Modern Rheumatology

VOLUME 35 SUPPLEMENT 2025

Japan College of Rheumatology

ABSTRACT SUPPLEMENT

The 69th Annual Scientific Meeting of the Japan College of Rheumatology
April 24 - 26, 2025 Fukuoka

JAPAN COLLEGE OF RHEUMATOLOGY ABSTRACT SUPPLEMENT

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Presidential Lecture

PL

Future Prospects of Rheumatology

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Conflict of interest: Yes

The rapid advancements in medical research emphasize the importance of pursuing patient-centered studies rather than research for the sake of research. At the 69th Annual General Assembly and Scientific Meeting of the Japanese College of Rheumatology, the theme "Future Prospects of Rheumatology" was chosen, and the key components necessary for designing this vision are reflected in the meeting's poster. The first component focuses on early diagnosis, disease onset prediction, and prevention by elucidating the interplay between genetic predisposition and environmental factors, coupled with the incorporation of "molecular medicine" in advancing clinical research. A notable example is the impact of the R4RA randomized trial based on RNA sequencing of synovial biopsy tissues. The second component highlights advancements in imaging diagnostics, beginning with evaluations of joint damage via plain radiographs (e.g., van der Heijde-modified Sharp score) and extending to CT, MRI, ultrasound, and PET imaging. Evaluating the efficacy of molecular-targeted therapies through imaging has become routine and continues to generate new research avenues. The third component pertains to progress in omics research. While ELISA remains the standard for assessing bioactive substances such as cytokines, chemokines, and growth factors in serum and other bodily fluids, cutting-edge array technologies now enable the stable analysis of over 1,000 bioactive substances from minimal sample volumes. Furthermore, advancements in multi-, trans-, and spatial omics allow for multi-layered biomolecular analyses, including genome and metabolite data, down to the single-cell level while incorporating spatial tissue information. The fourth component is the remarkable progress in AI and IoT. As Chair of the JCR Committee on AI, I have organized annual educational symposia on "AI-Driven Innovations in Rheumatology", where groundbreaking advancements in this field often leave one both amazed and overwhelmed. This underscores the critical importance of interdisciplinary collaboration, where leveraging one's expertise while engaging with researchers from other fields fosters new insights and their broader implications. To realize a brighter "Future Prospects of Rheumatology", internationalization is undeniably essential. Supported by AMED, my team —which includes internal and university researchers, intellectual property experts, antibody development specialists, and entrepreneurs—has been dedicated to drug discovery research for rare and intractable diseases. Whether we succeed remains uncertain, but our efforts aim to contribute to the envisioned Future Prospects of Rheumatology. This presentation will explore the Future Prospects of Rheumatology, reflecting on the speaker's experiences and perspectives.

Representative Session

RS

Precision Medicine for Immunological Diseases and Research on Human Immune System

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Conflict of interest: None

Precision medicine is a medical care that takes into account the patient's personal characteristics. Regarding immunological diseases, an understanding of immunological mechanisms is critical. Much of the progress in immunology has relied on studies of laboratory mice. However, the immune systems of mice and humans, which were separated tens of millions of years ago, cannot be considered identical. In fact, different numbers and functions of molecules have been reported. Further, laboratory mice are inbred and are not suitable for studying population diversity as in humans. Human immune diversity is reported to be strongly influenced by genetic factors, gender, age, and environment (especially gut bacteria). Genome-wide association studies (GWAS) have been used to analyze genetic variants (e.g., single nucleotide polymorphisms: SNPs) involved in human common diseases. Genetic variants found to be associated with a disease are likely to be the cause. Furthermore, many of the genetic variants shown in GWAS are reported to be quantitative trait loci (eQTLs) involved in different gene expression levels. eQTLs often work in specific cell types and epigenomics have been suggested as the possible mechanism. Based on these, we are producing new data sets of human immune system. For gene expression analysis in each subset of immunocompetent cells, we perform RNA-seq, determination of the 5' end of mRNA, ATAC-seq to detect open chromatin and histone modifications. Furthermore, proteome and lipidome of each subset can be integrated with genetic variant data to identify causal intermediate phenotypes. Proteins and lipids are closer to diseases than gene expression, different information could be obtained from gene expression analysis. Integrative studies of these data (multi-omics studies) are expected to reveal mechanisms of the human immune system and new therapeutic targets as well as information on precision medicine that cannot be obtained from mouse studies.

Special Symposium

SS2-1

Can we approach personalized medicine in rheumatoid arthritis despite lack of insights from modern molecular markers?

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Conflict of interest: Yes

The pathogenesis of rheumatoid arthritis (RA) is still enigmatic and causative and thus truly curative therapies are not in place. On the other hand, it is well established that (i) inflammation, such as by swollen joints and CRP, is the major driver of joint damage, (ii) cytokines like TNF and IL-6 are involved in the inflammatory response and (iii) autoantibodies, primarily rheumatoid factor (RF), may ignite and propagate these events. Consequently, abrogation of inflammation will eradicate the classical clinical signs of RA: pain and swelling and prevent joint damage, functional impairment and co-morbidities. Over the last decades, attempts to find predictive markers of response or good outcome by evaluating gene expression of cells from peripheral blood and synovial biopsies or multimolecular scores have sadly failed to surpass traditional predictors, such as normalization of joint counts and inflammatory markers or adjusting therapy in line with clinical scores and CRP- or RF-levels. One important means for therapeutic success, i.e. remission, is the treat-to-target strategy which calls for change of therapy if at least 50% reduction of disease activity has not been achieved within 3 months from starting a particular drug. However, the use of the right instrument is needed; as many effective agents, such as IL-6R- or JAK-inhibitors, affect the acute phase response (APR) directly and the DAS28 is heavily weighted on APRs, it should not any more be used to activity but rather scores recommended by ACR and EULAR, CDAI, SDAI and Boolean remission criteria. However, it has more recently been shown that using traditional biomarkers, CRP and RF, is also helpful. Patients with CRP >4 mg/dl will respond particularly well to IL-6 receptor blockade and patients with RF levels >200 IU/ml will respond better to Fc-free monoclonal antibodies than those containing an Fc-portion. Thus, given the lack of better molecular markers, following traditional clinical and laboratory measures along with the treat-to-target strategy allows one to achieve excellent outcome in the vast majority of RA patients.

SS2-2

75 years of glucocorticoid treatment: too early for a final ordeal

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Conflict of interest: None

In 1950 the Nobel Prize for phsyiology (medicine) was awarded for the discovery and application of glucocorticoids (GCs) in the treatment of patients with rheumatoid arthritis (RA). This prize was given rather early on, before all the negative effects of especially high doses of GCs became apparent. Since then discussion on the balance between beneficial and adverse effects has been ongoing. Are we able to make more final decisions yet? Probably not even now, but let me update you. I will discuss new insights into the mechanisms of action; quite some fundamental work has been done the last years. For many years there has been a plethora of reports on adverse events, that are quite often hard to interpret, especialy since bias by indication is difficult to rule out. Also dose and duration of GC therapy plays an important role in the occurence of adverse events. The most spoken off are cardiovascular, bone and infections. Since COVID there is especially emphasis on viral infections and vaccinations. Interesting data have been collected in elderly patients with RA that were not responding adequately to their DMARD and were started on an new DMARD and at that moment randomised to additional low dose GCs versus placebo. New insights in efficacy are limited, there is no doubt about the often shown efficacy of GCs in inflammatory rheumatic diseases. New insights have been collected on dosing in early RA, but also on tapering and stopping GCs in RA. Most clinical research deals with RA, but some studies in Polymyalgia Rheumatica and SLE are also of interest. Based on these and further insights into the mechanisms of action and efficacy versus adverse event of GCs, treatment recommendations have been adapted. In conclusion, GCs are still very valuable (and cheap) drugs that should be used with caution and knowledge, for the benefit of many patients.

SS2-3

CAR T-cells, BiTEs and more - are we on the road to cure of autoimmune diseases?

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Conflict of interest: None

This presentation will provide an overview of emerging therapeutic strategies in rheumatology, focusing on innovative approaches to treating autoimmune diseases like systemic lupus erythematosus (SLE), systemic autoimmune diseases and rheumatoid arthritis (RA). Key highlights will include: **Cellular Therapies:** CAR-T (Chimeric Antigen Receptor T-cell) therapies originally developed for treating leukaemia are now being explored in autoimmune diseases. They show promise in reducing autoreactive B cells and long-lived plasma cells, which are pivotal in disease pathology. The presentation will allude to the efficacy of CAR-T cells targeting CD19 and BCMA in achieving remission (and potentially a cure) in refractory autoimmune conditions. **Bispecific T Cell Engagers (BiTEs):** BiTEs, such as CD19xCD3 or BCMAxCD3 constructs, will be highlighted for their ability to deplete B cells by using T cells. Early clinical data suggests significant disease activity reduction in RA patients and individuals suffering from systemic autoimmune diseases. **Targeted Innovations:** New molecules, including engineered antibodies (such as those targeting CD19 or CD38), will be detailed for their role in modulating the immune response and reducing pathogenic antibodies. **Precision Medicine:** Future trends will focus on AI-driven personalized medicine and CRISPR-based gene-editing approaches to specifically eliminate autoreactive cells while preserving broader immune function. The lecture will address both the promise and complexity of these approaches, with discussions on challenges such as manufacturing costs, patient-specific factors, and potential side effects like cytokine release syndrome. The integration of haematology and oncology techniques in rheumatology highlights a transformative era in autoimmune disease management.

