypertension through echocardiography, and their interpretations differ based on the underlying disease. Exercise stress echocardiography is useful for detecting exercise-induced pulmonary hypertension, which is considered a precursor state of pulmonary hypertension. By applying appropriate indicators, stress levels, and assessments to the right patients, it is possible to identify individuals at high risk for future pulmonary hypertension, potentially improving patient prognosis and quality of life. Additionally, recent advancements in medical image analysis using artificial intelligence (AI) have been remarkable. Efforts are being made to detect pulmonary hypertension earlier and more easily using these tools. This presentation will focus on echocardiographic examinations (especially exercise stress) and AI-based methods aimed at early diagnosis of pulmonary hypertension. We aim to deepen understanding of their practical methods and interpretation of results.

## LS21-2

**Considering the optimal treatment for CTD-PAH and the positioning of selexipag - For the better lives for patients -**

Hideyuki Okada
Department of General Internal Medicine and Rheumatology, Gifu Prefectural General Medical Center

Conflict of interest: None

For rheumatologists, pulmonary hypertension (PH) should be a common disease. This is because if there is connective tissue disease (CTD), there is PH. PH also exists as an organ disorder of CTD. The first step in diagnosis is to notice symptoms that indicate the presence of PH among the seemingly flashy symptoms of CTD, such as interstitial pneumonia, nephrotic syndrome, high fever and severe skin rash. By being suspicious from the beginning that PH may coexist when examining patients with CTD, it is possible to diagnose the disease earlier. The existence of an immune mechanism behind such CTD-PAH has recently been actively discussed. It has also been frequently reported that dysbiosis in the intestinal flora is involved in the immune mechanism. (Nutrients. 2022; 14 (20): 4278.) Dysbiosis causes decreased production of short-chain fatty acids and increased TMAO and serotonin, increasing the permeability of intestinal epithelial cells and transferring intestinal bacteria, LPS, and various inflammatory cytokines to the lungs. This causes abnormalities in the pulmonary flora, leading to pulmonary perivascular inflammation and proliferation of pulmonary vascular smooth muscle cells. Furthermore, increased expression of HIF-1α in a hypoxic environment also activates the immune mechanism. Recently, various therapeutic drugs for PAH have

been introduced and the prognosis has improved dramatically, but the prognosis for CTD-PAH is still poor. Although the arrival of new biologics is imminent, it is currently necessary to normalize hemodynamics by making full use of existing PAH therapeutics. The 2022 ESC/ERS Guidelines state that the addition of Selexipag to ERA or PDE5 inhibitors is Class I, Level B, and is a beneficial, useful, and effective treatment combination. We, as rheumatologists, need to be familiar with the drugs currently available and how to use them, so that all patients who develop CTD-PAH can live a better life. We must strive to reflect this in our treatment.

## LS22-1

**COVID-19 Pandemic: Domestic and International Responses and Future Infectious Diseases**

Mugen Ujiie
National Center for Global Health and Medicine, Tokyo, Japan

Conflict of interest: None

The coronavirus disease 2019 (COVID-19), first reported in Wuhan, China, in December 2019, led the World Health Organization (WHO) to declare a 'Public Health Emergency of International Concern' on January 30, 2020, and left this declaration on May 5, 2023. As of May 8, 2023, COVID-19 was reclassified in Japan as equivalent to a category five infectious disease, similar to seasonal influenza. Since October 2021, the Omicron variant, first reported in South Africa, has become the predominant strain in the pandemic. This virus lineage has repeatedly shown a cycle of mutations leading to immune evasion and increased infections, followed by the strengthening of herd immunity, the subsiding of the outbreak, and the emergence of different viral strains. The COVID-19 vaccines, available since around December 2020, have significantly contributed to the acquisition of herd immunity and reduction in mortality rates. However, their effectiveness has been challenged by these mutations. Since the fall of 2022, adapting vaccines to match the prevalent virus variants has become a common strategy. This presentation will outline the knowledge gained from domestic and international COVID-19 preventive measures, including vaccines, and discuss future prevention strategies based on this evidence acquired. It will also introduce efforts to improve current vaccines and strategies to prepare for potential future respiratory virus pandemics.

## LS22-2

**Effectiveness and Safety of SARS-CoV-2 Vaccines in Immunocompromised Patients**

Tomomi Tsuru
PS Clinic, Fukuoka, Japan

Conflict of interest: None

The COVID-19 pandemic has been the most significant societal threat since the 1918 influenza pandemic. However, unlike the 1918 pandemic, the identification of the virus and the supply of vaccines were achieved in an extremely short time. This presentation introduces the development and mechanism of mRNA vaccines and discusses their effectiveness and safety in patients with autoimmune inflammatory diseases. In general, the development of vaccines requires a balance between effectiveness and safety. Live vaccines, such as those using attenuated viruses, sometimes pose risks of disease development, raising safety concerns. Subsequent vaccine development introduced non-living options, such as split vaccines or recombinant vaccines, but they often resulted in decreased immunogenicity. Adjuvants were then developed to enhance immunogenicity and are widely used today. However, it is essential to note that adjuvants, by nonspecifically inducing the immune system, carry the risk of triggering the onset or exacerbation of autoimmune diseases. mRNA vaccines provide the genetic information of antigens to the recipient, inducing antigen production in the recipient's cells. Due to the rapid analysis of the virus genome, antigen information can be obtained quickly, and as these vaccines do not rely on the use of living organisms, early delivery is possible. Additionally, the adjuvanticity of RNA and LNP (lipid nanoparticle) allows for the provision of highly immunogenic vaccines. In controlling the adjuvant effect, current mRNA vaccines use pseudouridine instead of uridine, resulting in acceptable side effects. While immunogenicity is observed in immunocompromised patients, it has been reported that the use of certain medications may reduce immunogenicity. On the other hand, concerns arise about the potential induction of existing or new autoimmune diseases by vaccine administration. Continued careful monitoring is deemed necessary as evidence continues to accumulate on this aspect.

## LS23-1

**Potential of Patient Education and Operational Efficiency Enhancement Using mymobility in APS Therapy**

Kazutoshi Kurokouchi
Department of Orthopaedic Surgery, Juko Osu Hospital

Conflict of interest: None

Platelet-rich plasma (PRP) therapy for knee osteoarthritis (OA) is a non-insured medical treatment, but it is increasingly recognized and used as an effective treatment for knee OA. Autologous Protein Solution (APS), also referred to as the next generation of PRP, is a solution refined by dehydrating PRP using a kit from Zimmer Biomet, concentrating proteins such as growth factors and cytokines. Since 2019, we have started APS therapy, and as of December 2023, we have performed APS therapy on 329 knees. For clinical evaluation of APS therapy, we use the knee injury and osteoarthritis outcome score (KOOS) and the numerical rating scale (NRS) for pain. For imaging, we use standing simple X-rays and 1.5T MRI, and since 2022, a 3D MRI imaging analysis system (Vincent) for detailed evaluation of cartilage. In Japan, medical costs are increasing due to aging population and advanced medical technology, while there is also a regional imbalance in medical resources. From the fiscal year 2024, reforms in doctors' working styles will be implemented, and a serious shortage of medical resources is a concern. The government is promoting medical digital transformation (DX) to improve the efficiency of healthcare. mymobility is an application that supports patients before and after treatment using smartphones, connecting medical professionals like doctors, PTs, and nurses with patients within the app, providing educational content and clinical scores. Previously, our outpatient service mainly used paper-based methods for explaining treatment contents and collecting clinical scores. We introduced mymobility's trial plan for knee OA patients receiving APS therapy in May 2023, registering 114 patients by December 2023. The introduction of mymobility's trial plan has realized the following benefits: 1. Regular educational contents are possible before APS administration, aiding patients' understanding of APS therapy. 2. Educational contents to patients have reduced the burden on doctors and medical staff in explaining APS therapy. 3. Automatic aggregation of scores such as KOOS and NRS is possible, making the work of doctors and medical staff more efficient. 4. Integration with healthcare apps on iPhones and Apple Watches has enabled monitoring of patient activity levels, allowing observation of changes in activity levels before and after APS therapy, and the effectiveness of APS therapy can be felt. In this presentation, I will discuss the utility and tasks of introducing mymobility at our hospital and the clinical outcomes of APS therapy.

## LS23-2

**Improvement of Patient Satisfaction with Total Hip Arthroplasty Using a Smartphone App (mymobility) and Its Application to Clinical Research**

Masahiko Mihara
Shonan Kamakura Joint Reconstruction Center, Kanagawa, Japan

Conflict of interest: None

mymobility (Zimmer-Biomet) is an app that enables preoperative and postoperative patient education to be provided with content and time periods set by the medical staff. The information provided is mainly educational menus and rehabilitation videos, which are sent to the patient's smartphone every preset day. The application can also be used to send questions and photos from the patient to the medical staff, who can reply to the patient's questions using the message function, as well as collect functional gait information such as JHEQ, HOOS, EQ-5D, etc. (PROMs), step count, walking speed, symmetry, etc. (limited to the iPhone), and perioperative gait analysis. The registration rate, frequency of use, and postoperative complications of mymobility were investigated for 1000 patients who underwent surgery between 2021 and 2022 and were able to be followed for at least two months after surgery. 527 of the 1000 patients

registered for mymobility. Of these, 319 actively used mymobility, 208 registered but did not use it at all or hardly at all, and 473 did not register. Postoperative complications were infection in 5 cases, dislocation in 3 cases, and symptomatic VTE in 0 cases, showing no significant difference between patients with and without mymobility use. Subsequently, the enrollment rate increased with ingenuity and effort, and by the time about 3 years had passed since the start of implementation, 1,200 patients had utilized mymobility. The message function was used by approximately one in six patients, and the number of unscheduled post-operative revisits decreased because it was no longer necessary to see the doctor if the consultation was completed on the application. Patient satisfaction with mymobility was generally favorable, and the ability to collect PROMs and perform perioperative gait analysis can be applied to clinical research. In this presentation, I will report on the effectiveness of mymobility and the recovery of gait function in our patients.

## LS24

**The Practical Application of Mepolizumab Therapy for EGPA**

Tomonori Ishii
Clinical Research, Innovation and Education Center, Tohoku University Hospital, The Practical Application of Mepolizumab Therapy for EGPA

Conflict of interest: Yes

Mepolizumab (MPZ) is a monoclonal antibody that binds with high specificity and affinity to interleukin-5 (IL-5). IL-5 is known to primarily regulate eosinophils in humans, and with the administration of MPZ, the number of eosinophils in the blood and tissues is reduced. This drug was initially approved for severe asthma, its indication was expanded to include Eosinophilic Granulomatosis with Polyangiitis (EGPA). Many patients with EGPA have difficult-to-control severe asthma, and with this approval expansion, it became possible to use three times the dose allowed for asthma patients. Indeed, it is a drug that powerfully controls such conditions, while also playing a significant role in reducing oral corticosteroids (OCS) dosage and preventing relapse. However, as it is a relatively new drug with a small patient base, there are still many unknowns regarding its long-term safety, effectiveness, and appropriate patient selection. The MIRRA study is an important piece of evidence as an RCT, but it is well-known for its patient selection bias, necessitating real-world data. In Japan, a registry of all EGPA patients receiving MPZ has been conducted, monitoring safety and efficacy over two years, with results reported. This report indicated that serious adverse events possibly related to the drug were only recognized in 1.7% of patients. Regarding efficacy, the dosage of OCS and blood eosinophil counts decreased, and the proportion of patients without clinical symptoms increased from 9.4% at the start of this drug administration to 30.1%. Currently, an observational study is being conducted to monitor the long-term progress over four year with interim data analyzed at three years of administration. The continuation rate for patients (119 cases) who received MPZ for more than 96 weeks and then continued for an additional 48 weeks was 95%. No adverse events reported during the observation period were determined to have a causal relationship with MPZ. Clinical symptoms of EGPA, EGPA-related events, and asthma exacerbations improved after MPZ administration compared to before. Meanwhile, the dosage of OCS continued to decrease as the duration of MPZ administration increased. Minimizing the dose of OCS is a long-term goal in the management of EGPA, and the setting of treatment goals is changing with the use of MPZ.

## LS25

**Simple RA treatment strategy for achievement of various REMISSION ~Joint Decision Making provided by JAK inhibitor monotherapy and ultrasound~**

Kenta Misaki
Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

Fourteen years have passed since the first EULAR recommendation was published for the treatment of rheumatoid arthritis (RA). We rheumatologists have experienced many paradigm-shifts in RA diagnosis and treatment over the past 14 years, and we have been able to achieve them in clinical setting for RA patients. However, the diagnosis of seronegative RA is still a difficult task even in the new era. One of the paradigm-shifts also in Japan over the past 14 years is the approval of musculoskeletal ultrasound (MSKUS) as an imaging approach to RA in addition to serological diagnostic procedures. MSKUS real-timely make it possible to depict abnormal findings that are difficult to determine by physical examination with no harm and make a huge contribution to the early diagnosis including seronegative RA. One of the major epoch-makings in the treatment of RA is the approval of JAK inhibitors (JAKi) in Japan in 2013. Upadacitinib (UPA), the fourth JAKi approved in Japan is focused not only as a next-generation JAKi with selectivity for JAK1 component but also as a new study outline in comparison to those other Biologics (Bio) and JAKi in world-wide clinical trials. Among them, the evidence of UPA monotherapy (SELECT-MONOTHERAPY) includes clinical remission assessments as well as patient -reported outcomes (PROs), and also includes original clinical evidence of JAKi monotherapy in Japanese patients. Furthermore, JAKi is one of the therapeutic agents will cut into the issues such as Difficult to Treat RA and Polypharmacy for RA patients in the new era. In this session, I would like to discuss about the topics which phase of the guidelines 2020 for the treatment strategy of RA UPA therapy should be adapted, the world evidence from 5 years of long-term UPA monotherapy, and the efficacy and safety, including structural remission, as revealed by the evaluation of UPA monotherapy using the MSKUS with some experiences of our own clinical trials.