SS2-4

The importance of preventing damage accrual in systemic lupus erythematosus (SLE)

Marta Mosca
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Conflict of interest: Yes

Despite the improvement of long term survival, SLE patients still experience an increased mortality and morbidity with respect to the general population as well as a poor quality of life. Therefore the aims of SLE treatments, according with the Treat to Target Recommendations as well as the EULAR Recommendations are “ensuring long-term survival, preventing organ damage, and optimizing health-related quality-of-life”. Damage accrual is one of the most important variables impacting on patients outcomes as there is a clear association between damage and reduced survival and burden of disease. Literature shows that damage, particularly cardiovascular or renal, is a strong predictor of mortality in SLE. In addition damage has an impact on physical and mental health of patients. It is well known that patients with SLE accrue damage very early in the disease course and this is related with the disease activity but also with treatment and comorbidities. Glucocorticoid (GC) therapy is strongly associated with damage accrual and comorbidities. Therefore it appears that in the management of SLE a balance between disease activity control, flare prevention, use of glucocorticoids and immunosuppressive therapy is needed to minimize damage accrual. According with the 2023 update of EULAR Recommendations for SLE management the following strategies can help in damage accrual prevention: early diagnosis and regular monitoring for organ involvement (for example kidney involvement), prompt introduction of immunosuppressive drugs and or biologics to control disease activity and minimize GC therapy, management of comorbidities, adherence to therapies, lifestyle indications. In summary, preventing damage accrual in SLE is essential for improving survival, maintaining quality

of life, and reducing the burden of the disease on individuals and healthcare systems.

SS3-1

Taming the Wolf- The Evolving Treatment Paradigm for Lupus Nephritis

Maria Dall'Era
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Conflict of interest: Yes

Lupus nephritis (LN) is the most common organ-threatening manifestation of SLE and affects up to 60% of people living with SLE. It continues to lead to increased morbidity and mortality, including end stage kidney disease. LN demonstrates a racial and ethnic disparity in that the incidence of LN is increaed and outcomes are worse in patients of self identified Black, Asian, and Hispanic race and ethnicity. In this presentation, I will start by discussing the epidemiology of LN and key principles of pathogenesis, including the immunologic and non-immunologic mechanisms of kidney injury. Against that background, I will then discuss the limitations of our conventional therapies and the data underlying the use of "triple therapy" with newer therapies such as voclosporin and belimumab. I will review the current guidelines for the treatment of LN, including the newly released 2024 ACR guidelines. Lastly, I will discuss selected emerging therapies in development, including the various modalities targeting B cells, such as CAR-T. The future is bright for the treatment of LN.

SS3-2

The evolving understanding of lupus pathogenesis

J Michelle Kahlenberg
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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a complicated autoimmune disorder with heterogeneous manifestations and treatment responses. In recent years, our group and others have identified critical intersects between environmental triggers such as microbes and ultraviolet light that push type I interferon (IFN) production and generate activation of innate and adaptive immune responses. In this talk, I will discuss recent discoveries in skin and systemic lupus biology and shed light on how type I IFN responses become skewed after environmental exposures and drive activation of lupus phenotypes.

SS4-1

Bridging the Gap: Pitfalls in Gout Management

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Conflict of interest: None

Gout is a treatable and curable disease. Undertreated hyperuricemia in gout can lead to joint damage and tophi deposition disease. This talk aims to discuss the evidence or clinical experience on the pitfalls or gaps in gout management that have prevented the health care specialist from more effectively managing gout. These include patient non-adherence, prescriber undertreatment, particularly at the primary care level where most patients are managed, multiple dose titrations needed to optimize monotherapy with urate lowering therapy (ULT) particularly allopurinol, potential toxicities and limited therapeutic choices. These have resulted in the unmet need for more rapid and significant clinical outcomes including less gout flare burden. ULT clinical trials have concluded that achieving target SUA <6.0 mg/dl achieved in 80-90% of subjects; flare burden reduction by 1-2 years of treatment. However, real world use of ULT results are far from this and targets are not achieved. There are diagnostic and therapeutic guidelines on gout from the APLAR, ACR, EULAR and other rheumatology leagues which can be referenced however these may not be enough to achieve the desired outcomes. Patient education is a strategy that has been identified to improve the gaps in gout management. Education on the following: gout as an acute and chronic disease, treat-to-target serum uric acid (SUA) 6.0 mg/dl or 360 umol/li, adherence to medications for prevention of flares and cure, facilitators and barriers to patient adherence, importance of lifestyle factors such as diet. Furthermore, nurse-led gout care has been shown to be efficacious and cost effective, regular clinic visits with SUA monitoring, dose titration until the desired SUA is achieved and treating co-morbid conditions are further strategies that can be applied.

SS4-2

comorbidities in idiopathic inflammatory myopathies

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Conflict of interest: None

With advances of knowledge in myositis specific antibodies, treatment strategies and new medications in idiopathic inflammatory myopathies (IIM), earlier diagnosis and better treatment algorithm is possible, thus improve the survival of patients with these rare diseases. Apart from treatment of the disease itself and its complications, frequent surveillance of associated comorbidities are essential to prevent damage and to improve the qualities of life. There is high prevalence of reduced bone mineral densities, osteoporosis and fracture rates in patients with IIM. Various traditional and disease specific factors are important contributing factors. Use of FRAX for assessment for risk of fractures in these groups of patients have certain pitfalls. Management of bone health should start early which include both non-pharmacological and pharmacological aspects. Exercise recommendations, fall prevention and correction of sarcopenia all carry significant roles in osteoporosis in IIM patients. Another comorbidity in IIM that are often missed in IIM are the cardiovascular comorbities. Although clinically significant heart involvement is uncommon in these patients, recent studies show an increased prevalence of traditional cardiovascular risk factors in both juvenile and adult DM. In IIM, treatment and detection of comorbidities are as challenging as the treatment of disease and updates in guidelines to tackle these problems are important.

SS4-3

Which test is Preferable for the Screening of Latent Tuberculosis in Refractory Spondyloarthritis Patients: Tuberculin Skin Test and or QuantiFERON TB Gold Test

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Conflict of interest: None

Background: This study aimed to determine the agreement between TST and QuantiFERON TB Gold Plus (QFT-Plus) positivity in refractory spondyloarthritis patients. **Methods:** A total of 51 consecutive refractory SpA patients of both genders were enrolled. Estimated sample size was 97. A model-based simulation test was used to convert the 51 sample data to 97 data using "R" software with "arm" and "Himise" package. In all patients' chest X-ray, TST and QFT-Plus test was done. Agreement between TST and QFT-Plus was evaluated using kappa statistics. To identify variables for TST or QFT-Plus positivity appropriate bivariate analysis was done with both primary and simulated data. Statistical significance was set at p-value < 0.05. **Results:** Out of 51 patients, TST was positive in 5 (9.80%) patients, 3 men. The QFT-Plus was positive in 8 (15.58%) patients, 4 men. Any test (TST or QFT-Plus) was positive in 13 (25.38%). Both tests were positive in 3 (5.89%) and negative in 41 (78.84%). Kappa agreement between TST and QFT-Plus test was κ=0.39. From simulated data, positive TST in 12 (12.37%), positive QFT-Plus in 16 (16.49%). Both tests were positive in 6 (6.19%) and negative in 75 (77.32%). Kappa agreement between TST and QFT-Plus test was κ=0.33. Mean age was 35.16±11.24 years, men 39 (76.5%). Among patients' 21.57% were tobacco users and 44 (86.27%) were BCG vaccinated. Ongoing drugs, SSZ (88.24%), MTX (16.69%) and steroid (3.92%). The SpA disease subtype, axial SpA (80.39%) and peripheral SpA (19.61%). The mean ASDAS-ESR and ASDAS-CRP were 4.01±0.71 and 4.90±0.88 respectively. Indipendent variables were not associated with TST and QFT-Plus positivity in both types of data except, female gender of simulated data, associated with

QFT-Plus positivity [OR=4.1, 95% CI=1.38-12.76; p=0.01]. **Conclusions:** In refractory SpA, poor agreement observed between TST and QFT-Plus test. No influence of BCG vaccination on TST positivity. Female gender may have effect on QFT-Plus positivity.

SS4-4

The Winding Path Towards Building the APLAR Systemic Sclerosis Incident Cohort

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Conflict of interest: Yes

Systemic sclerosis (SSc) is a heterogeneous autoimmune disease characterised by inflammation, fibrosis and vasculopathy. It has the highest mortality among autoimmune rheumatic diseases, with pulmonary complications being the leading causes of death. There is emerging data that Asians with SSc have more severe disease and higher mortality compared to patients of European-descent. SSc has distinct ethnic differences in disease behaviour, but there is to date, no large Asian SSc incident cohort. In this lecture, I will share the impetus and vision for embarking on this winding road towards building the APLAR SSc Incident Cohort (APSICC) and how this will address unmet needs and advance the care of SSc in the Asia-Pacific region.

SS4-5

Unveiling the pathology of axial spondyloarthritis in HLA-B27 negative patients through integrated analysis

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Conflict of interest: Yes

Axial spondyloarthritis (axSpA) is an autoimmune inflammatory condition primarily affecting the axial skeleton. Human leukocyte antigen B27 (HLA-B27) is a well-established genetic marker strongly associated with the development of axSpA. On the other hand, HLA-B27 prevalence varies depending on region and race, and the proportion of HLA-B27 negative axSpA patients is higher in Japan. HLA-B27 status could affect on the clinical features of axSpA, and surely it has been reported that axSpA without HLA-B27 has a poorer therapeutic response to TNF inhibitors than cases with HLA-B27. These observations suggest the diversity of the pathology that exists behind patientss currently clinically diagnosed as axSpA. To date, we have performed single-cell RNA sequencing (scRNA-seq) on peripheral blood mononuclear cells from 77 SpA spectrum cases and conducted an integrated analysis with clinical findings. Using a generalized linear mixed model (GLMM), we found that 1) patients with axial joint lesions had more plasmacytoid dendritic cells (pDCs) than cases with pure peripheral disease, 2) the number of $CD4^+$ T cells highly expressing downstream signals of type 1 interferon (IFN) (ISG^{hi} $CD4^+$ T cells) correlated with disease activity in HLA-B27-negative axSpA patients, but this relationship was not observed in HLA-B27-positive cases, and 3) pDCs were suspected to be one of the major sources of type 1 IFN production. The results indicate that type 1 IFN is deeply involved in the pathogenesis of axSpA, especially in HLA-B27-negative cases. Stratifying patients by HLA-B27 status and targeting type I interferon in HLA-B27-negative cases could enhance the development of precision medicine. In addition, a comparative study of the differences in the immunological dynamics of axSpA in Asia and the Pacific Rim will lead to deeper insight into the pathogenesis.

SS4-6

Identification of HDAC inhibitor targeting type I interferon and B-cell abnormalities in Systemic Lupus Erythematosus

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Conflict of interest: None

Objectives: This study aimed to identify drugs that can inhibit both type I interferon (IFN-I) and autoantibody production since over production of them is characteristic abnormality in systemic lupus erythematosus (SLE). **Methods:** We identified an inhibitor of IFN-I production from a chemical library of clinically approved drugs. Then, we examined its efficacy in suppressing the expression and phosphorylation of upstream signaling molecules for IFN-I, the differentiation of B cells into plasma cells, and autoantibody production. We also examined whether it could alleviate disease severity in SLE-prone mice, including *STING*-associated vasculopathy with onset in infancy (SAVI) mice and New Zealand Black/White F1 (NZB/W F1) mice. **Results:** Vorinostat, a clinically approved pan-histone deacetylase (HDAC) inhibitor, inhibited both IFN-I production and B-cell differentiation. Vorinostat inhibited *TBK1* phosphorylation and following *IRF3* nuclear translocation, and suppressed the expression of IFN-I-inducing molecules, such as *IRF5* and *IRF7*, and B-cell-related genes. Vorinostat ameliorated lung inflammation and fibrosis in SAVI mice by decreasing IFN-I. It also alleviated the mortality and severity of renal disease in NZB/W F1 mice by suppressing IFN-I induction and B-cell differentiation. Furthermore, it suppressed plasma cell differentiation in human B cells. **Conclusions:** Vorinostat simultaneously suppresses IFN-I production and B-cell differentiation via inhibiting *TBK1* phosphorylation and the expression of IFN-I- and B-cell-related genes. It should be considered as a novel therapeutic agent for SLE, as it is expected to benefit patients with SLE in need of more effective and better tolerated therapies.

TREG Session

TS-1

Systemic Lupus Erythematosus and Autoimmune Rheumatic Disorders

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Conflict of interest: Yes

This presentation will cover a variety of selevcted significant topics from the Convergence 24 meeting of the American College of Rheumatology. The primary focus will be on SLE, in particular, lupus nephritis, and will include results from the long term voclosporin trial, the effect of stoppng immunosuppression in patients, the effect of GLP-1 medications on renal outcome, new urinatry biomarkers and the recent ACR lupus nephritus guidelines. The presentation will also review abstracts on use of methotrxate in polymyalgia rheumatica (PMR), the efficacy of baricitinib, incidence of aortic complications in PMR and giant cell arteritis (GCA). Next, the presentation will cover selected topics in granulomatsis with polyangiitis (GPA), specifically corticosteroid use, lacy of efficacy of abatacept, topical niclosamide for the ENT manifestiations and the effficacy of plasma exchange (PLEX) in patients with diffuse alveolar hemorrhage (DAH). Finally, data will be presented on colchicine in Behcet Syndrome and efficacy of weight loss, disease activity and patient reported outcomes (PROs) in patients with autoimmune diseases taking newer weight loss therapy medications.

TS-2

New Molecules in Development for Rheumatic Diseases

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Conflict of interest: None

2024 witnessed an exciting expansion of information on the development of new molecules with novel mechanisms of action for the treatment of multiple rheumatic diseases as well as the transition of innovative mechanisms from other medical specialties to rheumatology. Although there has been the relatively recent approval of novel MOA for SLE, including belimumab and anifrolumab, many patients are still inadequately treated, particularly those lupus nephritis. The numerous positive reports of the use of CAR-T therapies, including anti-CD19, anti-CD20 and anti-BCMA molecules have suggested that many patients who haven't responded to currently approved therapies may be successfully treated with these CAR-T molecules. The duration of response and the safety of these procedures are still to be determined as to their accessibility. 2024 also saw the beginning of discussion on the effectiveness of Bi-specific T-cell engagers (BiTEs) which kill B cells by engaging T cells, for the treatment of immune mediated rheumatic diseases such as rheumatoid arthritis. In addition to CAR-T and BiTE therapies, results with other molecules targeting B cells including monoclonal antibodies to CD20, plasma cells and BAFF-R were presented. In addition, several novel MOA for SLE were reported including molecules targeting TLR7/8, CD40 ligand and TYK2. There were positive results in trials for Sjögren's Syndrome with a mAb to the neonatal Fc receptor and a mAb to CD40 as well as a different mAb to CD40 in RA. A device which causes stimulation of the vagus also reported positive results in a trial of patients with RA. And lastly, several positive reports of molecules for the treatment of OA were presented, Each of these concepts and molecules will be covered in this presentation.

TS-3

TREG session: ACR 2024, EULAR 2024 conference topics

Arthur Kavanaugh
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Conflict of interest: None

Progress in the Therapeutic Approach to Rheumatoid Arthritis (RA) Over the past few decades, thanks to efforts and collaboration from investigators around the world, there has been substantial progress in delineating the complex cellular and molecular mechanisms of RA. As a result, many therapeutic agents and treatment strategies have emerged and been brought to the clinic. This has allowed optimized clinical outcomes for patients affected by RA. With this success, the goals of therapy have been elevated, with remission now being considered the ultimate goal throughout the world. Despite significant advances, challenges remain as regards the optimal treatment of RA. Currently there are approximately 20 disease modifying antirheumatic drugs (DMARDs) available for treating RA, including biologic DMARDs, targeted synthetic DMARDs and older traditional DMARDs. However, RA is heterogeneous, and we still lack "precision medicine"; that is, we cannot know what the most effective and best tolerated therapy will be for an individual patient. 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 could actually be classified as 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.

TS-4

Spondyloarthritis

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Conflict of interest: Yes

Key abstracts from ACR 2024 on Spondyloarthritis, including Psoriatic Arthritis (PsA) and Axial Spondyloarthritis (AxSpA) will be discussed in this lecture. These abstracts were identified as being important for advancing the field of SpA and pertinent for practicing clinicians by the SpA working group of TREG. Topic areas will include criteria for "Difficult to Treat AxSpA", the AXIS study to define axial psoriatic arthritis (AxPsA), the relationship of inflammatory bowel disease and SpA, sex differences in SpA, emerging IL-17A&F and TYK2 inhibitors, efficacy and safety of dual biologic therapy in SpA, and TRBV9+ T cell targeting in treatment of AxSpA.

Symposium

S1-1

Glycobiology and maturation of AMPA during clinical suspect arthralgia to RA

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Conflict of interest: Yes

Rheumatoid Arthritis (RA) is a chronic inflammatory and destructive disease. During the last decades insight in pathogenesis and subsequent development of targeted therapies (especially monoclonal antibodies against cytokines and surface receptor on white blood cells) have dramatically improved outcomes for patients, the major developments will be reviewed. The phases of RA development are now well defined ranging from the mere presence of genetic risk factors to clinical suspect arthralgia to full-blown persistent RA. Moreover the maturation of the immuneresponse of the most specific autoantibody response to anti- citrullinated antigens has been studied in great detail which revealed that the antigen-biding site of these antibodies is glycosylated and this Fab-glycosylation is predictive of RA development. Moreover the first studies which focus on prevention of RA development have been published. These studies showed that prevention studies are possible and that RA development can be postponed but not prevented but the secondary endpoints (patient reported outcomes) showing clear suggestions of persistent disease modification. Interventional studies in undifferentiated arthritis and early RA patients aiming to reach clinical remission as defined by the absence of signs and symptoms, already showed that drug free remission can be achieved if patients are treated very early. The development of specific autoantibody profiles and the selection of B-cells specific for citrullinated antigens and subsequent specific mutations from germline sequences are now identified, opening the possibilities for more specific interventions in early disease. Examples of such interventions will be reviewed. An ideal intervention would be one that prevents the expression of the clinical entity we recognise as full-blown RA. Such intervention will halt the disease process in individuals from the 'phases' from the *pre-clinical status* [an individual with genetic risk factors & environmental risk factors that develops systemic autoimmunity] through the *clinical phases* [an individual will develop symptoms e.g. joint pain and stiffness, then arthritis finally to a disease to classified as RA.

S1-2

Characteristics of clinically suspect arthralgia that progresses to inflammatory/rheumatoid arthritis

Kei Ikeda
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Conflict of interest: Yes

The presence of joint swelling (clinical synovitis) is a prerequisite to classify a patient as having rheumatoid arthritis (RA) or early arthritis (EA) in 2010 ACR/EULAR RA classification criteria and 2016 update of the EULAR recommendations for the management of EA. Most patients who are eventually classified as RA or EA have a prodromal phase, in which they have some musculoskeletal signs and symptoms with no clinically swollen joints. These symptoms are called clinically suspect arthralgia (CSA). The characteristics of CSA have been defined by EULAR based on expert consensus: joint symptoms of recent onset (duration <1 year), symptoms located in MCP joints, duration of morning stiffness ≧60 min, most severe symptoms present in the early morning, presence of a first-degree relative with RA, difficulty with making a fist, and positive squeeze test of MCP joints. These symptoms and signs can be helpful in selecting patients at risk for RA but obviously not accurate enough to initiate treatment with DMARDs by themselves. RA-related autoantibodies and imaging findings have been shown to predict the development of inflammatory arthritis (IA) and RA in patients with CSA. Interestingly, not only synovitis, osteitis, and bone erosion, but also extra-articular lesions such as tenosynovitis and tendinitis have been shown to be predictive of IA/RA development. In addition, studies have demonstrated that some clinical features of CSA such as morning stiffness and difficulty with making a fist are associated with tenosynovitis rather than synovitis. These data indicate that tenosynovitis/tendinitis can be one of the earliest inflammatory lesions in RA and should be taken into account when diagnosing RA in practice and designing a trial for preclinical RA. These data also challenge the current notion that joint swelling, which usually does not reflect tendon lesions, should be the line that separates between preclinical RA and RA.