## LS26

**Management of rheumatoid arthritis-associated osteoporosis according to goal-directed treatment**

Tadashi Okano
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Conflict of interest: Yes

Rheumatoid arthritis is an autoimmune disease that causes chronic synovitis, leading to pain, swelling and functional impairment. In addition, patients with rheumatoid arthritis have high risk of osteoporosis due to frequency of female, inflammatory cytokines, long-term steroid treatment, limitation of activity and ageing. These factors can lead to a reduction in bone mineral density, resulting in an increased risk of fractures and reduced activities of daily life, as well as having a direct impact on patient survival. Considering this background, osteoporosis should be treated in patients with rheumatoid arthritis as well as disease activity. Bone densitometry examination is essential for the treatment of osteoporosis and plays an important role not only in the diagnosis of osteoporosis but also to assess the efficacy of therapeutic agents. The concept of goal-directed treatment has recently been proposed for the selection of therapeutic drugs. This is a new approach in which individual patient treatment goals are clearly defined and strategies are developed to achieve them. In the choice of drugs for osteoporosis treatment, a wide variety of treatment options are available, such as anti-resorptive therapies including bisphosphonates and denosumab, bone anabolic agent including teriparatide and romosozumab. Aggressive therapeutic intervention with osteogenesis-promoting agents such as romosozumab is particularly warranted in osteoporotic patients at imminent fracture risk (Imminent Fracture Risk). These agents are known to promote a strong increase in bone density and reduce fracture risk. The choice of treatment drugs should be based on the latest clinical data and the individual patient's situation. This seminar will include new findings in the diagnosis and treatment of patients with rheumatoid arthritis-associated osteoporosis.

## LS27

**Stable, safe, and inexpensive drug treatment for rheumatoid arthritis 2024-Considering the benefits of TNF inhibitors-**

Yuji Hirano
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Conflict of interest: Yes

It is no exaggeration to say that a paradigm shift in drug treatment for RA began with the clinical approval of etanercept (ETN) in the US in 1998. ETN, a fully human soluble TNFα/LTα receptor, has provided us with a wealth of clinical evidence and ushered in a new era. The first thing

that comes to mind is the excellent joint destruction suppressing effect, the possibility of discontinuing anchor drug MTX, and the possibility of reducing or discontinuing ETN. It was later demonstrated by Ishii that TNF is strongly involved in the abnormal enhancement of osteoclast function caused by RANKL. Although new types of drugs have been introduced one after another, TNFi still have many advantages. Examples of ETN include low placental penetration and high clinical continuity rate. According to "Considerations for targeted therapy in patients with inflammatory arthritis with a history of malignant tumors" presented at EULAR 2023, TNFi should be used in patients with a history of solid tumors as first line. This is considered to be an important guideline in Japan, where the aging of the population continues to progress. A further advantage of current TNF formulations is the availability of biosimilars (BS). Japan's population will continue to age in the future, and the decline in economic power and the resulting reduction of the medical economic burden will become an urgent issue. One countermeasure is the active use of BS. In our department, we feel that there is a particularly strong need for BS among patients in their 40s and 50s, who still have to pay for children. ETN is approved in the package insert at a dose of 25 mg per week. A post-hoc analysis of the Japanese ETN phase III trial showed that there was no statistically significant difference in disease activity suppression effect when comparing ETN 20 mg/w and 50 mg/w. In this lecture, I would like to consider the merits of TNF inhibitors and the similarities between stable, safe, and inexpensive drug treatment.

## LS28-1

**The mechanism of action of anifrolumab in the pathophysiology of systemic lupus erythematosus**

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Conflict of interest: Yes

Systemic Lupus Erythematosus (SLE) is an autoimmune disease, and its pathophysiology involves immune cells and inflammatory cytokines. In particular, type I interferon (IFN) is believed to play a central role in the onset and various pathologies of SLE, contributing to the promotion of autoimmune responses and tissue inflammation. The treatment goal for SLE is achieving remission. To achieve remission and control disease activity with reducing glucocorticoid doses, anifrolumab has several evidences. On the other hand, the pathophysiology of SLE is heterogeneous, and it is still uncertain which type of SLE cases anifrolumab may be the optimal choice for. This presentation aims to introduce the current understanding of the role of type I IFN in the pathophysiology of SLE and discuss the best use of anifrolumab in view of its pathophysiology.

## LS28-2

**Positioning of anifrolumab in real-world clinical practice**

Tsuneo Kondo
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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a heterogeneous and complex autoimmune disease with variable manifestations and progression. Hydroxychloroquine and corticosteroids are first-line agents. Depending on the severity of the disease and the extent of organ involvement, immunosuppressive drugs step up to first and second-line agents. Anifrolumab, a type I interferon inhibitor approved in Japan in September 2021, is a therapeutic agent for SLE with an unprecedented mechanism of action. This presentation will discuss the role of type I interferon in the pathophysiology of lupus and the evidence that led to the approval of anifrolumab, particularly the TULIP2 and TULIP-LTE studies. In addition to standard therapy, anifrolumab appears to reduce corticosteroid requirements, reduce lupus disease activity, particularly cutaneous and musculoskeletal symptoms, and has an acceptable safety profile. We present the status of 51 SLE patients treated with anifrolumab at our institution and discuss the current real-world clinical status of anifrolumab in light of the EULAR recommendations 2023 update.

## LS29-1

**Molecular-targeted therapy considering immunopathogenesis in psoriatic arthritis**

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Conflict of interest: None

Spondylarthritis (SpA) is a representative highly heterogeneous disease. Activation of the IL-23/Th17 axis plays a vital role in the pathogenesis. Our results of peripheral blood lymphocyte phenotyping conducted on 54 healthy controls, 775 cases of rheumatoid arthritis (RA), and 150 cases of SpA patients confirmed a characteristic increase in activated Th17 cells in SpA. Recently, various molecular target drugs [TNF-i, IL-17A-i, IL-12/23 (p40)-i, IL-23 (p19)-i, IL-17 receptor-i, JAK-i] have become available for SpA (PsA). However, even when these drugs are used, the MDA achievement rate in clinical trials and clinical practice remains at about 1/3. The therapeutic goal of simultaneously improving various symptoms has not been fully achieved. On the other hand, peripheral blood comprehensive immunophenotyping conducted on 30 healthy controls, 33 PsA cases, and 22 PAO cases revealed that an increase in activated Th17 cells is typical in PsA/PAO, but there may be a higher dependence on activated Th17 cells in PAO. We also revealed that each drug has a different impact on immune phenotypes. It was shown that the immunological diversity of each patient (each disease) and the characteristics of each molecular target drug may influence the therapeutic response of individual diseases and patients. Based on this background, we have been practicing precision medicine using molecular target drugs for PsA. PsA can be classified into four subgroups based on helper T cell phenotype, and strategic treatment based on this classification using TNF-i, IL-17-i, and IL-12/23 (p40)-i demonstrated higher effectiveness. Furthermore, by using serum IL-22 as a biomarker, it became possible to use TNF-i and IL-17-i differentially, and it was shown that the PsA patient population could be stratified into TNF type and IL-17 type. Patient stratification and the selective use of molecular-targeted drugs are highly effective and additionally provide new insights into pathogenesis.

## LS29-2

**Importance of diagnosis and therapeutic strategies for IL-17 inhibition in axial spoindyloarthritis**

Tetsuya Tomita
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Conflict of interest: Yes

Spondyloarthritis is a group of diseases with a diverse clinical presentation, including inflammatory back, peripheral arthritis, uveitis and inflammatory bowel disease. In 2008, ASAS proposed classification criteria for axial spondyloarthritis, which includes AS that meets the revised NY criteria for sacroiliac joint X-ray and non-radiographic axial spondyloarthritis. Recent advances in the pathogenesis of spondyloarthritis have demonstrated the importance of IL-23/17 axis and IL-17 is a known cytokine that directly affects bone resorption and formation and is considered an effective therapeutic target in axial spondyloarthritis. 2022 ASAS-EULAR treatment recommendations for axial spondyloarthritis state that NSAIDs should be the first-line drug therapy and biologics (TNF inhibitors, IL-17 inhibitors) or JAK inhibitors should be considered if adequate disease activity control cannot be achieved, with biologics being preferred. In Japan, however, TNF inhibitors are not approved for nr-ax SpA and IL-17 inhibitors should be considered. If the expected therapeutic effect is not achieved, the diagnosis should first be reviewed. Secukinumab, the first IL-17 inhibitor indicated worldwide for the treatment of somatic spondyloarthritis, has been shown to improve clinical symptoms, as well as objective measures such as MRI, and to inhibit the progression of joint destruction by simple radiography after long-term use. Furthermore, with safety, the incidence of inflammatory bowel disease is less than 1%, a trend similar to that observed with other IL-17 inhibitors. Psoriatic arthritis has also recently become a major problem in terms of axial joint morbidity, and the 2022EULAR recommendations also recommend IL-17 inhibitors as first-line treatment in PsA patients with axial disease who have had an inadequate response to NSAIDs. The rationale for this is the MAXIMISE study,

which evaluated the efficacy of secukinumab in the management of somatic symptoms in psoriatic arthritis (PsA), the only RCT to evaluate the efficacy of a biologic in the management of somatic symptoms in PsA and the only RCT to evaluate the efficacy of a biologic in a population with high activity of inflammatory back pain, with multiple clinical and Significant improvements in imaging endpoints were demonstrated. IL-17 inhibitors are considered a useful treatment option in the treatment of axial spondyloarthritis.

## LS30

**~Kidney Ages as People Age~ Treatment Strategies for Elderly Rheumatoid Arthritis Considering Pharmacokinetics**

Naoki Sawa
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Conflict of interest: Yes

In "Tsurezuregusa", Yoshida Kenko stated that it would be desirable to die before reaching even forty years of age, but in modern Japan, less than 40% of the population is under 40. The aging trend is even more pronounced in cases of rheumatoid arthritis (RA), with reports indicating that over 70% of RA patients are over 60 years old, and the prevalence of RA is higher among the elderly. Since the lungs and kidneys are organs that experience significant functional decline with age, special attention is required for these two organs in the treatment of elderly patients with rheumatoid arthritis (RA). Particularly in RA cases, it has been reported that the frequency of comorbid chronic kidney disease (CKD) and the progression of its stages increase with aging. Furthermore, in elderly RA patients, a lower muscle mass often results in no apparent increase in serum creatinine, indicating potential underlying renal function decline. In such cases, measuring serum cystatin C becomes necessary for the detection of renal dysfunction. Recently, RA activity has been reported to be an independent risk for CKD progression. Therefore, management of disease activity is important to prevent CKD progression in RA patients. On the other hand, the use of NSAIDs and methotrexate (MTX) is limited in RA patients with renal dysfunction, either by reducing or withholding their use. This presents a dilemma for many rheumatologists, and in cases of RA with concurrent CKD, the use of biologic agents or JAK inhibitors is often necessary. Considering the aforementioned characteristics of the elderly, (1) a wide safety margin, (2) maintenance of efficacy as a single agent, and (3) a low renal excretion rate are desirable characteristics of drugs for elderly rheumatoid arthritis patients. In this presentation, we will discuss treatment strategies for rheumatoid arthritis that take into account changes in physiological functions associated with aging.

## LS31

**Latest Treatment Strategies for Rheumatoid Arthritis: From Biological Agents to JAK Inhibitors**

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Conflict of interest: Yes

The initial management of rheumatoid arthritis (RA) involves various considerations, including the time from onset to treatment initiation, joint prognosis, disease activity, complications, intentions regarding pregnancy, and the urgency of achieving remission. Personalized medicine is crucial, often starting with selective monotherapy using oral disease-modifying antirheumatic drugs (DMARDs) for efficacy, and setting criteria for combination therapies. Dosage decisions are vital, not only to improve remission induction rates with oral DMARDs but also to influence future treatments with biological agents and JAK inhibitors. Early treatment typically combines long-term disease controllers, such as oral DMARDs, biologics, and JAK inhibitors, with immediate anti-inflammatory agents like NSAIDs and steroids as part of a comprehensive care approach. The primary goal is to induce remission quickly, maintain it with minimal pharmacotherapy, and tailor treatments to the patient's specific background. Personalized medicine also takes into account drug costs and the necessity for adjunct therapies. With biologics and JAK inhibitors, such as tofacitinib, tailored pre-treatment screening and ongoing monitoring after administration are required. Biologics have shown potential for a 'bio-free' status and dose reduction during the maintenance phase, which necessitates evaluating each drug's unique risks, including infections. Etanercept is often preferred for patients at risk of secondary inefficacy due to its dosing flexibility, short half-life, and low development of neutralizing antibodies. For JAK inhibitors like tofacitinib, which have demonstrated non-inferior efficacy compared to biologics, optimal patient identification is essential given their broad cytokine inhibition. Tofacitinib also presents the possibility of discontinuing methotrexate after efficacy onset, as recent studies indicate. These evolving insights necessitate a reassessment of each drug's role in current RA therapy, directing treatment decisions based on the latest evidence.