S1-3

Omics analysis of synovial tissue opens up a new era for rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a multifactorial autoimmune disease that develop against the background of genetic predisposition and environmental factors. From the early stage of onset, various immune cells (e.g., T cells, B cells, monocytes) and mesenchymal cells (e.g., synovial fibroblasts) are activated mutually through cell-cell adhesion and humoral factors in the RA joints, and these "immune-mesenchymal interactions" form a local inflammatory environment. Recently, global efforts have been made to stratify RA patients and comprehend their pathology in real time by analyzing synovial tissues taken by ultrasound-guided needle biopsy. Synovial information has provided us with insight into the local immunological dynamics that occur from the early stage of the disease and the potential for modification with therapeutic agents. Moreover, some clinical trials have reported that focusing on the heterogeneity of synovial cells between cases may lead to the selection of optimal therapeutic strategy. Collectively, from the maturation of techniques to safely and effectively extract synovial tissue, to the development of single-cell multi-omics technologies, we are now entering a stage where the knowledge gained can be applied in clinical practice. In this presentation, I will provide an overview of recent findings from synovial tissue research along the timeline of RA, and introduce the efforts being made by the Japan Autoimmune Disease Consortium (Alliance of Japanese Autoimmunity Gene eXpression research; AJAX) to overcome intractable condition.

S1-4

Bone erosion and microarchitecture changes in inflammatory arthritis analyzed by HR-pQCT

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Conflict of interest: None

High-resolution peripheral quantitative computed tomography (HR-pQCT) is an advanced three-dimensional imaging technique with superior sensitivity in assessing bone. It exhibits higher sensitivity in detecting erosions compared to conventional radiography (CR), MRI, and CT, and enables the evaluation of bone microarchitecture parameters such as volumetric bone mineral density, trabecular bone volume fraction, and trabecular thickness. HR-pQCT facilitates independent measurement of specific parameters of bone erosion, including width, depth, and volume, while simultaneously revealing the status of bone microarchitecture. The relationship between bone microarchitecture and bone destruction is not fully elucidated; however, considering that periarticular osteoporosis precedes erosion, and that early periarticular osteoporosis predicts the progression of joint destruction, it is hypothesized that improving bone microarchitecture may result in subsequent erosion suppression or repair effects. Furthermore, detection of deterioration of bone microarchitecture without bone erosion may be valuable in predicting the development of rheumatoid arthritis (RA) in early arthritis. Utilizing HR-pQCT, we have investigated the effects of several pharmaceutical agents, focusing on changes in bone microarchitecture and bone erosion. These studies revealed that the depth of bone erosion was numerically more repaired in patients treated with conventional synthetic disease-modifying antirheumatic drugs (cs DMARDs) plus denosumab compared to those without denosumab, accompanied by significant improvement in bone microarchitecture. Furthermore, abatacept prevented the progression of bone erosion, including

new occurrences, and prevented the deterioration of bone strength independently of synovitis compared to csDMARDs. Additionally, other studies employing HR-pQCT demonstrated not only more numerous and larger cortical interruptions but also impaired vBMD and microstructure in patients with RA, both with and without visible erosions on CR, compared to healthy subjects. In this talk, I will provide a comprehensive review of the advancements in bone microstructure assessment in rheumatoid arthritis as elucidated through HR-pQCT imaging, as well as an examination of pharmaceutical interventions that have demonstrated more nuanced effects when evaluated using HR-pQCT technology.

S1-5

Optimizing Molecular Targeted Therapies in Rheumatoid Arthritis: Insights from Registry Studies

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Conflict of interest: Yes

Registry studies have significantly advanced our understanding of how to optimize molecular targeted therapies in rheumatoid arthritis (RA). They have contributed to patient stratification by identifying specific serum markers or patient characteristics that respond best to particular biologics or JAK inhibitors. For instance, in patients with high inflammatory levels, such as those having elevated CRP or inflammatory anemia, IL-6 inhibitors have shown better clinical response than TNF inhibitors (TNFi), aligning with the role of IL-6 in inducing acute phase inflammatory proteins like CRP or hepcidin. JAK inhibitors were effective in patients with inadequate response to TNFi because Type 1 and Type 2 interferon signatures are upregulated after TNFi treatments. The response to biologics is influenced not only by the target molecules but also by the structural characteristics of biologic IgG. Our ANSWER cohort study revealed that in patients with high rheumatoid factor (RF) levels, TNFi without the Fc portion of IgG was more effective than TNFi with IgG Fc, because IgG Fc of biologics was recognized by RF and degraded in macrophages, leading to reduced concentration of biologics and impaired efficacy. Thus, we can optimize the treatment of RA by referring to the evidence obtained from cohort studies. In this seminar, I will introduce the real-world evidence revealed by large RA registries in Japan and discuss how to optimize molecular targeted therapies to promote precision medicine in RA.

S2-1

Establishment of the Concept of Nephro-Rheumatology

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Conflict of interest: None

Nephro-rheumatology is a novel specialty bridging rheumatology and nephrology. While diseases such as systemic lupus erythematosus, rheumatoid arthritis, and ANCA-associated vasculitis frequently involve renal complications, advances in precise and effective immunosuppressive therapies have improved acute kidney injury outcomes. However, with an aging society, the number of rheumatic disease patients with chronic kidney disease (CKD) is increasing. The KDIGO 2024 guidelines emphasize the importance of personalized medicine in CKD management. As renal dysfunction influences the selection of immunosuppressants and targeted therapies, establishing personalized CKD management strategies specific to rheumatic diseases is crucial. Based on this background, Nephro-rheumatology addresses the following challenges: 1. Elucidating mechanisms of kidney injury in rheumatic diseases: Investigating direct effects of rheumatic diseases activity and medications on renal function using urinary biomarkers and pathological specimens 2. Understanding pharmacokinetics in patients with kidney dysfunction: Establishing appropriate usage guidelines for csDMARDs, immunosuppressants, and b/tsDMARDs according to renal function 3. Management of CKD in rheumatic diseases: Implementing personalized medicine through medical teams led by rheumatologists and nephrologists, developing treatment strategies incorporating new drugs such as SGLT2 inhibitors and non-steroidal MRAs As a future subspecialty of rheumatology, we aim to establish evidence-based clinical guidelines and implement personalized medicine. Through research, clinical practice, and education, we will contribute to developing optimal medical care systems for rheumatic disease patients with kidney complications.

S2-2

Chronic Kidney Disease in Rheumatology

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Conflict of interest: None

In rheumatology, chronic kidney disease (CKD) requires attention, as even with normal renal function, persistent proteinuria or urinary abnormalities for over three months constitutes a CKD diagnosis. Proteinuria above 0.15 g/gCr increases risks of end-stage renal disease, cardiovascular mortality, and overall mortality. Patients with rheumatic diseases meeting CKD criteria face poor prognosis, managing CKD alongside disease control is important. Given the complexity of CKD management, this symposium discusses key monitoring and management strategies for mild to moderate CKD (eGFR 45-59 ml/min/1.73 m^2) in rheumatology patients. Rheumatoid arthritis patients with CKD frequently experience combined inflammatory and renal anemia, often complicated by iron deficiency, affecting erythropoiesis-stimulating agent efficacy. Additional considerations include mineral bone disorder (MBD) and the emerging role of sodium-glucose cotransporter-2 (SGLT2) inhibitors, though their efficacy and safety remain uncertain in rheumatic diseases due to limited trial data. This overview aims to integrate novel therapies, including angiotensin receptor neprilysin inhibitors (ARNIs) and Hypoxia-inducible factor-prolyl hydroxylase (HIF-PH) inhibitors, into a practical CKD management framework for rheumatic care.

S2-3

Chronic kidney disease in rheumatoid arthritis ~ why kidney fails in patients with rheumatoid arthritis

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Conflict of interest: None

Rheumatoid arthritis (RA) is an autoimmune disease caused by genetic and environmental factors disrupting self-tolerance, leading to rheumatoid factor and anti-cyclic citrullinated peptide antibodies. It primarily affects small joints, causing chronic inflammation. Treatment requires long-term management and is often accompanied by complications. Recent studies show RA patients are at higher risk of kidney function decline and chronic kidney disease (CKD) compared to healthy individuals. The introduction of tDMARDs has significantly improved RA disease activity, reflected in reduced secondary amyloidosis in renal biopsies since 2000. However, the aging RA population and later onset ages have caused CKD prevalence to rise, increasing risks for end-stage renal disease (ESRD) and mortality. Data from the NinJa (National Database of Rheumatic Diseases in Japan) cohort show eGFR <60 mL/min/1.73 m^2 cases increased from 19% in 2012 to 29% in 2020. Over half of RA patients aged 75+ now have eGFR below 60 mL/min/1.73 m^2. Declining kidney function complicates the use of anchor drugs like methotrexate and some csDMARDs and tDMARDs, worsening disease activity and advancing progression to difficult-to-treat RA (D2TRA). Therefore, understanding the mechanisms behind CKD onset in RA patients is crucial to improving kidney and survival outcomes. Evidence-based strategies are also needed to manage RA effectively in CKD and ESRD cases. This presentation will discuss recent research on CKD prevalence and its changes over time in RA patients, factors contributing to CKD onset, and strategies for managing RA with CKD. Emphasis will be placed on balancing safety with effective disease control to improve outcomes for RA patients with CKD.

S2-4

Key Renal Pathological Features and Differences in Treatment Guidelines for ANCA-Associated Nephritis

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Conflict of interest: Yes

ANCA (anti-neutrophil cytoplasmic antibody) was first reported in 1982 by Davies et al. (1) and became widely recognized in 1984 when Hall et al. introduced the term “antineutrophil cytoplasmic antibody (ANCA)” (2). This discovery led to the establishment of ANCA-associated vasculitis (AAV), encompassing pauci-immune necrotizing glomerulonephritis and systemic vasculitis, significantly advancing understanding of its pathophysiology. Renal involvement is the most common organ manifestation of AAV, affecting approximately 70% of cases, with 60% presenting as rapidly progressive glomerulonephritis (RPGN). RPGN is defined by nephritic urinary findings and rapid renal failure progression, with an eGFR decline of over 30% within three months. Pathologically, ANCA-associated nephritis is characterized by necrotizing crescentic glomerulonephritis, a key indicator of disease severity. Despite numerous studies, no consensus has been reached on renal prognosis and optimal treatment strategies (3, 4). The 2020 Japanese RPGN Clinical Practice Guidelines, revised from the 2017 version, aim to assist not only nephrologists but also rheumatologists and non-specialists. These guidelines emphasize early diagnosis and treatment, recommending cyclophosphamide or rituximab for induction therapy, combined with glucocorticoids. Maintenance therapy options include azathioprine or mycophenolate mofetil. Compared to the international KDIGO 2021 Guidelines (5). This presentation will discuss the essential pathological features of ANCA-associated nephritis for rheumatologists and compare the treatment strategies outlined in the 2020 Japanese guidelines and KDIGO 2021 Guidelines, highlighting areas of consensus and ongoing challenges. References 1. Brit Med J 1982; 285: 606. 2. Aust N Z J Med. 1984 Jun; 14(3): 277-8. 3. Nephrol Dial Transplant 1996; 1989-95. 4. J Am Soc Nephrol 2010; 21: 1628-36. 5. Kidney Int. 2021 Oct; 100(4): 753-779.

S2-5

Comprehensive Management Approaches for Preventing Chronic Kidney Disease Progression in Lupus Nephritis

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Conflict of interest: Yes

Lupus nephritis (LN), associated with systemic lupus erythematosus (SLE), is a severe autoimmune disease affecting multiple organs, particularly the kidneys. Progression to chronic kidney disease (CKD) significantly impacts the long-term prognosis of LN patients. LN poses a high risk of irreversible renal decline, and as CKD advances, the risks of cardiovascular disease and infections increase. Patients with an initial estimated glomerular filtration rate (eGFR) below 75 mL/min/1.73 m^2 have a notably higher risk of CKD progression, making eGFR monitoring during the first year of treatment crucial. Early risk stratification and intervention can delay CKD progression, potentially enhancing quality of life and survival. LN treatment centers on immunotherapy to control SLE activity, with careful immunosuppressive management. However, factors like hypertension, obesity, and dietary habits also influence CKD progression, necessitating comprehensive lifestyle management. Weight control, blood pressure management, dietary guidance, and early introduction of renin-angiotensin system and SGLT2 inhibitors can help preserve renal function and slow CKD progression. Reducing proteinuria remains a key indicator of LN treatment efficacy. Proteinuria reflects not only SLE activity but also kidney function decline, highlighting the importance of interventions to reduce it. Additionally, disease recurrence exacerbates cumulative renal damage, making relapse prevention a critical therapeutic goal. Addressing lifestyle-related conditions, such as diabetes and obesity, is essential in preventing CKD progression in LN patients. Collaboration between rheumatologists and nephrologists can enhance comprehensive management of immune and non-immune risk factors. This presentation will explore key CKD management strategies in LN, based on current evidence, and outline novel approaches aimed at improving outcomes.

S2-6

IgG4-related disease and the kidney

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Conflict of interest: Yes

In 2006, as a young doctor at Nagoya University, I (the first author) encountered a renal tissue specimen with an unusual interstitial lesion. The patient exhibited elevated serum creatinine and IgG levels, along with hypocomplementemia. I reported, “Extensive cell infiltration and progressing fibrosis are noticeable in the interstitium. Fluorescence staining suggests IC-mediated injury, but the renal biopsy does not identify the systemic disease”. My supervisor referenced a report by Kambham N et al. titled ‘Idiopathic hypocomplementemic interstitial nephritis with extensive tubulointerstitial deposits’ (Am J Kidney Dis. 2001), which matched my histological findings. In hindsight, these cases were IgG4-related tubulointerstitial nephritis (IgG4-TIN). The concept of systemic IgG4-related autoimmune disease emerged from cases of autoimmune pancreatitis (AIP) with high serum IgG4 and IgG4-positive plasma cell infiltration. In 2004, two TIN cases associated with AIP were reported, recognizing the kidneys as targets in this systemic disease, highlighting my knowledge gap. Today, these systemic diseases, characterized by hyper-IgG4emia and IgG4-positive plasma cell infiltration, are known as IgG4-related disease (IgG4-RD), with renal manifestations termed IgG4-related kidney disease (IgG4-RKD). This session will cover the history of the disease concept, clinical epidemiology, microscopic and macroscopic findings, treatments, and their responses. It will include our renal biopsy cases before and after glucocorticoid administration and data from the renal biopsy registry at our university and Nagoya University-related facilities from a nephrologist’s perspective.

S3-1

Environment and Exposome in Rheumatoid Arthritis

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Conflict of interest: Yes

The exposome integrates the variety and accumulation of exposures (external and internal) to which an individual is submitted to from conception to death. Exposome may therefore be a useful tool for understanding the diversity of these factors and their role in the pathophysiology of rheumatoid arthritis (RA). Life is perceived as a continuum of cumulative changes, with key periods of disruption (e.g. birth, adolescence, pregnancy, prolonged treatment). The combination of these changes and the external signals that cause them constitute an individual’s exposome, which is constantly changing and expanding throughout life. Thus, measuring the exposome requires specific tools and approaches as well as a global perspective. RA, a complex pro-inflammatory autoimmune disease with a genetic component and for which a large number of environmental factors have already been incriminated is an appropriate field of application for the exposome. Environment is a part of exposome and is a significant player in RA. The most studied **specific external exposure** is active smoking, but many others are involved, namely dust, coal, or air pollution. Diet and infections have also a major impact on RA. **General external exposures** are also important, many of them might influence RA course since they are linked to central nervous system: a meningeal lymphatic network allows the passage of immune cells from the cerebrospinal fluid to the cervical lymph nodes. Reciprocally, macrophages communicate with neurons. Since then, the concept of an interface between stress or other pshychological factors modulated by the brain via the autonomic nervous system and immunity has emerged. Development of new research strategies in RA pathophysiology studies should mainly involve large-scale multidisciplinary collaboration in order to share technologies and large cohorts. Involvement of other fields of sciences (social, human, ecology, anthropology, artificial intelligence) is also a prominent issue.

S3-2

Pathogenesis of enthesitis and secondary synovitis

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Conflict of interest: None

Up until the end of the 20th Century, enthesitis was viewed as an interesting clinically useful but a relatively infrequent lesion in the Spondyloarthropathy (SpA) spectrum disorders including ankylosing spondylitis and psoriatic arthritis. Its role as the key to unlocking the pathogenesis of SpA seemed unlikely since the actual insertion point itself had fibrocartilage only and was devoid of immune cells in healthy humans. Fast forward a quarter of a century and the enthesis is not centre stage in all aspects of SpA immunopathogenesis and therapy. How did this come about? First, the advent of fat suppression MRI and ultrasound has shown that enthesitis and associated anchorage point osteitis is common in the axial and peripheral skeleton in AS and PsA and other SpA family members. Secondly, imaging in humans shows a large burden of subclinical enthesopathy in psoriasis and that this is linked to later PsA evolution. Thirdly, the nature of the enthesis as not just a mere insertional point but as an "enthesis organ" and "synovio-entheseal complex" and the recognition that entheses are prone to microdamage and micro-inflammation in a biomechanically associated way has provided a robust pathology model for all SpA manifestations including, not just focal enthesitis, but also synovitis, dactylitis, osteitis, periostitis and other SpA associated lesions. Fourthly, insights in man have allowed studies in several animal models including TNF transgenic mice and IL-23 overexpression murine models that show a primary enthesitis with entheseal stromal or peri-entheseal resident lymphocyte release of pro-inflammatory cytokines as a primary event with the development of a secondary synovitis. Thus, the enthesis point of anchorage is the eye of the hurricane towards and immunological mediate inflammatory arthritis with shared synovial yet distinct inflammatory features from other inflammatory arthropathies.

S3-3

Recent progress and future potential in the imaging of inflammatory arthritis

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Conflict of interest: None

Clinical imaging in rheumatology has evolved over the centuries, and novel imaging modalities, including musculoskeletal ultrasonography (MSUS) and magnetic resonance imaging (MRI), are widely used in the 21st century. With the increase in availability of molecular target-specific therapies, including biologic agents and Janus kinase (JAK) inhibitors, the therapeutic outcome of inflammatory arthritis has changed, and early and accurate diagnosis of inflammatory rheumatic diseases has become more important. Given this situation, MSUS, which is a portable, convenient, noninvasive, and cost-effective imaging technique, plays an important role in the diagnosis of rheumatic diseases. MSUS can be used to detect subclinical inflammation and to accurately determine the distribution of joint involvement and inflammation sites in each joint. Definitive diagnosis for patients with early arthritis should be made after noting their history and performing clinical examination, laboratory testing, and additional procedures. However, MSUS is an extension of physical examination, and it can provide a further opportunity and motivation to consider differential diagnoses rather than a conclusive diagnosis. This session provides an overview of the main studies focusing on the value of MSUS in the assessment of the patients with inflammatory arthritis including rheumatoid arthritis, spondylarthritis and other rheumatic diseases, and we are discussing the future potential of usefulness of MSUS in specific settings especially assessing the patients with difficult to treat rheumatoid arthritis and precision medicine using ultrasound guided synovial biopsy.