## LS32

**Mechanisms of Joint Destruction in Rheumatoid Arthritis and Strategies for Mitigation: Optimizing Rheumatoid Arthritis Treatment through Cohort Studies**

Kosuke Ebina
Graduate School of Medicine Orthopaedic Surgery, Osaka University

Conflict of interest: Yes

In the 2020 Rheumatoid Arthritis (RA) treatment guidelines, the treatment goals for RA are clearly defined as "improvement in clinical symptoms (clinical remission) and suppression of joint destruction (structural remission), and beyond that, prevention of physical disability and improvement in life prognosis." According to the 2020 Rheumatoid Arthritis Report, RA patients have been reported to have the highest expectations of treatment to halt the progression of joint destruction (structural remission). In clinical practice, however, a significant proportion of RA patients in Japan are aged 70 or older, as stated in the 2020 Rheumatoid Arthritis Treatment Guidelines. This includes challenging cases where treatment intensification with anchor drugs such as methotrexate is difficult due to high disease activity, renal dysfunction, or pulmonary complications. There are also cases where joint destruction and physical functional impairment progress, despite achieving clinical remission criteria based on inflammation markers in blood tests and composite measures, often due to 1) a lack of understanding and assessment of the mechanism and risk of joint destruction progression, 2) inadequate evaluation of small joint inflammation in the hands and feet, and difficult-to-observe deep joint inflammation (e.g., shoulder and hip joints), and 3) a lack of treatment strategies independent of steroids in the elderly. These issues can be attributed to one of the factors. To address these issues and meet the treatment demands of RA patients, it is considered important to 1) implement appropriate early treatment interventions taking into account age and the risk of joint destruction progression, and 2) conduct regular assessments of the risk of joint destruction progression. Additionally, after achieving low disease activity or remission as mentioned above, the concept of "Beyond remission" is also emphasized, considering the reduction of medication for safety and reduced medical costs. This presentation will provide an overview of the latest topics on the mechanism of joint destruction in RA and the optimization of RA treatment, including the data from the Kansai multi-center ANSWER cohort.

## LS33

**Efficacy of early intervention for systemic sclerosis associated pulmonary arterial hypertension**

Yasushi Kawaguchi
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Conflict of interest: None

Systemic sclerosis (SSc) is a collagen disease in which vascular damage and fibrosis affecting multiple organs are involved in the main pathogenesis. Specific autoantibodies are observed in SSc. Complications related to life prognosis of SSc include interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), and pseudoobstruction associated with lower intestinal lesions. PH in SSc includes PAH (Group 1), PH associated with SSc-ILD (Group 3), and PH associated with cardiac lesions in SSc (Group 2). Pulmonary vein lesions were also observed, and PVOD-like pathology (Group 1) must also be considered. Although rare, pulmonary thromboembolic PH (Group 4) is also experienced. Among the autoantibodies expressed in SSc, the antibodies associated with PAH

complications are anti-centromere antibodies and anti-U1-RNP antibodies. Therefore, early diagnosis of SSc in which these autoantibodies are expressed has become possible using echocardiography, serum NT-proBNP, and %DLco. Diagnosis of PAH requires cardiac catheterization, and the mean pulmonary artery pressure (mPAP) is 25 mmHg or higher and the pulmonary artery wedge pressure is 15 mmHg or lower. Current treatment with pulmonary vasodilators has been shown to be effective for Groups 1 and 4. If SSc-PAH is diagnosed as the main cause, combination therapy with pulmonary vasodilators should be performed at an early stage. Several therapeutic drugs have been developed in three systems: endothelin (ET)-1, cGMP, and cAMP, which are involved in pulmonary vasoconstriction and dilation. Early combination therapy uses drugs that treat the ET-1 and cGMP pathways. A combination of macitentan and riociguat, among others, is used as the drug. If the effect is insufficient, a three-drug combination treatment including selexipag, which works on the cAMP pathway, is performed. We believe that the prognosis of SSc-PAH will improve if these treatments are started at a stage when mPAP or pulmonary vascular resistance is low.

## LS34

**Treatment of rheumatoid arthritis in an Aging Society: Toward Enhancing Its Sustainability**

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Conflict of interest: Yes

The treatment of RA has made great progress. The treatment strategy for RA has been well established and supported by a large body of evidence. Japan has entered a hyper-aged society, and it is reported that approximately two-thirds of RA patients are aged 65 years or older. Older age is a risk factor for RA treatment. Evidence for the treatment of elderly patients is limited. Therefore, how to safely sustain treatment is a major challenge. To increase the sustainability of RA treatment, it is important not only to extend life expectancy but also to extend healthy life expectancy. In addition to the maintenance of physical function, the maintenance of mental functions such as social activity and cognitive function, as well as social support such as drug costs and nursing care costs are extremely important. In this super-aged society. Health care economic aspects cannot be avoided. Perspectives such as frailty and sarcopenia, concepts related to physical and mental vulnerability due to aging, are essential for extending healthy life expectancy. Therapeutic intervention for osteoporosis must also be strengthened. The use of so-called generic drugs is useful to reduce medical costs, which are also a social issue. National policies are also making a major shift toward the use of generic drugs. On the other hand, there have been incidents of concern about the quality of generic drugs. Biosimilars are required to undergo clinical trials to verify that they are as effective as the brand-name drug. Efforts should be made to properly explain biosimilars to patients and incorporate them into their treatment. In this seminar, we would like to consider ways to improve the sustainability of RA treatment.

## LS35-1

**Practice and challenges of computer-assisted total hip arthroplasty**

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Conflict of interest: Yes

Advances in computer technology have made it possible to plan component placement in preoperative planning for total hip arthroplasty (THA) to minimize implant impingement during activities of daily living. CT-based navigation is useful for accurately carrying out these preoperative plans, and surgery can be performed with an accuracy of 2 to 3 degrees in angle and 2 to 3 mm in distance. In recent years, robotic surgery has been introduced, making it possible to perform more precise and safer surgeries. We started robotic arm-assisted THA in 2019, and in an accuracy survey of the initial 100 cases, the absolute value of the difference (error) between the preoperative plan and postoperative CT measurement was 1.2° on an average in the cup inclination angle. The average error of cup anteversion angle was 1.8°, which was better than that of CT-based navigation. The major advantage of robotic surgery compared to CT-based navigation is that in navigation, outliers of 5° or more and less than 10° were observed in approximately 10% of cases for both cup inclination and anteversion angles, whereas in robotic surgery, however, not a single case was observed. In addition, because the cup provides a secure press fit, many cases do not require the use of screws, which reduces the possibility of vascular damage. These are particularly effective in minimally invasive surgeries performed using small incisions. As it becomes possible to perform such highly reproducible surgeries, the importance of preoperative planning has become increasingly recognized. Ideally, it is not a uniform plan for all cases, but an optimal preoperative plan for each individual case; however, to do so, it is necessary to analyze the factors of each case and reflect them in the preoperative plan. In THA, the effects of pelvic tilt, which are affected by posture and spinopelvic alignment, and postoperative changes in pelvic tilt are discussed on the pelvic side, and the effects of femoral rotation and other factors are concerned on the femoral side. In this seminar, we report on the practice and challenges of computer-assisted THA.

## LS35-2

**Computer-assisted total knee arthroplasty with patient specific surgical plan**

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Conflict of interest: None

Computer Assisted Surgery (CAS) for total knee arthroplasty (TKA) was started from navigation system to achieve accurate bone resection and evaluate the intraoperative factors. Advanced CAS technology of robotics for TKA has been introduced into Japan in 2019. Mako knee systems (Mako; Stryker) is Computed Tomography (CT)-based robotic arm-assisted system has three main features; three dimensional preoperative surgical plan, intraoperative modification of its pla based on the intraoperative soft tissue balance, and robotic-arm assisted bone resection. The clinical results after comparison between the robotics TKA (RA-TKA) and CT-free navigated TKA (navigated-TKA) at our institution found that RA-TKA reduced the coronal alignment outliers, and blood loss, and coordinated to the adequate bone resection thickness, compared to the navigated-TKA. RA-TKA also reduced the deviation of soft tissue balance and the incidence of worse maximum flexion angles cases than in navigated-TKA. However, RA-TKA with conventional alignment and soft tissue balance theories will never achieve improved clinical outcomes with better patient-reported outcomes and long-term survivorship. The trends in TKA surgery are shifting from the consistent target alignment to the personalized target alignment, and the personalized target alignment in CAS surgery were called “Functional alignment (FA)”. FA is proposed to achieve native alignment, joint line obliquity and height, and adequate soft tissue balance by adjusting the implant position using CAS technology with minimizing the periarticular soft tissue release. FA is expected to improve the clinical outcomes. CAS in TKA is still no more than the one of methods to reproduce the operative plan. To maximize the benefit of CAS, the focus should be shift toward the advancement of surgical plan. The plan is expected to be sophisticated by using the advanced technology such as big data including the comprehensive patient factors.

## LS36

**What we can do to bring the standard of care for lung cancer patients with autoimmune diseases**

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Conflict of interest: Yes

Autoimmune diseases (AIDs) and cancer have become an interdisciplinary treatment challenge, especially with the advent of immunotherapy;

AIDs are well known to be complicated by malignancies, with rheumatoid arthritis being second only to malignant lymphoma in the incidence of lung cancer. Conversely, rheumatoid arthritis has the highest frequency of AIDs complicated by lung cancer. Cancer immunotherapy is a treatment that activates or utilizes the immune system in body to kill cancer cells. Immune checkpoint inhibitors (ICIs) have emerged as a breakthrough immunotherapy that offers superior therapeutic effects after a long period of inadequate clinical efficacy. In addition, ICI-based cancer immunotherapy has been shown to significantly improve long-term survival (with expectation of cure in some cases) as well as to reduce tumor size not seen with conventional drug therapy. In Japan, 8 ICIs are currently approved for various types of cancer, and in just 8 years since the approval of nivolumab in September 2014, immunotherapy with ICIs has established itself as the standard of care for cancer and has become a central part of cancer treatment. ICI is an antibody that targets CTLA-4 and PD-1/PD-L1 and activates cytotoxic T lymphocytes by releasing suppressive signals by CTLA-4 and PD-1 in the immune system, thereby exerting an anti-tumor effect through cellular immunity. The anti-tumor effect of ICI caused by the release of negative immune signals is the opposite of immunosuppression, which is a treatment for AID caused by the breakdown of immune tolerance and the establishment of autoimmunity. Toxicities caused by ICI are mainly considered immune-related adverse events (irAEs), meaning that they are off-target effects of an excessively activated immune system. ICIs inhibit negative immune signaling and elicit immunity, resulting in T-lymphocyte activation, decreased immune tolerance, inflammatory cytokine production and autoantibody production, which in turn leads to autoimmune-like adverse events due to immunogenic inflammation of organs. Patients with AID are usually excluded from prospective clinical trials due to concerns for safety and flares of the underline AID when using ICIs. There is limited evidence supporting the use of ICI in cancer patients with AID. However, evidence is gradually accumulating through registry studies and retrospective studies. I hope that this seminar will help to deepen cooperation and collaboration among doctors in the treatment of cancer patients with AIDs, and lead to the development of cancer treatment.

## LS37

**Vaccination Strategies for herpes zoster in Patients with Rheumatic Diseases: Current Insights and Practices**

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Conflict of interest: Yes

The Varicella-zoster virus (VZV) causes chickenpox during initial infection, followed by a latent infection of ganglion cells in the cerebrospinal cord, resulting in herpes zoster (HZ) due to immunosuppressive conditions linked with aging, stress, and medication. The impact of reduced quality of life linked to post-HZ neuralgia is significant and should not be underestimated. VZV is the only vaccine-preventable herpes virus, and its vaccination is crucial. It has been widely acknowledged that HZ is primarily increased due to age-related immunocompromised immunity, as well as hematopoietic stem cell transplantation and hematologic malignancies. However, the elevated occurrence of HZ among autoimmune diseases, besides systemic lupus erythematosus, lacks acknowledgment. During the clinical trials with Janus kinase (JAK) inhibitors for rheumatoid arthritis (RA), the unusually high frequency of HZ garnered significant interest. The incidence of HZ was notably higher in individuals receiving JAK inhibitors during clinical trials conducted in Western countries when compared to those receiving traditional anti-rheumatic drugs. Furthermore, in Japanese subjects, the frequency of HZ during the same trials was roughly double that observed in the Western countries. As a result, the occurrence of HZ is a common concern while initiating JAK inhibitors. However, the occurrence of HZ is 2-3 times higher in patients with immune-mediated inflammatory diseases, including RA, compared to the general population, even prior to the approval of JAK inhibitors. Hence, it is crucial to recognize the rising incidence of HZ in immune-mediated inflammatory diseases, with or without JAK inhibitors. This is an important time to discuss measures to be taken in actual clinical practice in light of the expansion of Shingrix vaccination eligibility in 2023. Unlike a cure, vaccination serves as a precautionary measure against public health issues by curbing the onset of diseases. Thus, it can be challenging for patients to observe definitive benefits. It can be challenging for healthcare professionals to persuade patients to agree to costly vaccinations unless they are able to illustrate the necessity from a long-term standpoint. Hence, this presentation intends to suggest a proposal for the administration and explanation of the HZ vaccine based on clinical trial outcomes, as well as insights from clinical studies conducted in the fields of rheumatic diseases that can facilitate further discussion.

## LS38

**Current treatment strategies for rheumatoid arthritis -Focus on JAK inhibitors-**

Tsutomu Takeuchi
Saitama Medical University/Keio University

Conflict of interest: Yes

The advent of biologics has led to a paradigm shift in rheumatoid arthritis (RA) treatment, making it possible to aim for clinical remission, structural remission, and functional remission. Furthermore, oral JAK inhibitors appeared in Japan approximately 10 years ago, and treatment options to achieve and sustain remission have been expanded. On the other hand, achieving and sustaining of remission in daily clinical practice is not enough, and challenges remain in the implementation of Treat to Target (T2T). 2019 update of the EUALR recommendations recommended that biologics or JAK inhibitors be administered in Phase2 if treatment with MTX is started, and the treatment target is not achieved within 6 months. However, based on the results of the ORAL Surveillance study, the 2022 update revision specified that consider use of a JAK inhibitors only after risk assessment in Phase2. The importance of shared decision making (SDM) is also addressed in the revised EULAR recommendations. The JAK inhibitor Upadacitinib (UPA) exerts its anti-inflammatory effects by potently inhibiting JAK1 and thereby inhibiting the signaling of cytokines involved in the pathology of RA. In the phase3 SELECT study, the efficacy and safety of UPA were investigated in RA patients with diverse background characteristics, and the usefulness of UPA in combination with csDMARDs including MTX or without MTX. UPA was also directly compared with biologics in different patient backgrounds (inadequate responders to MTX or biologics). Although the pooled analysis of clinical studies showed an increased risk of herpes zoster, safety needs to be evaluated based on the results of all case post-marketing surveillance in Japan. In this lecture, we will discuss treatment strategies for achieving and sustaining remission, as well as discuss the clinical significance and safety profile of UPA and the positioning of JAK inhibitors in RA treatment strategies, based on the latest evidence, including long-term results from the Phase3 clinical studies of UPA.

## LS39-1

**How to view HCQ retinopathy in ophthalmology considering long-term management**

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Conflict of interest: None

Eight years have passed since ophthalmologists began screening for retinopathy in patients taking hydroxychloroquine (HCQ). With the remarkable advances in imaging modality, the prevalence of HCQ retinopathy was found to be higher than previously thought. HCQ retinopathy presents with a characteristic bull's eye (target maculopathy). Unfortunately, discontinuation of the HCQ at this stage does not stop the deterioration of the retinopathy. Around 2010, it became clear that detection of focal thinning of the retina by spectral-domain optical coherence tomography (SD-OCT) and detection of a slight decrease in visual field sensitivity by visual field testing are useful in the early detection of retinopathy. It is essential that ophthalmologists regularly examine patients taking HCQ to ensure that they do not miss early findings of HCQ retinopathy, and that HCQ prescribers also ensure that their patients receive regular eye examinations. It is not recommended to immediately discontinue HCQ when HCQ retinopathy is suspected. The patient should continue to be examined closely to make a definitive diagnosis of retinopathy. Ophthalmologists need to work closely with the HCQ prescribing physicians to discuss the possibility of reducing or stop HCQ based on the degree of damage caused by HCQ retinopathy. Unfortunately, clear diagnostic criteria based on

structural and functional abnormalities of HCQ retinopathy have not yet been established or standardized, and objective numerical guidelines for drug reduction or withdrawal at the onset of HCQ retinopathy are not clear. We would like to emphasize the importance of close collaboration between the prescribing physician and the ophthalmologist, including the patient, in the long-term management of patients with SLE. In this seminar, I would like to present a summary of the accumulated knowledge on HCQ retinopathy and consider what more is needed to make the HCQ safer and more effective in its long-term use.

## LS39-2

**Role of hydroxychloroquine in long-term management for SLE**

Shingo Nakayamada
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Conflict of interest: Yes

The pathogenesis of systemic lupus erythematosus (SLE) is characterized by immune complexes consisting of antigens, activation of dendritic cells and autoreactive T cells and overproduction of autoantibodies secreted from activated B cells. The prognosis of SLE has dramatically improved because of the widespread uptake of glucocorticoid and immunosuppressants, with survival rates reported to be 50%-70% after 20 years, given the age at onset, these survival rates are relatively low. As glucocorticoids and immunosuppressive drugs are non-specific therapeutic agents that cause many adverse reactions, the development of drugs aiming to control specific abnormal immune network is anticipated for the treatment of SLE. The EULAR recommendations for the management of SLE updated in 2023 stated that glucocorticoids should be used for short-term to control active disease; taper to ≦ 5 mg/day as quickly as possible and discontinue, if possible. Same as the 2019 recommendations, the antimalarial drug hydroxychloroquine (HCQ) remains the first-line drug. HCQ accumulates in lysosomes of antigen-presenting cells, such as plasmacytoid dendritic cells, and its mechanism of action is to inhibit interferon production and antigen-presenting functions by increasing pH and inhibiting TLR signalling. HCQ is useful not only for improving cutaneous and joint symptoms of SLE, but also for preventing recurrence, organ damage, thromboembolism and cardiovascular events. On the other hand, the risk of retinal damage due to long-term use of HCQs must be considered. In this seminar, we would like to discuss the role of HCQ in long-term management for SLE.

## LS40

**The 2024 Noto Peninsula Earthquake and the Importance of Rehabilitation Medicine**

Isao Matsushita
Department of Rehabilitation Medicine, Kanazawa Medical University

Conflict of interest: Yes

In a large-scale disaster, people affected by the disaster are forced to live in evacuation centers for long-term. Especially in the case of elderly persons in large-scale disasters, the isolation and inactivity become more serious, and the resulting disaster-related deaths occur. The Japan Rehabilitation Assistance Team (JRAT) was established in the wake of the Great East Japan Earthquake to prevent inactivity and disaster-related deaths among the vulnerable and elderly victims of large-scale disasters, and to help them rebuild independent lives. The Noto Peninsula Earthquake occurred at 4:10 p.m. on January 1, 2024. The magnitude 7.6 earthquake caused extensive damage to homes and lifelines. After the disaster, 404 evacuation centers were set up and 33,530 people evacuated. Noto Peninsula area has a high aging population and lifelines were severely damaged, Ishikawa Prefecture set up a 1.5 evacuation center at the Ishikawa Sports Center in Kanazawa City on January 8, and wide-area evacuation of disaster victims from the Noto area was implemented. The Ishikawa JRAT established a Disaster Response Headquarters on January 3, and in cooperation with regional JRATs of each prefecture, has been working at evacuation centers in the Noto region and Sports Center to improve the environment, perform rehabilitation triage of victims, prepare welfare equipment, and support evacuees' activities and participation. By March 15, 2024, a total of more than 4,500 JRAT members have worked to support disaster victims. In this session, I would like to report on how JRAT operated during the Noto Peninsula earthquake and discuss the importance of rehabilitation support in the event of a large-scale disaster.

# Evening Seminar

## ES1-1

**Challenge to unmet needs in rheumatoid arthritis with methotrexate and TNF inhibitors**

Yuko Kaneko
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine

Conflict of interest: Yes

Rheumatoid arthritis is a disease with chronic destructive arthritis as the predominant pathology. Its symptoms include not only persistent joint pain, but also irreversible functional impairment and extra-articular symptoms associated with joint destruction, which have a significant impact on patients' quality of life and life expectancy. Rheumatoid arthritis used to represent an intractable immune disorder, but its treatment underwent a paradigm shift about 20 years ago. Remarkable progress has been made due to the establishment of small-dose intermittent methotrexate administration and the development of molecularly targeted therapies that directly inhibit pathologically important molecules, such as biologics and JAK inhibitors, which have a good balance of efficacy and safety. Once rheumatoid arthritis has been diagnosed, remission can now be achieved by following a treat-to-target strategy, aiming for clinical remission and making full use of these drugs in appropriate therapeutic interventions. However, behind the improvement in the quality of life and long-term prognosis of rheumatoid arthritis patients, there are still unmet needs, such as multidrug-resistant D2T cases, drug side effects and the management of elderly-onset cases. Appropriate use of methotrexate and TNF inhibitors is also important to reduce side effects and avoid creating D2T cases. Today, I will present past and current evidence on methotrexate and TNF inhibitors and discuss how to address those unmet needs.

## ES1-2

**Future issues in the treatment of rheumatoid arthritis: considering the role of JAK inhibitors**

Kimito Kawahata
Rheumatology and Allergology, St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan

Conflict of interest: Yes

The results of rheumatoid arthritis treatment have changed significantly due to the widespread use of methotrexate, the advent of molecular-targeted drugs, and the implementation of T2T strategies. In the Ninja cohort, the CDAI remission rate has significantly increased from 8.8% in 2002 and 26.4% in 2011 to 38.6% in 2019. As a result, mHAQ decreased from 0.70 in 2002 and 0.48 in 2011 to 0.37in 2019, and the average age at death, which is an important outcome, increased from 70.6 years in 2002-2004 and 73.6 years in 2010-2011 to 77.4 years in 2018-2019. However, activities of daily living and life prognosis continue to improve. On the other hand, many issues remain in the treatment. Clinical remission, particularly the induction of remission in patients with early rheumatoid arthritis, still requires further improvement. Furthermore, there is a need to expand medical care that also focuses on patient-reported outcomes. This has a major impact on patient satisfaction. To achieve this, it is necessary to provide care for pain, fatigue, and stiffness, which requires efforts across the entire clinical practice, from communication between patients and doctors to treatment. Furthermore, there is insufficient data regarding the treatment of patients with special patient backgrounds, such as those with interstitial pneumonia or a history of malignancies, and this is an important topic for future clinical research. Furthermore, as the population continues to age, the actual situation of rheumatoid arthritis patients who are no longer being treated by specialists should be clarified in the future. In this lecture, I would like to discuss the role that JAK inhibitors, particularly upadacitinib, should play in addressing these issues.

## ES2-1

**Recent real-world evidence of baricitinib treatment in patients with rheumatoid arthritis ~ Japanese PMS data and the RA-BE-REAL study ~**

Takao Fujii
Rheumatology and Clinical Immunology, Wakayama Medical University, Wakayama, Japan

Conflict of interest: Yes

Difficult-to-treat RA (D2T-RA) is one of the recent topics in rheumatoid arthritis (RA). Although the causes of D2T-RA are multifactorial, it might suggest a therapeutic limit for biological disease-modifying antirheumatic drugs (bDMARDs). Currently, nine original bDMARDs (boDMARDs) are now approved in Japan and a plenty of evidence has been published for each bDMARD. On the other hand, there are still unmet medical needs in RA and there are cases in which sufficient response cannot be obtained even by the administration of bDMARDs with different modes of action (MOA). JAK inhibitors are a new class of DMARDs that are totally different from bDMARDs. Although their efficacy has been well proven, some concerns regarding long-term safety have been reported. Therefore, JAK inhibitors are often used in cases where bDMARDs including TNF inhibitor are ineffective. In Japan, post-marketing all-case surveillance (PMS) is conducted for all JAK inhibitors with the main purpose of evaluating safety, and baricitinib is the second JAK inhibitor for which all-case surveillance has been completed. In addition, the new real-world evidence of efficacy (RA-BE-REAL study) was recently developed in Europe. Baricitinib is the JAK inhibitor for which evidence of dose reduction has also been shown (RA-BEYOND study). In this presentation, we would like to discuss the more appropriate use of baricitinib in phase II to overcome the unmet needs in RA.