S3-4

Cutting-edge of the treatment of arthritis: Bridging the gap between RCTs and real-world clinical practice through cohort studies

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Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), the availability of various molecular-targeted therapies has expanded, yet approximately 20% of patients in clinical practice still fail to achieve low disease activity (Yamanaka et al., Modern Rheumatology, 2020). One contributing factor is the increasing prevalence of patient populations, such as the elderly or those with comorbidities, who are typically excluded from randomized clinical trials. This trend underscores the growing importance of cohort studies to provide real-world evidence in RA care. In 2016, we initiated the ANSWER Cohort (Kansai Consortium for Well-being of Rheumatic Disease Patients), a multicenter cohort study led by orthopedic and immunology specialists across nine institutions in the Kansai region, including Osaka University, Kyoto University, Osaka Metropolitan University, Osaka Medical and Pharmaceutical University, Kansai Medical University, Kobe University, Nara Medical University, Kinki University, and Osaka Red Cross Hospital. To further enhance this research, the ANSWER Cohort Consortium was established as a non-profit organization in December 2018. Currently, we are collecting and longitudinally maintaining data from approximately 10,000 RA patients at each clinical visit, enabling physician-led studies addressing clinical questions relevant to RA management. To streamline data collection and improve data quality, some data management tasks are outsourced, and data managers assist with data extraction. This symposium will provide an overview of the latest findings from the ANSWER Cohort, shedding light on the current status and challenges in RA management in Japan.

S3-5

Unmet needs in the current treatment of arthritis and enthesitis

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Conflict of interest: Yes

Although most of the patients with immune-mediated arthritis and enthesitis achieve the treatment goal within a year, at least 10% of the patients are classified as difficult-to-treat/manage. Some of the patients show persistent and refractory inflammation in and around the joints which requires adjustment of disease-modifying antirheumatic drugs (DMARDs). Before switching to DMARDs of similar or different mode of action, we need to evaluate whether the current dose of ongoing DMARDs is sufficient for the patients or not, because insufficient dosing of DMARDs is a critical issue in current treatment with targeted therapies. Difficult-to-treat/manage patients without objective signs of inflammation may not be suitable for current measures of clinical disease activity and other therapeutic options than DMARDs should be considered for those patients. Future directions include an intensified use of current biological/targeted synthetic (b/ts)DMARDs and their combination use in addition to novel b/ts DMARDs.

S4-1

Imaging of connective tissue diseases related intersting lung diseases

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Conflict of interest: Yes

CT findings of connective tissue diseases related interstitial lung diseases (CTD-ILD) are classified into usual interstitial pneumonia (UIP) pattern, fibrosing non-specific interstitial pneumonia (FNSIP) pattern, organizing pneumonia (OP) pattern, diffuse lymphoid hyperplasia (DLH) pattern, fibrosing OP (FOP) pattern, and diffuse alveolar damage (DAD) pattern according to their pathological backgrounds. Common CT findings of UIP pattern are lower lobe predominant subpleural heterogeneous reticulation with traction bronchiectasis and honeycombing. FNSIP pattern shows lower lobe predominant peribronchovascular ground-glass attenuation (GGA) and reticulation with traction bronchiectasis on CT. Subpleu-

ral sparing is also common in FNSIP pattern. DLH pattern depicts thickening of interlobular and bronchovascular bundles, centrilibular branching structures and areas with GGA. Cysts are commonly seen in DLH pattern. OP pattern shows patchy either peripheral or peribrocnhovascular areas of airspace consolidation on CT. Common CT findings of FOP are bilateral synmetrical peribronchovascular areas of air space consolidation with traction bronchiectasis and perilobular opacites. DAD pattern shows areas of airspace consolidation and GGA with traction bronchiectasis and severe local loss of volume. Although FNSIP pattern is common in all CTDs, prototype of CT findings of FNSIP is seen in SSc. UIP and OP pattern is often seen in RA. DLH pattern is common in SjS while FOP pattern is in PM/DM.

S4-2

The importance of lung biopsy on interstitial lung disease associated with connective disease

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Conflict of interest: None

In this session, I will discuss the significance of lung biopsy in interstitial lung disease associated with connective tissue diseases (ILD-CTD). Below are the main roles and importance of pathological interpretations. **1. Treatment plan** The antifibrotic agents have significantly changed the treatment plan for chronic interstitial pneumonia (IP). In particular, if a pathological usual interstitial pneumonia pattern is present, it suggests a poor prognosis and can be a basis for the use of antifibrotic agents. If there are many fibroblastic foci, there may be a risk of acute exacerbation or rapid progression of fibrosis. **2. Evaluation of lesions other than interstitial pneumonia** Changes in hemodynamics may be detected histologically even before pulmonary hypertension becomes clinically evident. **3. Evaluation of complications** There are many pathologies associated with treatment of CTD, such as infections and drug-induced pneumonia. Infection is often the main cause of acute exacerbations of ILD-CTD. **4. Assessment of treatment efficacy** It is also useful for assessing the effectiveness of treatment. In particular, in CTD, the condition may change due to treatment, so it is reasonable to adjust the treatment method according to the change in condition. **5. Exclusion of malignant tumors** Many deaths in CTD are due to malignant tumors, so it is important to detect the malignant tumors. In particular, malignant lymphoma associated with methotrexate and lung cancer are frequent. **6. Evaluation of CTD features** There are many cases where CTD is strongly suspected histologically even if the diagnostic criteria are not met. **7. Other** ILD-CTD have many variations. Although ILD-CTD has common pathologies, there are many atypical pathologies. There are still many unknown pathologies of CTD, and it is believed that lung biopsy suggests many clues to improving the prognosis of CTD patients.

S4-3

Evaluation of connective tissue disease-associated interstitial lung disease

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Conflict of interest: Yes

Management of connective tissue disease-associated interstitial lung disease (CTD-ILD) necessitates a comprehensive approach that combines clinical evaluation, imaging, and physiological assessment to monitor disease progression accurately, understand pathophysiological changes, and determine the achievement of therapeutic goals. Clinical evaluation involves monitoring changes in symptoms such as cough and dyspnea. Additionally, assessing quality of life through patient-reported outcome measures is crucial for a holistic understanding of the patient's health status. Imaging primarily utilizes HRCT to classify ILD patterns and quantify changes. Physiological Assessment includes pulmonary function tests and the six-minute walk test. A singular assessment method is insufficient for the accurate evaluation of CTD-ILD; therefore, integrating multiple assessment modalities is imperative. Notably, certain phenotypes within chronic fibrosing ILD exhibit progressive fibrosis, leading to poor prognosis regardless of the underlying disease. This understanding has led to the proposal of concepts such as progressive fibrosing interstitial lung disease (PF-ILD) and progressive pulmonary fibrosis (PPF). Although there are differences between these criteria, they all fundamentally rely on clinical, imaging, and physiological evaluations. In recent years, the role of serum biomarkers has garnered increasing attention. In Japan, biomarkers such as KL-6, SP-D, and SP-A are utilized as indicators reflecting prognosis and disease progression in ILD. It is expected that employing biomarkers enables personalized tailored pathophysiological assessment. This lecture will provide an in-depth discussion on the application and interpretation of various indicators used in the management of CTD-ILD.

S4-4

Myositis-associated interstitial lung disease

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Conflict of interest: Yes

Polymyositis/dermatomyositis (myositis) is characterized by autoimmune myositis and extramascular manifestations including skin rash, arthritis/arthralgia, interstitial lung disease (ILD), cardiomyopathy, dysphagia, and intestinal ulceration. Characteristics of myositis-associated ILD (myositis-ILD) such as disease behavior, morphological pattern on chest HRCT, and treatment response, are highly variable among myositis patients. The assessment of ILD status before treatment initiation and monitoring during follow-up period is crucial to prevent ILD progression. According to 2020 guide for the diagnosis and treatment of ILD associated with connective tissue disease (CTD-ILD) which a joint effort of the Japan College of Rheumatology and Japanese Respiratory Society, the therapeutic algorithm for myositis-ILD consists of disease behavior: acute/subacute ILD or chronic ILD, and myositis autoantibody profile: presence or absence of anti-MDA5 and anti-ARS. Clinicians can use this algorithm to formulate therapeutic strategy taking into account prognostic factors and initial treatment response. Afterward, the British Society of Rheumatology and American College of Rheumatology published clinical guidelines for myositis including myositis-ILD and CTD-ILD, respectively. These guidelines provided a separate therapeutic algorithm for rapidly progressive ILD (RP-ILD). Furthermore, various predictive models for the development of RP-ILD or fatal outcomes have been created using cohort databases. Therefore, the management of RP-ILD in myositis patients is considered pivotal in clinical practice. Reports on the usefulness of JAK inhibitors, rituximab, antifibrotics, or plasmapheresis for patients with myositis-ILD are accumulating. The purpose of this symposium is to present the therapeutic algorithm for myositis-ILD based on the 2025 guide for the diagnosis and treatment of CTD-ILD and to compare the 2025 and 2020 versions.