## ES2-2

**Baricitinib versus TNF-inhibitors in Patients with Rheumatoid Arthritis: a Pragmatic, Multicenter, Real-Life Study in a Treat-to-Target Setting after failing csDMARDs**

Mart AFJ van de Laar[1,2,3,4]
[1]Department Psychology, Health and Technology, University of Twente, The Netherlands, [2]Transparency in Healthcare bv, The Netherlands, [3]Department of Medical Cell BioPhysics & TechMed Center, University of Twente, The Netherlands, [4]Erasmus School of Health Policy and Management, Erasmus University, Rotterdam, Netherlands

Conflict of interest: Yes

RA Guidelines advise T2Tprinciples. If the target is not achieved with csDMARD, adding a TNF-inhibitor (TNFi) or a JAK-inhibitor are advised options, considering risks and contraindications. While RCT comparing Bari (citinib) and Adalimumab provided insight into the efficacy under trial conditions, safety of Bari is demonstrated in long-term exposure databases. The reproducibility in real-life remains unclear up to present. To compare efficacy of starting Bari versus TNFi, after csDMARDs, in a real-life T2T setting. b/tsDMARD-naïve RA patients failing to respond to csDMARDs, when pretreated according to T2T principles, disease duration ≦5 years and no contraindications to b/tsDMARD were included. Patients were treated open, using T2T principles, by their physician with a TNFi or Bari. Patients were seen at 0 and 12-weekly until week 48. Assessment was performed at each visit including PROMs. The primary endpoint was NI (&superiority) of Bari versus TNFi with respect to the ACR50 response at week 12. The ACR50 responses were compared. The NI margin for baricitinib was set at -12%. Linear mixed models were used to analyze the other outcomes over the 48 weeks. 199 patients who received a first dose of TNFi (n=102) or Bari (n=97) were included. Baseline was comparable between groups. At 12 weeks, the 95% CI for the difference in the ACR50 response was above zero, in both the PP and ITT. Hence, Bari was found to be NI and superior to TNFi. Other clinical and PRO-measures over the 48 weeks showed, most often statistically, superior responses of Bari over TNFi. (S)AE were comparable in both groups. The PerfectRA study provides real world evidence of superiority of Baricitinib to TNFi in csDMARD refractory RA patients. Analysis of the 2nd endpoints were consistently in favor of the group that started Bari, without unexpected safety signals.

## ES3-1

**Symposium for rheumatoid hand in JCR2024~Surgical treatment of elderly RA patients (RA + OA hand surgery)~**

Yoshiya Arishima

Kohshinkai Ogura Hospital, Kanoya, Japan

Conflict of interest: None

Advances in multidisciplinary treatment for rheumatoid arthritis (RA) have improved the life expectancy of RA patients, and we rheumatology surgeons have more and more opportunities to operate on elderly patients. Nowadays, bone quality has improved, even in the elderly, and we are less likely to encounter extremely fragile joints, such as the mucilaginous type, as in the past. Intraoperatively, there is no synovitis in the joint, and more and more cases present with joints that look like osteoarthritis (OA). In large joints, we have experienced a small number of cases in which knee and hip joint replacements can be performed using the same surgical techniques as for regular OA. On the other hand, hand RA surgeries, are not always handled in the same way as OA. In other words, it is necessary to deal with each case individually, depending on the presence or absence of soft tissue contractures, conditions of adjacent joints, and lesions in other fingers and wrist joints. The theme of this year's panel discussion is "Surgical treatment of elderly RA patients (RA + OA hand surgery). Dr. Takashi Masatomi will present a case of "thumb CM joint," Dr. Natsuko Nakagawa will present a case of "wrist joint," and Dr. Yoshitaka Hamada will present a case of "PIP and DIP joint" and discussed treatment strategies unique to RA, which are different from OA, we would like to deepen the discussion with the participating doctors using the answer pad. In special lectures, Dr. Ryo Oda will talk about "joint-sparing surgery of the hand" and Dr. Asami Abe will talk about "hand echo". We hope that many medical and surgical doctors interested in the rheumatoid hand will attend and help to improve the prognosis of RA patients.

## ES3-2

**Rheumatoid arthritis and joint ultrasonography, rheumatoid arthritis and biologics, both inseparable**

Asami Abe
Department of Rheumatology, Niigata Rheumatic Center, Shibata, Niigata, Japan

Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has changed significantly with advances in therapeutic drugs. By providing powerful treatment at an early stage of onset, it is possible to create a state in which there is almost no joint destruction, and the patients are possible to live as before the onset of the disease. However, there are still cases in which the timing of treatment is delayed and the treatment does not proceed well due to complications, resulting in joint destruction. Joint ultrasonography is said to be a stethoscope for rheumatologists because it does not involve radiation exposure, is simple, low-cost, and can be performed on any joint regardless of the location of the examination. Furthermore, the quality of images has improved remarkably due to advances in machinery, and it has established a solid position as a diagnostic imaging. However, it often depends on the experience and skill of the examiner. There is also data showing that the combination of joint ultrasonography and joint palpation in patients with rheumatoid arthritis has improved the palpation technique of examiners, which has shown its usefulness. Arthritis of the fingers and inflammation of the flexor tendons, which are common initial symptoms of RA, can be confused with other diseases. In daily practice, many patients complain of functional disorders such as pain on the volar side of the fingers and difficulty bending. In postmenopausal women, it is often due to thickening of the ligamentous tendon sheath (A1 pulley), which causes finger extension and flexion disorders. Flexor tendon synovitis may also be an early symptom of RA. Swelling and pain can also be considered as early symptoms of psoriatic arthritis dactylitis. Other examples include osteoarthritis of the fingers and arthritis. The flexor tendon of the fingers is located on the palmar side of the finger, but it is a little deeper, so it is less visible from the surface of the skin than the extensor tendon. Anatomically, the flexor digitorum superficialis and the flexor digitorum profundus are covered by ligamentous tendon sheaths and synovial tendon sheaths. Recently, it has been found that inflammation around the flexor tendon appears as an early symptom of psoriatic arthritis, and joint ultrasonography has made it easier to diagnose. Based on the above, as a rheumatic surgeon, I will describe the usefulness of joint ultrasonography.

## ES3-3

**A new surgical strategy pioneered by biological agents, the possibility of joint-preserving surgery**

Ryo Oda, Naoki Okubo, Shogo Toyama, Daisaku Tokunaga, Kenji Takahashi
Department of Orthopaedics, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Conflict of interest: None

RA develops in the hands, causing characteristic deformities that are often difficult to treat, and is called rheumatoid hand to distinguish it from other hand deformities. As the disease progresses, it interferes with daily life, so it is important to provide appropriate treatment at the appropriate time. In recent years, with the advent of biological agents and the unrelenting efforts of hand surgeons, the results of rheumatoid hand surgery have gradually improved, leading to a highly recommended treatment with high patient satisfaction. Furthermore, even if diagnosis and treatment were performed in accordance with the guidelines, deformities and functional impairments in the upper limbs, especially the hands, were shown to worsen over time. Therefore, it is necessary to perform therapeutic intervention at an appropriate time to prevent deterioration of upper limb function and to perform functional reconstruction. As for the surgical method, the ideal first choice would be soft tissue reconstruction from the perspective of joint preservation, which is a common cause of rheumatoid foot. Even in RA, where joint destruction is said to be the essence of the disease, joint-preserving surgery, a new surgical strategy pioneered by biological agents, has become a realistic option. Since progression of deformity and residual pain are problems in RA, it is necessary to appropriately evaluate age, degree of bone destruction, joint pain, disease activity, etc., and select the timing and method of surgery. If joint destruction has progressed, arthrodesis, arthroplasty and joint replacement may be combined to improve the function of the hand, taking into consideration the condition of adjacent joints, and surgical methods should be selected with long-term results in mind. Furthermore, to improve surgical outcomes, it is important not only to be proficient in surgical techniques but also to accurately judge the local condition and decide on the surgical method. In addition to providing appropriate drug therapy to prevent further deformities from occurring, interventions such as braces and surgery should be performed at the appropriate timing for functional restoration of hands that have already developed. In other words, it is expected that "total management of rheumatoid hand" will be established.

## ES4-1

**Discovery of nanobody molecules (VHH) and their application to antibody drugs**

Yuji Ito
Graduate School of Science and Engineering, Kagoshima University

Conflict of interest: None

Antibody drugs have developed rapidly over the last two decades to such an extent that they account for five of the top 10 drugs in global drug sales, showing great achievements. Antibodies are protein molecules that bind specifically to antigens and eliminate them; hence, antibody drugs exert high efficacy owing to their high molecular targeting capacity. Antibodies also have multiple mechanisms of action as a drug, which adds to their efficacy. Targeting, signaling, and blocking antibodies, etc. are differentiated based on the characteristics of their mechanisms. VHH, a low-molecular-weight antibody, differs from the ordinary IgG antibody and consists of two heavy chains with defects in the $CH_1$ domain of the heavy chains. VHH can be humanized, and its application as a therapeutic drug has been investigated via attenuating VHH antigenicity during human administration. The VHH antibody has a low molecular weight of approximately 13000-15000, and is characterized by high tissue permeability after administration. In addition, the structural characteristics of a single domain enable the enhancement of the antibody function via antibody engineering, such as enhancing their affinity for antigens via connecting single domains. Ozoralizumab (OZR), an anti-tumor necrosis factor (TNF)-α drug, was the first VHH drug released in Japan. OZR has a structure of three VHHs linked by a linker. The first and third VHHs recognize and bind to TNF-α and the second VHH recognizes and binds to human serum albumin (HSA) in the blood. Binding to HSA in a mouse surrogate anti-

body of OZR has been reported to overcome the short blood half-life, which is a drawback of low-molecular-weight antibodies. In this lecture, I wish to discuss the discovery of heavy chain antibodies, the development of VHH antibodies, and the commercialized nanobody product OZR.

## ES4-2

**Latest Findings regarding a Novel TNF Inhibitor, Ozoralizumab**

Tsutomu Takeuchi[1,2]
[1]Saitama Medical University, [2]Keio University

Conflict of interest: Yes

Symptomatic treatment with drugs such as nonsteroidal anti-inflammatory drugs and steroids has previously been the mainstay of treatment for rheumatoid arthritis (RA). However, the advent of biologics (biological anti-rheumatic drugs) has enabled the achievement of a realistic goal of remission by strongly inhibiting the progression of joint destruction. Furthermore, the advent of JAK inhibitors, which are small-molecule oral drugs with the same efficacy as biologics, has greatly expanded the drug treatment options for RA. Such progress in therapeutic drugs has established a treat-to-target strategy for RA treatment. Although biologics and JAK inhibitors are highly effective, their cost is high. Therefore, further issues for treatment have emerged, such as predicting the therapeutic effect of each drug, stopping/reducing drug dosage after remission, and prolonging dosing intervals. Long-term treatment strategies are required for various existing anti-rheumatic drug types. Tumor necrosis factor (TNF) inhibitors first appeared among the anti-rheumatic biologics and JAK inhibitors. Based on long-term experience and sufficient clinical evidence, they are positioned as first-line drugs for standard treatment with biologics. The usage of TNF inhibitors has already been established based on their efficacy and safety. Nevertheless, many studies have been conducted and new evidence has been reported. In this seminar, I will review the development of RA treatment, the role of TNF inhibitors in treatment, and the usage of these drugs in actual clinical practice. In the latter half of the seminar, I will introduce data from two Japanese clinical studies of a newly launched TNF inhibitor, ozoralizumab: the OHZORA study (in combination with MTX) in patients receiving MTX-IR, and the NATSUZORA study in patients not receiving MTX. I will also discuss ozoralizumab administration during RA treatment.

## ES5

**ICAP recommendation update - how can we maximize clinical significance of antinuclear antibody (ANA) test -**

Tsuneyo Mimori
Takeda Clinic for Rheumatic Diseases

Conflict of interest: None

Anti-nuclear antibody (ANA) test detects autoantibodies against nuclear antigens and is ordered when systemic autoimmune diseases such as connective tissue diseases are suspected. Since ANA test uses HEp-2 cells as substrates, it can detect autoantibodies that react with antigens in the cytoplasm as well as in the nucleus. However, in Japan most laboratories have not reported cytoplasmic patterns in detail. The International Consensus on ANA Patterns (ICAP) was organized to discuss an international consensus on cell staining patterns observed in the indirect immunofluorescent assay (IFA) using HEp-2 cells and to promote harmonization. ICAP also proposed recommendations related to ANA testing and reporting. In Japan, some laboratories have started implementing detailed reporting based on ICAP recommendations in ANA test reports since October 2023. In this session, the domestic and international movement of ICAP harmonization and the clinical utility of ANA tests will be discussed.

## ES6-1

**Hot Topics in Osteoimmunology**

Masayuki Tsukasaki
Department of Osteoimmunology, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo

Conflict of interest: Yes

In rheumatoid arthritis, synovial fibroblasts function as the main source of osteoclast differentiation factor RANKL which causes bone damage. However, the precise molecular mechanism underlying RANKL expression has remained poorly understood. Recently, we identified a synovial fibroblast-specific RANKL enhancer involved in bone damage associated with rheumatoid arthritis (Yan et al., Nature Immunology 2022), an osteocyte-specific RANKL enhancer responsible for physiological bone metabolism (Yan, Tsukasaki* et al., Bone Research 2023) and a periodontal ligament/osteoblast-specific RANKL enhancer involved in bone damage associated with periodontitis (Ando, Tsukasaki* et al., in revision). These data highlight the cell type- and context-dependent machinery underlying RANKL regulation. The periosteum, a membranous tissue covering the outer surface of bones, houses a unique class of osteogenic stem/stromal cells that contribute to fracture repair. We recently found that periosteal stem cells contribute to physiological bone elongation (Tsukasaki et al., Nature Communications 2022) and that stromal cells in the periosteum possess a capacity to inhibit tumor progression (Nakamura, Tsukasaki* et al., in revision), shedding light into the unexpected functions of the periosteum as the key component of the osteoimmune system. In this seminar, I will introduce the current hot topics in the osteoimmunology field by focusing on the synovium, periosteum and RANKL biology.

## ES6-2

**Current status and future of precision medicine in rheumatoid arthritis**

Keishi Fujio
Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo

Conflict of interest: Yes

In rheumatoid arthritis (RA), the high efficacy of biologics and oral JAK inhibitors has contributed to improved outcomes, but there are still cases of inadequate response to drug therapy. The reason for such heterogeneity in response is assumed to be the heterogeneous and highly individualized nature of the pathogenesis of RA, which involves a variety of immune cells. At present, it is difficult to predict therapeutic response in advance, and how to use different types of molecular-targeted drugs is also a clinical issue. Recent advances in genome-wide association analysis, next-generation sequencing, flow cytometry, etc. have made it possible to precisely evaluate the human immune system, at least at the research level. In particular, the finding that different synovial cell phenotypes respond differently to treatment with molecularly targeted drugs is a major step forward. The combination of such information with clinical cohorts will greatly contribute to the elucidation of new pathophysiology, disease stratification, and therapeutic development in RA, and is expected to be applied to precision medicine through new stratification of rheumatoid arthritis patients using biomarkers. Even in peripheral blood, which is relatively easy to analyze, it is becoming clear that dendritic cell subsets and the percentage of various T cells are associated with resistance to treatment. In this lecture, the need for stratified medicine in the treatment of rheumatoid arthritis will be discussed, including the current status and future prospects of the genetic analysis approach in particular.

## ES7-1

**Significance of Proteinuria in the Treatment of Lupus Nephritis**

Keiju Hiromura
Department of Nephrology and Rheumatology, Gunma University Graduate School of Medicine

Conflict of interest: Yes

In lupus nephritis, immune complexes including anti-dsDNA antibodies and DNA are deposited in the glomerular capillary walls and mesangial regions, causing glomerular damage through the activation of complement and infiltration of inflammatory cells. As a result, proteinuria occurs. Even with mild vascular lesions (corresponding to ISN/RPS classification Class I/II), some patients exhibit significant proteinuria, suggesting that glomerular epithelial cells may be damaged by mechanisms other than immune complex deposition, a condition known as lupus podocytopathy. Proteinuria is an important indicator of renal involvement in patients with SLE. In healthy individuals, proteinuria is less than 0.5 g/day, while the Japanese

designated intractable disease diagnostic criteria (ACR classification criteria 1997 edition), EULAR/ACR classification criteria 2019 edition consider proteinuria of 0.5 g/day or more as a criterion for renal involvement. Furthermore, proteinuria is an important indicator of treatment responsiveness and prognosis prediction in lupus nephritis. Proteinuria of 0.3-0.5 g/day has been used as one of the indicators of complete remission. Subsequent post-hoc analysis of the ELNT and ALMS trials data indicated that proteinuria of less than 0.7-0.8 g/day after 12 months of initial treatment is a good predictor of long-term renal prognosis. Based on this, the EULAR/ERA-EDTA lupus nephritis treatment recommendations 2019 edition set treatment goals including maintaining renal function and reducing proteinuria by 25% within 3 months, 50% within 6 months, and proteinuria/urine Cr to 0.5-0.7 g/gCr or less within 12 months. On the other hand, there are reports that earlier (within 3 months) or more substantial proteinuria remission (less than 0.15 g/day) leads to long-term suppression of renal relapse and organ damage in SLE. This seminar will explain the significance of proteinuria in the treatment of lupus nephritis, incorporating the latest findings.

## ES7-2

**Pathophysiology of SLE/Lupus Nephritis from Podocytes**

Kunihiro Ichinose
Department of Rheumatology, Shimane University Faculty of Medicine, Japan

Conflict of interest: Yes

Lupus nephritis (LN), associated with systemic lupus erythematosus (SLE), is a condition that significantly impacts patient prognosis. In particular, the impairment of glomerular epithelial cells, known as podocytes, is key to understanding the pathology of LN. Podocytes, situated above the glomerular basement membrane, extend octopus-like projections and function as a barrier against proteinuria. The mechanisms of podocyte damage, including dedifferentiation, detachment, and cell death, lead to proteinuria and irreversible glomerular damage, which contribute significantly to the progression of LN. Moreover, podocytes express immune-related molecules such as CD80/CD86, MHC Class II, FcRn, TLRs, NLRP3, and CaMK4, deeply involving them in the inflammatory response of autoimmune diseases. Notably, the activation of the NLRP3 inflammasome promotes the production of IL-1β through caspase-1, contributing to the increased inflammation and cellular damage in LN. The inhibition of podocyte-specific CaMK4 has been shown to contribute to the maintenance of the cytoskeleton and improvement of proteinuria, promising a new therapeutic approach. Additionally, tacrolimus as a calcineurin inhibitor (CNI), is reported to improve proteinuria through the protection of podocytes, promoting recovery post-glomerular damage and consequently reducing inflammation. The protective function of CNI in podocytes represents a new development in the treatment of renal diseases. Furthermore, the changes in podocytes during the progression of the disease, such as dedifferentiation and re-entry into the cell cycle, are garnering attention, with the activation of the JAK/STAT3 pathway and miR-92a suggesting potential control over these processes. This presentation aims to provide a detailed account of these molecular mechanisms and the interaction with podocytes, offering a new perspective on the understanding of pathology and the development of treatment strategies for LN.

## ES8-1

**Management Tips of Respiratory Tract Infections in Patients with Rheumatoid Arthritis**

Kazuko Yamamoto
University of the Ryukyus

Conflict of interest: Yes

Rheumatoid arthritis (RA) is frequently associated with lung involvement, and it is known that respiratory disease is the main cause of death among RA patients in Japan, unlike in Europe and the U.S. Immune disorders caused by RA itself, as well as biologic agents (BIOs) and steroids used to treat RA, can contribute to respiratory tract infection (RTI) and affect the prognosis of patients. Management of RTI is particularly important in patients with RA. Worldwide studies of novel coronavirus infection (COVID-19) have showed that RA itself is not a risk for severe disease. However, RA with high disease activity, the elderly, and patients being treated with immunosuppressive drugs are at risk for severe disease of COVID-19. These RA patients have a low antibody-producing response to the SARS-CoV-2 vaccines and require prompt antiviral therapy, even if they are mildly ill at the time of COVID-19 diagnosis. Two years have passed since the omicron mutant strain became endemic, and routine vaccination against the SARS-CoV-2 mutant strain will be an important practice for RA patients in the future. Pneumonia complicating RA patients is a serious problem with a high mortality rate. Our study showed that approximately 10% of RA patients with BIO developed pneumonia over a 3-year period, and that the presence of pre-existing pulmonary lesions was the most relevant risk factor for developing pneumonia. Vaccination to prevent pneumonia may be particularly important for RA patients with preexisting lung lesions. The treatment of RA-associated pneumonia should be based on the classification of nursing home-acquired pneumonia. Antimicrobial therapy should be given with attention to the higher mortality rate and isolation of drug-resistant organisms compared to usual community-acquired pneumonia. Pulmonary nontuberculous mycobacterial (pNTM) disease is also a major problem in RA patients. Early diagnosis by microbiology testing and chest imaging is important because of its high prevalence and frequent worsening during RA treatment. Antimicrobial therapy for pNTM is necessary, taking into account of drug interactions with RA medications. Depending on the status of pNTM disease, treatment for RA may have to be modified or discontinued. In patients with RA, differentiation of pNTM from other microbial infections and mixed infections are also often problematic. In this lecture, I would like to discuss the managements of RTI in RA patients, showing the latest evidence and data from our study.

## ES8-2

**Short-term epigenetic memory in innate immune cells after consecutive BNT162b2 mRNA vaccination**

Atsushi Kumanogoh, Yuta Yamaguchi, Yasuhiro Kato
Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine, Osaka University, Osaka, Japan

Conflict of interest: None

Since the start of the coronavirus disease 2019 (COVID-19) pandemic in December 2019, more than 700 million people have been infected, and by the end of 2022, more than 6 million people had died. As part of the effort to combat the COVID-19 pandemic, vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were rapidly developed. mRNA-based vaccines that encode the SARS-CoV-2 spike protein were one of the first administered and have shown its efficacy. Consecutive mRNA vaccinations elicited both innate and adaptive immune responses. However, it remains unclear whether the enhanced innate immune responses are accompanied by epigenetic modulation and whether these effects persist in such cases. Using RNA-seq, and ATAC-seq, our research revealed that BNT162b2 mRNA vaccination upregulated antiviral and IFN-stimulated gene expression in monocytes with greater effects after the second vaccination than those after the first vaccination. Transcription factor-binding motif analysis identified enriched IFN regulatory factors and PU.1 motifs in accessible chromatin regions. Notably, although consecutive BNT162b2 mRNA vaccinations enhanced innate immune responses and caused epigenetic changes in monocytes, these effects occurred only transiently and disappeared 4 weeks after the second vaccination. Additionally, single-cell RNA sequencing analysis indicated that a similar gene signature was impaired in the monocytes of unvaccinated COVID-19 patients with acute respiratory distress syndrome. These findings underscore the role of the importance of the innate immune response in the determination of COVID-19 severity but indicate that, unlike adaptive immunity, innate immunity is not sustained despite consecutive vaccinations. This study, focusing on innate immune memory, may provide novel insights into the vaccine development against infectious diseases.

## ES9-1

**The Potential of IL-6 in Autoimmune Diseases from the Perspective of new imaging modality**

Georg Schett
Department of Internal Medicine 3 Rheumatology and Immunology, Friedrich Alexander University Erlangen-Nürnberg, Germany

Conflict of interest: Yes

Rheumatoid arthritis (RA) is a systemic, inflammatory disease causing joint inflammation and bone loss. Key in managing RA is the correct identification and monitoring of bone erosions, indicative of progressive arthritis and linked to functional impairment. High Resolution-peripheral Quantitative Computer Tomography (HR-pQCT) is effective in evaluating peripheral bone microarchitecture and assessing bone changes in RA. Proinflammatory cytokines, particularly TNF-alpha and IL-6, trigger bone erosions by disturbing local bone metabolism. The anti-IL-6 receptor antibody tocilizumab (TCZ) has been found to repair existing bone erosions in RA patients, suggesting a homeostatic role of IL-6 in bone. IL-6 inhibition is also central to treating giant cell arteritis (GCA), a condition with limited treatment options. IL-6 is a key mediator of vascular inflammation in GCA patients, with levels correlating with disease activity. GiACTA trials reveal that TCZ, received weekly or every other week, combined with a 26-week prednisone taper, outperforms either 26-week or 52-week prednisone tapering plus placebo in inducing sustained glucocorticoid-free remission in GCA patients. TCZ reduces vascular inflammation faster than methotrexate or prednisolone monotherapy, and lowers the cumulative prednisolone dose, enabling most patients to stop prednisolone, thus avoiding its side effects. This symposium will explore new possibilities related to IL-6 for tissue regeneration in inflammatory diseases like RA and GCA.

## ES9-2

**The Role of IL-6 in the etiology of rheumatoid arthritis**

Satoshi Kubo
Department of Molecular Targeted Therapies, University of Occupational and Environmental Health, Japan

Conflict of interest: Yes

Rheumatoid arthritis (RA) disproportionately affects relatively young women, significantly impacting their lives due to irreversible joint destruction. The incidence of RA in monozygotic twins is around 15%, indicating a combination of genetic predisposition and environmental factors triggering an exaggerated immunoallergic response. Genome-wide association analyses (GWAS) have identified disease susceptibility genes for RA, and with GWAS involving 250,000 individuals, the genetic background is nearly unveiled. However, gaps persist in understanding genetic predisposition, particularly regarding rare nonsynonymous substitution mutations not captured by GWAS. Meanwhile, Japan has approved four classes of molecular targeted therapies for RA, all considered as targeting the etiologies of RA. IL-6 signaling inhibition, implemented in daily practice since 2008, has accumulated 15 years of evidence. IL-6 plays diverse roles in immunity, inflammation, and regeneration, and its signaling inhibition is now insurance-covered for adult Still's disease, giant cell arteritis, and Takayasu's arteritis. This presentation will delve into the significance of IL-6 in RA, drawing on genetic predisposition, treatment outcomes, and immunophenotyping results.

## ES10-1

**New insights into the roles of Janus Kinases for the pathogenesis of rheumatoid arthritis**

Yoshinori Matsumoto
Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Faculty of Medicine, Dentistry and Pharmaceutical Sciences

Conflict of interest: Yes

Significant progress in the treatment of rheumatoid arthritis has been achieved through the appropriate use of methotrexate and the advent of biologics/JAK inhibitors. Rheumatoid arthritis is now in an era in which remission is possible, and fewer patients present with significant joint deformities as in the past, but there are a certain number of patients with difficult-to-treat rheumatoid arthritis (D2TRA) in whom controlling joint destruction is challenging. In patients with comorbidities and organ damage, there are cases where a reduction in treatment intensity becomes inevitable. In addition, with the increase in the number of elderly rheumatoid patients in recent years, interstitial pneumonia and impaired renal function have made the use of methotrexate difficult in some cases. In order to achieve clinical and structural remission in a larger number of patients and to help them return to social activities, it is necessary to select appropriate diagnosis and treatment from the early stage of disease onset and to deal with difficult-to-treat cases such as those with organ complications and coexisting chronic infectious diseases. The onset and pathogenesis of rheumatoid arthritis are complicated by environmental factors such as tobacco, periodontal disease, and intestinal microflora, in addition to genetic factors, and inflammatory cytokines produced by abnormal activation of innate and acquired immune systems are involved. They stimulate immune cells and synovial fibroblasts, and RANKL/MMP production induces bone and cartilage destruction. VEGF production is also known to contribute to pannus formation. In recent years, the detailed regulatory mechanism of RANKL/MMP-3 has been gradually elucidated, and treatment that addresses not only bone destruction but also cartilage destruction is required to suppress joint destruction. JAK is a tyrosine kinase, a substrate protein, and phosphorylates/activates the transcription factor STAT, a substrate protein, downstream of receptors for many inflammatory cytokines and growth factors, thereby increasing the expression of target cytokine genes. From these actions, JAK is known to be directly/indirectly involved in various pathological states of rheumatoid arthritis, and JAK is also thought to be involved in pain stimulation in rheumatoid arthritis. In this seminar, based on recent reports, I will summarize the roles of JAK in the pathogenesis of from a basic perspective.