S4-5

Interstitial lung disease associated with systemic sclerosis

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Conflict of interest: Yes

Systemic sclerosis (SSc) is characterized by a triad including fibrosis of the skin and systemic organs, peripheral circulatory disorders, and autoantibody production. Interstitial lung disease (ILD) is the most common cause of death as well as the most prevalent pulmonary involvement in SSc. Thus, predicting the clinical course and appropriate treatment are indispensable for improving the prognosis of SSc. In the management of SSc-ILD, the extent of the lesion is evaluated first using high-resolution CT, followed by anticipating the risk of progression by disease stage, clinical features, biomarkers, and pulmonary function test. Based on these evaluations, the indication for pharmacotherapy is determined. Five drugs are currently recommended for the treatment of SSc-ILD, including mycophenolate mofetil, cyclophosphamide, tocilizumab, rituximab, and nintedanib. However, the efficacy of these drugs is limited to "slowing the decline" of pulmonary function. Further evidence regarding new treatments and combination therapies is therefore required. This seminar will

introduce the latest evidence regarding the diagnosis, risk assessment, and treatment of SSc-ILD.

S4-6

Diagnosis and Treatment of Interstitial Lung Disease Associated with Rheumatoid Arthritis

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Conflict of interest: None

Interstitial lung disease (ILD) is one of the poorest prognostic complications of rheumatoid arthritis (RA). RA-ILD is encountered more frequently in daily practice due to the large number of patients compared to other rheumatic diseases. Risk factors for acute exacerbation or poor prognosis in RA-ILD include elder age, methotrexate (MTX), extensive pulmonary fibrosis, poor diffusion capacity, and a usual interstitial pneumonia (UIP) pattern on high-resolution CT (HRCT). Evaluation of extent and patterns of RA-ILD is important at the diagnosis. Although there is a large body of evidence for treatment of RA, there are few randomized controlled trials (RCTs) in RA-ILD. As with idiopathic interstitial pneumonia, treatment strategies are based on disease behavior. In the acute and subacute ILD, infections and drug-induced lung injury should be differentiated and treatment with glucocorticoids and immunosuppressive drugs is initiated depending on the severity of the disease. In chronic ILD with progressive diseases, therapeutic intervention should be considered. Several perspectives, including clinical symptoms, imaging, respiratory function, and serological markers are performed to evaluate disease progression and phenotypes by multidisciplinary discussion (MDD) on a 3-6 month interval. Immunosuppressive drugs are initiated in RA-ILD with cellular/inflammatory phenotype and antifibrotic agents are in those with fibrotic phenotypes. There is insufficient evidence for immunosuppressive therapy for RA-ILD. The antifibrotic agent, nintedanib, has been reported to be effective in reducing FVC decline and the risk of acute exacerbations and death in subgroup analyses of RCTs. Recent reports addressed that MTX therapy is not a risk for the progression and acute exacerbation of ILD. MTX therapy, the use of immunosuppressive agents and antifibrotic agents, or the combination of the two, in RA-ILD remain a future issue.

S5-1

The importance of patient-reported outcomes in clinical practice

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Conflict of interest: None

Rheumatoid arthritis was once an intractable disease, but the establishment of the T2T strategy, quantification of the condition using comprehensive disease activity assessment indices and the development of highly effective molecular-targeted drugs have advanced its treatment to the extent that the aim of clinical remission in all patients is now advocated as a treatment goal. At Keio University Hospital, 65% of the approximately 2500 patients with rheumatoid arthritis have achieved clinical remission. On the other hand, it has been highlighted that even when clinical remission is achieved, symptoms such as pain and fatigue remain and some patients are more distressed than the medical profession would have thought. Patient-reported outcomes have therefore been in the spotlight in recent years for their usefulness. Patient-reported outcomes are the same as patient-reported outcomes (PROs), patient-oriented assessments, etc., and refer to subjective assessments of health status made directly by patients themselves, without the involvement of a doctor. Historically, health status in the medical field has been assessed from the perspective of the physician. In recent years, the importance of evaluations that index subjective opinions from the patient's perspective as well as objective indicators from the medical practitioner's perspective has been reassessed and tends to be actively incorporated into the evaluation of drug efficacy. In fact, the FDA recommends setting PROs as clinical trial endpoints; PROs include symptom severity, treatment satisfaction, function and health-related quality of life, which can be used as indicators for determining treatment efficacy by scientifically evaluating the impact of the disease on life and ensuring reliability and validity, thereby promoting patient-participatory clinical trials and practice in This leads to the implementation of patient-participatory clinical trials and medical practice. In the field of rheumatic diseases, the visual analogue scale (VAS), morning stiffness time, etc. were incorporated as patient-oriented assessments from a relatively early stage, but in daily clinical practice, joint findings and blood test findings tended to be more important. However, several studies, including a report from our hospital, have shown that there is often a significant discrepancy between patient and physician assessment. In this presentation, I will outline recent findings on patient-reported outcomes in rheumatic diseases and consider how they should be used in routine practice to maximise patient quality of life.

S5-2

The Importance of Early Treatment in Difficult-to-Treat Rheumatoid Arthritis (D2T-RA)

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Conflict of interest: Yes

Rheumatoid arthritis (RA) management hinges on early diagnosis and timely pharmacological intervention to maximize patient quality of life (QOL) and reduce disease activity. Despite advances in treatments achieving remission or low disease activity for many, challenges persist, particularly for patients with difficult-to-treat rheumatoid arthritis (D2T-RA). These individuals often experience treatment-resistant disease due to factors like comorbidities and economic constraints, significantly impacting QOL. Preventing D2T-RA is critical, as this group exhibits lower treatment responsiveness and worse outcomes. Early intervention is vital for reducing disease activity, preventing joint damage, and lowering the risk of developing D2T-RA. Research highlights the importance of early treatment, with studies showing that delays, such as a three-month postponement in initiating methotrexate (MTX), can increase the risk of D2T-RA. Early control of immune overreaction is thought to minimize disease complexity and progression. Key risk factors for D2T-RA include high disease activity, respiratory comorbidities, and seropositive status. Precision medicine tailored to patient-specific conditions is essential, emphasizing standard treatment with adequate MTX dosing. For patients unable to use MTX, early adoption of molecular-targeted therapies is recommended. Despite current limitations, optimizing available treatment strategies is crucial to preventing D2T-RA and improving QOL. This presentation addresses the need for early treatment strategies to prevent D2T-RA, aligning with the broader therapeutic goal of enhancing patient outcomes and QOL.

S5-3

Evidence and practice of treatment of older rheumatoid arthritis patients

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Conflict of interest: Yes

Compared with younger patients, older rheumatoid arthritis (RA) patients have more comorbidities such as chronic kidney disease, chronic lung disease, cardiovascular disease, osteoporosis, and malignancy, and are at higher risk for serious infections while receiving disease modifying anti-rheumatic drugs (DMARDs). There are few randomized controlled trials (RCTs) in older RA, and sub-analysis of RCTs of biological DMARDs (bDMARDs) and JAK inhibitors have evaluated efficacy and safety in RA patients older than 65 years. Safety analyses have also been conducted from insurance databases in the U.S., the U.K., Canada, and Japan, primarily regarding safety in older RA. These analyses have shown that bDMARDs and JAK inhibitors are effective in older RA compared to placebo. Safety has also been confirmed for bDMARDs in the older population compared to csDMARDs, including MTX, or in multivariate risk factor analyses, although older patients have more serious adverse events than younger patients. Long-term treatment with JAK inhibitors in older RA patients at risk for cardiovascular events has been shown to potentially increase the incidence of cardiovascular disease and malignancy compared with long-term treatment with TNF inhibitors. Evidence for the efficacy and safety of

concomitant use of glucocorticoids in older patients with RA has also been presented. Prospective observational studies and RA registry, mainly in Japan, have revealed the actual treatment status of older RA patients with MTX, bDMARDs, JAK inhibitors, and glucocorticoids in daily clinical practice. In addition to analyzing data on late-onset RA from existing large cohorts representing Japan, we are conducting a new multicenter prospective cohort study of late-onset RA. In this symposium, we will introduce these evidences on older RA patients and discuss the unmet-needs of treatment in order to achieve an increase in healthy life expectancy of older RA patients.

S5-4

Management of patients with RA and other complications

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Conflict of interest: Yes

In our super-aged society, RA patients without complications are in the minority, and many RA patients have multiple comorbidities. In patients with renal dysfunction, a careful choice of drug and its dosage is needed, and in those with respiratory complications, attention should be paid to the risk of respiratory tract infections due to a decreased respiratory barrier function and to the prevention of airway diseases and interstitial lung disease (especially acute exacerbation in the latter case). Collaboration with cardiology is essential for patients with cardiovascular disease and the use of drug with a potential risk of cardiovascular exacerbation should be avoided as much as possible. Current or prior malignancy is an important issue, and although the overall impact of therapeutics on tumor immunity remains unclear, preference should be given to agents with a good evidence base for malignancy. The same is true for preexisting lymphoproliferative disease, and such patients should not be (re)treated with methotrexate. It should be noted that RA itself is a high-risk disease, and remission (or at least low disease activity) of RA should be a top priority. The problem of polypharmacy is becoming more and more serious, and the role of pharmacists will become even more important in terms of drug interactions. Thus, the importance of total management is acknowledged in RA patients, and close collaboration among multiple disciplines and professions will be the key to success.