## ES10-2

**Therapeutic strategy of JAK inhibitor for consideration of safety issue**

Hironari Hanaoka
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Conflict of interest: None

The treatment of rheumatoid arthritis (RA) has undergone a paradigm shift with the advent of biologic agents. However, there remains a subset of patients with difficult-to-treat RA (D2TRA) who do not respond well to multiple biologic agents, making their treatment challenging. Janus kinase (JAK) inhibitors are positioned in the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) treatment recommendations at a similar level to biologic agents and are expected to be effective for D2TRA. Tofacitinib was first approved for RA treatment in 2013, and by 2023, a total of five JAK inhibitors are available. While they have shown the convenience of oral administration, JAK inhibitors have a safety profile that differs from biologic agents, necessitating cautious use. Concerns have been raised based on the results of the ORAL Surveillance trial, which primarily evaluated long-term safety, regarding major cardiovascular events, malignancies, and herpes zoster. In response to these concerns, in 2021, the European League Against Rheumatism (EULAR) issued a consensus statement regarding the use of JAK inhibitors for immune-mediated inflammatory diseases, including rheumatoid arthritis. This statement provides expert opinions on the safety of JAK inhibitors across diseases and addresses risk assessments related to age, smoking, cardiovascular events, thromboembolic events, malignancy screening, and vaccination. Additionally, recent sub-analyses of the ORAL Surveillance trial have provided detailed risk assessments for major cardiovascular events and malignancies. While the long-term safety of JAK inhibitors is a critical issue, it is important to note that most international data do not include specific data for Japanese patients with rheumatoid arthritis. Therefore, there is a need for large-scale data collection targeting Japanese patients to better understand the safety of JAK inhibitors. This discussion aims to consider the safety of JAK inhibitors and the corresponding strategies.

## ES10-3

**The effectiveness of JAK inhibitor: perspectives from real-world data**

Akira Onishi
Department of Advanced Medicine for Rheumatic Diseases, Kyoto University Graduate School of Medicine

Conflict of interest: Yes

Based on the results of the ORAL Surveillance trial, the European

League Against Rheumatism (EULAR) recommendation 2022 for the management of rheumatoid arthritis (RA) was updated as "If the treatment target is not achieved with the first csDMARD strategy, when poor prognostic factors are present, a bDMARD should be added; JAK inhibitors may be also considered, but pertinent risk factors, such as major adverse cardiovascular events (MACE), malignancy, and thromboembolism must be taken into account." in the phase II. On the other hand, some patients with RA remain symptomatic despite treatment based on the currently recommended treat-to-target (T2T) strategy. This subgroup of patients is clearly defined by the EULAR Task Force as difficult-to-treat rheumatoid arthritis (D2T RA). D2T RA is defined as: "(1) Treatment according to EULAR recommendation and failure of ≧2 bDMARDs/JAK inhibitors with different mechanisms of action after failing csDMARD therapy; (2) Signs suggestive of active/progressive disease, defined as ≧1 of 5 signs; and (3) the management of signs and/or symptoms is perceived as problematic by the rheumatologist and/or the patient." Several cohort data indicate that D2T RA accounts for approximately 10% of all RA cases. D2T RA is a heterogenous population, including patients with difficulty in controlling arthritis due to resistance to DMARDs, drug adverse effects, comorbidities, and poor adherence, and non-inflammatory conditions such as pain due to fibromyalgia, osteoarthritis, and psychiatric disorders including depression and anxiety. This presentation will focus on D2T RA and comorbidities such as interstitial lung disease and renal dysfunction that may contribute to D2T RA, making it difficult to use methotrexate (MTX), and introduce the effectiveness of JAK inhibitors from real-world data.

## ES11

**Osteoporosis Management in Elderly Rheumatoid Arthritis Patient**

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Conflict of interest: Yes

Japan has one of the longest life expectancies in the world, but at the same time, the aging rate is increasing at an unprecedented level. Reflecting this aging population, rheumatoid arthritis (RA) patients are also aging. According to *NinJa*, a national database of RA patients, the average age of the entire cohort in 2020 is 67.3 years, nearly five years older than it was 10 years ago. The proportion of elderly RA patients is also increasing, with about 1/3 of all patients in the 2020 data being late-onset RA patients aged 75 years or older, and a very high 16.2% of patients being 80 years or older. Osteoporosis is known to have a high complication rate in RA patients. Osteoporosis in RA presents a complex disease picture, with the coexistence of periarticular osteoporosis, which occurs early in the disease onset, and systemic osteoporosis. Periarticular osteoporosis is characterized by a decrease in subchondral trabecular bone volume early in the course of the disease, which is thought to be due to increased bone resorption and suppression of bone formation by inflammatory cytokines, as well as steroid use and decreased exercise load due to pain. Systemic osteoporosis is also thought to be related to inflammatory cytokines, steroid use, immobility, and vitamin D deficiency due to short daylight hours. RANKL (receptor activator of nuclear factor kappa B ligand)-mediated osteoclast differentiation and activation is known to be involved in the progression of osteoporosis and bone destruction in RA patients. Denosumab, a fully human monoclonal antibody to RANKL, is known not only to increase bone mineral density in RA patients, but also to inhibit the progression of bone erosion. However, it is known that vertebral fractures increase and bone erosion progresses after discontinuation of denosumab, Therefore, the use of appropriate osteoporosis and anti-rheumatic drugs is required. The combination of anti-osteoporosis drugs and anti-rheumatic drugs may enable more appropriate disease management in RA patients.

## ES12-1

**Treatment strategy of axial spondyloarthritis from the viewpoint of its pathogenesis: Exploration for the optimal use of upadacitinib**

Yuya Tabuchi
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Conflict of interest: Yes

Axial spondyloarthritis (axSpA) has been defined according to the classification criteria by the Assessment of SpondyloArthritis International Society (ASAS) (2009). In addition to the onset under the age of 45 and back pain that persists for more than three months, either the combination of sacroiliitis on imaging (X-ray or magnetic resonance imaging) and at least one spondyloarthritis (SpA) feature or that of HLA-B27 positivity and at least two SpA features is required to classify patients into the axSpA group. "The SpA features" comprise inflammatory back pain, arthritis, enthesitis of the heel, uveitis, dactylitis, psoriasis, Crohn's disease/ulcerative colitis, good response to NSAIDs, family history for SpA, and the elevated level of C-reactive protein. This indicates that there are likely to be a variety of immunological profiles among patients with axSpA. In the ASAS-EULAR recommendation for the management of axSpA updated in 2022, JAK inhibitors have been added besides "the current therapy" by TNF inhibitors or IL-17 inhibitors in phase 2, which is adopted when the treatment goal is not achieved by physiological therapy and NSAIDs in phase 1. The approval of JAK inhibitors for axSpA and their advent in recommendations can be a boon to patients with unmet needs in the treatment of axSpA. As for rheumatoid arthritis, a head-to-head RCT named SELECT-COMPARE has shown that there is a group where patients improve after switching from a TNF inhibitor (adalimumab) to a JAK inhibitor (upadacitinib), and vice versa. The same thing is likely to happen in the management of axSpA, considering its immunological heterogeneity. In this session, I will discuss which patients with axSpA are more suitable for upadacitinib, which has been approved for ankylosing spondylitis, non-radiographic axial SpA, and psoriatic arthritis in the area of SpA in Japan, considering the pathogenesis of axSpA in addition to its effectiveness and safety.

## ES12-2

**The treatment strategy for PsA, as a multi-domain disease -Toward achieving MDA-**

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Conflict of interest: None

Psoriatic arthritis (PsA) is a multi-domain disease with heterogeneous condition. PsA most commonly occurs in patients with psoriasis. Enthesitis is a key feature of PsA. Enthesitis could elicit epientheseal bone marrow edema, synovial joint inflammation, tendinitis and peritendinitis. It is pointed out that enthesitis in the distal interphalangeal joints could lead to nail involvement. Enthesitis is greater prevalence in lateral epicondyle, greater trochanter and Achilles tendon. Axial disease can occur, with some experiencing cervical involvement. Understanding of the clinical features is essential to the diagnosis of PsA. There is no consensus of treatment goals. Treat-to-target (T2T) concept has not been fully implemented for PsA. The definition of Minimal Disease Activity (MDA) encompasses several domains of disease involvement. The MDA has been considered a useful target by both the patient and physician. Given the heterogeneity of disease involvement, GRAPPA treatment recommendations for PsA 2022 update utilize a domain-based approach. The etiological events of PsA could be variable in the specific disease domains. As a multi-domain disease, the pathogenesis of PsA involves multiple cytokines, many of which utilize Janus kinase (JAK) pathway. Multiple cytokines signaling blockade by JAK inhibitors could be a promising therapeutic choice across a broad spectrum of first-line treatment to so-called "Difficult-to-treat PsA". The GRAPPA recommends the use of JAK inhibitors as first-line therapy in up to 5 domains. In this seminar, we will introduce the results of SELECT-PsA1/2 trial for the JAK inhibitor Upadacitinib, including improvements in multiple domains, and achievement of MDA, as well as the results of the integrated safety analysis. We also introduce our cases. Based on these, we consider the details to discover the value of Upadacitinib for T2T approach to improve outcomes in patients with PsA.

## ES13-1

**Inhibition of joint destruction by using methotrexate and TNF inhibitors**

Masaru Kato
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ro, Japan

Conflict of interest: Yes

In recent years, many drugs have become available to treat rheumatoid arthritis (RA). However, there is still little knowledge to make them applied in a precision medicine. The combination of methotrexate (MTX) and TNF inhibitors may be an ideal treatment of RA because it is more likely to lead to bio-free remission, MTX inhibits IL-6, and MTX suppresses the generation of anti-drug antibodies. In osteoclast differentiation, which plays a central role in joint destruction that occurs in RA, not only RANKL but also TNFα and IL-6 function as important effectors. Further, TNFα and IFNγ activate synovial fibroblasts, which act as a main source of RANKL in the joints. Recent evidence indicates that some TNF inhibitors, even as monotherapy, exhibit a high efficacy in RA. In this seminar, we will introduce and discuss the latest findings regarding the effect of MTX and TNF inhibitors against joint destruction in RA.

## ES13-2

**Rheumatoid sarcopenia and TNF~TNF destroys muscle~**

Masahiro Tada
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Conflict of interest: Yes

Early diagnosis, early treatment, Treat to Target, and bs/ts DMARDs have led to the induction and maintenance of remission in patients with rheumatoid arthritis (RA). The quality of life (QOL) has become comparable to that of healthy individuals, and lifestyles have become more diverse. The prevalence of sarcopenia in RA is 35%, which is higher compared to 10% in healthy individuals. There is a mutual relationship between RA and sarcopenia, and the coexistence of both is defined as rheumatoid sarcopenia. TNF decreases muscle mass in animal models and basic research. TNF induces MuRF-1 and Atrogin-1 via NF-κB, inhibiting muscle synthesis, and it also inhibits transcription factors that induce muscle synthesis, such as MyoD and Myogenin. TNF has a catabolic effect on muscles. In high disease activity patients, elevated TNF values in the blood and joints are likely to contribute to muscle mass reduction and the development of sarcopenia. In clinical practice, the non-use of biologic agents has been reported as a risk factor for sarcopenia in RA. Furthermore, reports of increased muscle mass have been observed in RA patients treated with TNF inhibitors. Based on both basic research and clinical practice, the use of TNF inhibitors lead to increased muscle mass and the suppression of sarcopenia. To increase muscle mass in RA patients, it is essential to control disease activity, reduce and stop glucocorticoid, exercise, and nutrition. The EULAR 2021 recommendations for lifestyle and work participation, "Exercise is beneficial not only for the symptoms and progression of rheumatic diseases but also for overall health." They also recommended "A healthy and balanced diet is integral to lifestyle improvement for people with rheumatic diseases." We will examine the impact of TNF on muscles in RA, the importance of preventing sarcopenia, and the effects of exercise and nutrition, based on a review of the literature. We look forward to discussing these topics with all of you.

## ES14-1

**Treatment strategies considering the life stages of young rheumatoid arthritis (RA) patients -Issues in RA treatment for the WoCBA generation-**

Yuri Hiramatsu
Rheumatism and Collagen Disease Internal Medicine, Osaka Medical and Pharmaceutical University

Conflict of interest: None

Women go through various life stages (puberty, sexual maturity, menopause, early adulthood, and old age) accompanied by changes in female hormones. One of the major life events for women is pregnancy and childbirth. In patients with RA Although unplanned pregnancies are extremely common, accounting for approximately half of all pregnancies, we often experience patients who are unable to get pregnant due to vague and severe anxiety about pregnancy and childbirth. Recently, the importance of preconception care (PCC) has been pointed out both in Japan as a whole and in the field of collagen diseases. For patients with chronic diseases, regardless of whether or not they currently wish to become pregnant, PCC is aimed at providing 1) general health education (understanding lifestyle habits, childbearing age, etc.) as early as possible, as well as 2) preparations for pregnancy. By providing two-step care: disease management (developing mutual understanding between medical professionals and patients regarding diseases, treatments, and timing of pregnancy), patients can plan their pregnancy with peace of mind. It has been reported that RA with high disease activity in the pre-pregnancy stage is associated with decreased fertility and a high risk of miscarriage, premature birth, and low birth weight even after pregnancy, whereas RA with stable disease activity Pregnancy outcomes for complicated pregnancies are similar to those for other pregnancies. It is recommended to continue treating to target, paying attention to the safety of both mother and baby, from before pregnancy, throughout pregnancy, and even while breastfeeding. Since young RA patients have a long period of disease, it is important for medical professionals and patients to share correct knowledge and life plans, to sufficiently suppress disease activity from the early stage of onset, and to select treatments that take into account various future life events. In this presentation, we will consider treatment strategies for young women with rheumatoid arthritis.

## ES14-2

**Unraveling the Potential of Certolizumab Pegol Based on Its Structural Properties: Results from the ANSWER Cohort**

Ryu Watanabe
Department of Clinical Immunology, Osaka Metropolitan University Graduate School of Medicine

Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has advanced dramatically with the advent of biologic agents and JAK inhibitors. However, even with these agents, there are cases in which disease activity is not adequately controlled. In addition, a patient profile has been identified in which administration of JAK inhibitors is not desirable from a safety perspective. Thus, an in-depth understanding of characteristics of both the patients and the therapeutic agents will enable optimal drug selection for patients with RA. TNF inhibitors have demonstrated long-term efficacy and safety for patients with RA. Among them, certolizumab pegol (CZP) has no Fc portion, has data on placental transfer, and is used in young female patients. In addition, PEGylation prolongs its half-life and increases its hydrophilicity, making it more likely to accumulate at inflammatory sites. Furthermore, the efficacy of TNF inhibitors with the Fc portion is generally known to be reduced in patients with high titers of rheumatoid factor (RF), but CZP does not decrease blood drug concentration even in patients with high titers of RF and is effective regardless of RF levels. In this seminar, the potential of CZP based on its structural properties will be discussed along with the data of CZP in the Kansai Multicenter Cohort (ANSWER cohort).

## ES15

**Mechanisms and Countermeasures for Bone Fragility Associated with Steroids, RA, Psoriasis, and Lifestyle-related Diseases: A Paradigm Shift in Osteoporosis Treatment Opened by Artificial Intelligence (AI) and Mass Spectrometry**

Mitsuru Saito
Department of Orthopaedic Surgery, Jikei University School of Medicine, Tokyo, Japan

Conflict of interest: Yes

Bone quality is thought to encompass the structural and material properties of bone that are affected by turnover rate. The concept of bone quality is included in Japanese Guideline for Osteoporosis prevention and treatment. Evidence has accumulated that collagen cross-links play important roles in bone strength. We have demonstrated that the quantitative and qualitative deterioration of lysyl oxidase controlled and non-enzymatic cross-links (Advanced glycation end products, AGEs, Pentosidine) of collagen in patients with osteoporotic femoral neck fracture cases might be affected by hyperhomocysteinemia (Saito M, Calcif Tissue Int, 2006) oxidative stress vitamin B status (Saito M, Osteoporos Int, 2006). Recently

Shiraki et al. demonstrated that a functional polymorphism in methylenetetrahydrofolate reductase (MTHFR) polymorphism T allele (C677T) may be a risk factor for future fracture in addition to the traditional risk factors (Shiraki M, Saito M, et al., J Bone Miner Metab, in press). In addition we have reported that a higher urinary pentosidine was an independent risk factor for vertebral fracture in a 5-year prospective study in Japanese women (Shiraki M, Saito M, et al., J Bone Miner Metab, 2008). If confirmed in large prospective trials measurement of serum homocysteine and serum or urinary excretion of pentosidine might be characterized as markers reflecting bone collagen deterioration.

## ES16-1

**Therapeutic strategy for psoriatic arthritis with heterogeneity**

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Conflict of interest: None

PsA (Psoriatic arthritis: Psoriatic arthritis), a subtype of SpA (spondyloarthritis), is a disease that causes joint symptoms mainly in enthesitis and is estimated to be present in 10~15%, or approximately 50,000 patients, of patients who develop psoriasis vulgaris in Japan. It is a disease with heterogeneity, such as peripheral arthritis, spondyloarthritis (SpA), enthesitis, and dactylitis, in addition to psoriatic skin lesions and nail lesions. Since PsA presents with various symptoms, early diagnosis is not easy, and comprehensive management including skin findings and physical functions as well as multiple domains of arthritis and enthesitis and comorbidities is required to achieve the treatment goal, minimal disease activity (MDA). Since the number of reports varied among domestic surveys, intervention for early diagnosis is necessary also in terms of preventing irreversible joint destruction. In addition, in recent years, it has also been revealed that PsA patients are at high risk of MACE (Major Adverse Cardiovascular Events) associated with obesity, complications of metabolic syndrome and lifestyle-related diseases, and systemic inflammation, and the necessity of cooperation with other departments including cardiovascular internal medicine is increasing from the viewpoint of management of systemic inflammatory symptoms. In this lecture, we explain treatment and collaboration for early diagnosis and systemic inflammation control from the respective perspectives of rheumatologists and dermatologists.

## ES16-2

**Effects of Apremilast and Unmet Needs in Behcet's Disease**

Hiroaki Dobashi, Risa Wakiya
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Conflict of interest: None

Behcet's disease is an intractable disease with paroxysmal repeated inflammatory lesions in the oral mucosa, skin, eyes, and vulva. It was proposed as a new disease by dermatologist Hulusi Behcet in 1937. It occurs between the ages of 20 and 40 and is more common in areas along the Silk Road, such as Asia, the Eastern Mediterranean area, and the Middle East. The diagnosis is made in consideration of the major symptoms of painful aphthous ulcers of the oral mucosa, skin symptoms, uveitis, and genital ulcers and the accessory symptoms of the nervous system, blood vessels, intestine, epididymitis, and arthritis. However, recent reports have shown significant changes in the clinical features of Behcet's disease. However, even though the phenotype has changed, each of these disease domains has a significant impact on QOL of patients with Behcet's disease. Treatment requires therapeutic strategies for the significant disease domains in each case. The application of many therapeutic agents, including biologics and PDE4 inhibitors, has focused on the burden of aphthous ulcers and arthritis, previously endured by patients in the treatment of Behcet's disease, and has allowed for improved patient quality of life. However, the efficacy of PDE4 inhibitors for domains other than aphthous ulcers has not been fully elucidated. In this seminar, we will outline the current status of Behcet's disease treatment and treatment strategies, and discuss future issues through presentations by our department at ACR and EULAR held last year.

## ES17-1

**Aiming for Beyond T2T - From the Perspective of Subjective Symptoms**

Kei Ikeda
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Conflict of interest: Yes

Advances in drug therapy for rheumatoid arthritis have made it possible to achieve and maintain clinical remission in many patients. Achieving and maintaining clinical remission using a comprehensive index such as SDAI or a Boolean remission criterion is expected not only to reduce the progression of joint destruction but also to prevent further decline in physical function in many patients so that it leads to maximize quality of life in the long term. However, it has been shown that even in patients who have previously achieved clinical remission, certain subjective symptoms (pain, fatigue, stiffness, etc.) remain. On the other hand, in recent years, the ACR/EULAR announced to relax the criteria for patient general assessment, which reflects the subjective symptoms of the patient, in the Boolean remission criteria (Boolean 2.0). This will result in more patients with subjective symptoms meeting the Boolean criteria, suggesting that such subjective symptoms are not for a target of treatment intensification. Is that notion really correct? In this talk, we will discuss this question from the perspective of the causes of subjective symptoms, the long-term goals of rheumatoid arthritis treatment, and patient-doctor communication. Regarding communication in particular, we would like to present the results of our recent validation study of the subjective symptom evaluation tool "Okomarigoto check sheet" (copyright: Japan College of Rheumatology) and discuss the meaning of Beyond T2T.

## ES17-2

**Arthritis and Brain**

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Conflict of interest: Yes

The EULAR definition of difficult-to-treat rheumatoid arthritis (D2TRA) includes residual symptoms of controlled activity, such as pain, fatigue, and depression, which reduce the quality of life and are all associated with the brain. Thus, the problem with this definition of D2TRA is that amelioration of arthritis symptoms does not necessarily translate into improved brain symptoms, suggesting that arthritis symptoms and brain symptoms are not linked. We used a questionnaire to identify patients with RA who were in a state of central nervous system (CNS) sensitization. CNS sensitization is a condition in which abnormal CNS function results in hypersensitization of pain reception and other pathways. We identified 39 patients with CNS sensitization among 240 patients with RA. Those with CNS sensitization had a lack of improvement in the quality of life after treatment that reduced the arthritis activity. The similarity of these 39 patients to benchmark D2TRA patients was noteworthy. Thus, a proportion of patients with RA is thought to have some CNS abnormality. We thus analyzed the brains of arthritis model mice and found activated microglia (neuroinflammation) in the area postrema (AP), which is a sensory periventricular organ. This lesion was associated with decreased appetite and depression observed in arthritic mice. STAT3 activation was also found in the AP region. This neuroinflammation in the AP is thought to be caused by peripheral inflammation (arthritis) transmitted to the brain, but interestingly, this altered state in the brain is also influenced by factors other than arthritis. Trends in cytokines in the brain were examined. Abnormal IL-6 expression was found prior to the onset of arthritis; in arthritic mice, the trends in the joints and brain did not coincide. Since JAK inhibitors exert a positive effect on PRO, we administered baricitinib, a JAK inhibitor, to arthritic mice. Baricitinib had an effect on decreased appetite and depression in arthritic mice. It is currently hypothesized that the small molecule baricitinib enters directly into the AP and suppresses microglial activation. The brain is an important physiological compartment involved in RA, a systemic disease. It is important to carefully examine the brain in addition to the joints, because RA-related trends in the joints and brain do not always coincide.

## ES18-1

**Treatment goal in the management of spondyloarthritis**

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Conflict of interest: Yes

Spondyloarthritis, including psoriatic arthritis, is a chronic inflammatory disease associated with joint destruction, osteogenesis and ankylosis due to systemic arthritis. Patients with the diseases suffer from pain, deformity, and reduced quality of life. Their prognosis was poor due to a lack of effective treatments, but in recent years, their treatment has made remarkable progress with the introduction of validated disease activity measures and the development of drugs that directly inhibit cytokines important in the pathogenesis of the disease. In the management of spondyloarthritis, the assessment of disease activity is critical. Spondyloarthritis involves joints, periarticular sites, and extra-articular organs, and worldwide recommendations recommend that clinical signs and symptoms, blood tests, and imagings should all be assessed. Various disease activity measures have been proposed, and patient-reported outcomes, such as the degree of back pain, duration of morning stiffness and overall assessment by the patient, are also important. This presentation will discuss disease activity assessment and patient reported outcomes and their characteristics in spondyloarthritis, including psoriatic arthritis.

## ES18-2

**Pathologic significance of IL-17A&F in the spondyloarthritis disease spectrum**

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Conflict of interest: Yes

The spondyloarthritis (SpA) disease spectrum comprises a heterogeneous range of tissue dysfunctions. Tissue lesions include cutaneous psoriasis, synovitis, enthesis, dactylitis, axial disease and can also associate with uveitis and inflammatory bowel disease. Compelling evidence implicates cytokine dysregulation as a critical part of the pathogenesis of SpA, notably differentially impacting discrete target tissue, with clinical consequence. Whereas long standing data confirm a role for TNF in mediating effector biology, more recently a vital role for the IL-17 superfamily in SpA pathogenesis has emerged, mediated by both IL-23 dependent, and independent pathways. In particular, IL-17A and IL-17F are members of this cytokine family which are present and bio active in a range of tissues in SpA. Both function as essential synergistic partners with other inflammatory cytokines to fundamentally regulate immune and stromal cell lineages e.g. keratinocytes, fibroblasts, osteoclasts, and thereby promote tissue inflammation, damage and remodelling. Given their dual expression and functional profile, optimal suppression of the IL-17 superfamily in SpA tissue likely requires inhibition of both IL-17A and IL-17F.

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**RS** .... **Representative Session**

**SS** .... **Special Symposium**

**TS** .... **TREG Session**

**S** .... **Symposium**

**EL** .... **Educational Lecture**

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