S5-5

Rheumatology rehabilitation treatment aimed at maximizing QOL

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Conflict of interest: None

Paradigm shift in the treatment of rheumatoid arthritis has induced remarkable in pharmacotherapy. However, all patients are not in remission and joint destruction is not prevented totally. With the advent of a super-aging society, the number of elderly-onset RA patients is increasing and the number of young-onset RA patients is aging. Complications of osteoporosis, osteoarthritis, sarcopenia, and frailty due to decreased activity, low nutrition and muscle volume, depressive symptoms, and cognitive decline are also increased in late-onset patients with RA. Internal disorders make it increasingly difficult to administer strong drug therapy, and non-drug treatment, especially rehabilitation therapy, is becoming increasingly important to maximize quality of life. However, according to the Rheumatology report by the Rheumatology Friendship Society, while the percentage of patients receiving rehabilitation therapy was 46.2% in 2000, this percentage has been declining year by year, decreasing to 23.6% in 2020. This is partly because the number of patients who do not need rehabilitation treatment has increased due to the paradigm shift in treatment, but on the other hand, there were also opinions that it is difficult for patients to receive rehabilitation therapy due to their insurance. On the other hand, according to the 2022 National Health and Nutrition Survey Report by the Ministry of Health, Labour and Welfare, even in the general population, 35.5% of men and 31.5% of women have an exercise habit, and this percentage is decreasing year by year, especially for women. In patients with RA, furthermore, it is estimated that they spend less time exercising and walking than the general population. So it seemed important to motivate, appropriate programs, and maintain motivation for rehabilitation therapy. In this symposium, we would like to deepen the discussion with the participating doctors on rehabilitation therapy aimed at maximizing QOL.

S5-6

Toward expansion of the range of QOL -Orthopaedic surgery-

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Conflict of interest: None

The therapeutic targets of clinical practice in rheumatoid arthritis (RA) may be varied among patients and medical professionals. As evidenced in the white paper of RA, pain may be the first target when the pain is severe, or the resolusion of complications such as lung disorders may be the most important target when the complication is a heavy burden for the patient. However, functional impairment must be one of the most serious targets for patients and medical professionals due to the facts that RA is a joint disorder and that joint destruction and deformity is one of the distinctive manifestations of the disease. Especially, the severer the conditions of the patient are, or the longer the duration of the disease lasts, more serious the target of the patient becomes. The white paper previously mentioned shows that many issues in ADL and QOL still exist among the patients. When considering the therapies for the issues, medical treatment with anti-rheumatic disease-modifying drugs must be the most effective one for resolution of the problems in ADL and QOL, but if anything remains after the treatment, orthopaedic surgery is the most powerful treatment option toward expansion of the range of QOL. This lecture will show how and when the orthopaedic operations can expand the range of QOL in details, descriving specific examples.

S6-1

Development of a Japanese Familial Mediterranean Fever Model Mouse and Novel Therapeutic Strategies for Drug Discovery

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Conflict of interest: Yes

Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disease caused by MEFV gene mutations, common in Mediterranean coastal regions. FMF pathology involves abnormal activation of inflammatory molecules and immune cells, essential for inflammation control. MEFV encodes pyrin, a key inflammation regulator. Pathogenic mutations cause dysfunctional pyrin, leading to excessive inflammation and periodic fever, abdominal pain, and joint pain. In Japan, specific MEFV gene variants, especially the E148Q mutation in exon 2 and M694I mutation in exon 10, are commonly found in FMF patients. These mutations, prevalent in Japanese FMF cases, are believed to uniquely influence disease pathology. This study aimed to develop a knock-in mouse model with these human MEFV mutations to replicate Japanese-type FMF pathophysiology and enhance understanding of the disease. This mouse model replicates FMF inflammatory responses and febrile episodes, offering a tool for studying disease mechanisms. Mice homozygous for the human MEFV M694I mutation showed reduced survival, poor weight gain, and elevated inflammatory cytokines, linking chronic inflammation to tissue damage. This phenotype mirrors FMF patient symptoms, highlighting the model's relevance for Japanese-type FMF research. Regarding drug discovery, we aimed to enhance both the efficacy and safety of colchicine, which is the primary treatment for FMF. Although colchicine is widely used as a first-line treatment, its broad systemic effects and the risk of adverse effects with long-term use present challenges. In this study, we developed a novel therapeutic approach by encapsulating colchicine in a nanolipogel coated with an antineutrophil antibody, enabling targeted delivery to neutrophils. This nanolipogel has the potential to efficiently deliver drugs to target cells in the bloodstream, reducing side effects while enhancing therapeutic effica-

cy. This presentation summarizes these research findings using FMF mouse models and outlines new insights into the pathophysiology of Japanese-type FMF and potential therapeutic strategies.

S6-2

Development of a new treatment targeting the active inflammatory cytokine IL-18

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Conflict of interest: None

IL-18 is classified within the IL-1 cytokine family based on its amino acid sequence homology. IL-18 is synthesized as a biologically inactive IL-18 precursor (193 amino acids in humans). It requires processing by caspase-1/4 to bind to its receptor. The enigma of how IL-18 is secreted outside the cell despite the absence of a signal peptide was solved by discovering gasdermin D. In numerous diseases, including adult-onset Still's disease, rheumatoid arthritis, interstitial pneumonia, ulcerative colitis, Crohn's disease, multiple sclerosis, and diabetes, elevated serum IL-18 levels are observed, positioning the IL-18 protein as a promising therapeutic target. One drug discovery strategy involves the use of IL-18 binding protein (IL-18BP), an endogenous soluble factor that specifically inhibits IL-18 activity, while another strategy employs monoclonal antibodies. Administration of IL-18BP has been shown to significantly ameliorate conditions in mouse models of experimental arthritis, colitis, interstitial pneumonia, type 1 diabetes, and other diseases. There are two potential approaches with monoclonal antibodies: one involves using an antibody that recognizes both the IL-18 precursor and active IL-18, and the other involves using an antibody that targets only active IL-18. Certain cells, such as Kupffer cells, constitutively express IL-18 precursors. To mitigate the risk of antibody consumption due to the large quantities of IL-18 precursors released from cells damaged by inflammation, we generated mouse monoclonal antibodies that specifically recognize active IL-18, not inactive IL-18 precursors. We have already observed amelioration in the pathological conditions of mouse models of interstitial pneumonia, ulcerative colitis, Crohn's disease, multiple sclerosis, and other diseases using an antibody that exclusively recognizes active IL-18. This antibody has been humanized. We are conducting preclinical research in collaboration with Nagasaki University, Nagoya University, and Shimane University to expedite its application in humans. I would like to discuss the current progress with you.

S6-3

Development of new treatments for idiopathic multicentric Castleman disease

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Conflict of interest: None

Idiopathic multicentric Castleman disease (iMCD) is a rare inflammatory disease characterized by enlarged lymph nodes. It affects around 1,500 people in Japan. If not treated appropriately, iMCD can lead to organ damage and secondary amyloidosis, compromising quality of life and even shortening life expectancy. The involvement of interleukin-6 (IL-6) in the pathogenesis of iMCD has been reported, and tocilizumab and siltuximab are used. Although IL-6 inhibitors are effective, there are refractory cases, and chemotherapy is sometimes administered. Furthermore, in Japan, subcutaneous tocilizumab is not approved for iMCD. Because of the need for frequent outpatient visits for intravenous administration, some patients seek orally available drugs. Understanding the disease mechanisms has led to attempts to regulate various targets. Targeting B cells, clinical trials of rituximab, thalidomide, cyclophosphamide, bortezomib, and Bruton's tyrosine kinase inhibitors for iMCD are conducted worldwide. In addition, the mechanistic target of rapamycin (mTOR), contributing to T-cell activation and cell proliferation, is involved in the pathogenesis of the disease. Clinical trials are conducted for its inhibitor, sirolimus, in the US and Japan. It has been reported that Janus kinase (JAK) 1 and JAK2, which are downstream of IL-6, cause activation of mTOR and signal transducer and activator of transcription 3, and some cases treated with ruxolitinib, a JAK1/2 inhibitor, are reported. A clinical trial of filgotinib, a JAK inhibitor already approved for rheumatoid arthritis and ulcerative colitis, has been conducted. iMCD is highly specialized, with the pathological findings of the lymph nodes being important for diagnosis. Therefore, building a cooperative system between specialists for this disease and the many facilities involved in patient recruitment is essential. In parallel with elucidating the pathogenesis, it is anticipated that various treatments will be developed for iMCD.

S6-4

Identification of Therapeutic Targets in VEXAS Syndrome Through Multi-Omics Analysis Based on Clinical Data

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Conflict of interest: None

VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is a newly identified autoinflammatory disorder with poor prognosis, first described in 2020. It is caused by somatic mutations in *UBA1* gene on the X chromosome. This disease frequently presents systemic inflammatory symptoms and hematological abnormalities. However, its pathogenesis remains poorly understood. While high-dose steroids show some efficacy, inflammation often relapses during tapering, highlighting the need for the development of effective and tolerable alternative therapies. To identify therapeutic targets, understanding the molecular mechanisms underlying the disease is essential. Recently, transcriptome analysis has emerged as a powerful tool in genomic drug discovery and was considered applicable to the development of novel treatments for VEXAS syndrome. Peripheral blood samples from 5 patients with VEXAS syndrome and 3 healthy controls were used to isolate PBMCs, monocytes, neutrophils, and plasma. RNA sequencing (RNA-seq) and proteomic analysis were conducted. Single-cell RNA-seq was performed on samples from 2 patients and 1 healthy control to identify disease-specific therapeutic target molecules. However, cross-sectional analysis posed challenges due to noise caused by differences in patient backgrounds, disease activity, and treatment regimens. To overcome these limitations, longitudinal analysis was conducted. Blood samples and clinical information were repeatedly collected from 13 VEXAS syndrome patients during clinical visits, and whole-blood RNA-seq was performed. As controls, samples from 18 patients with autoinflammatory diseases suspected of having VEXAS syndrome but negative for UBA1 mutation and 10 healthy individuals were included, generating 119 gene expression datasets. To quantify disease activity, a novel score, VEXASCAF was developed. (Kirino et al., Rheumatology, 2024) Genes strongly correlated with this score were identified, and those consistently overexpressed in VEXAS syndrome were further selected using previously obtained omics data. This study demonstrates the integration of clinical data with multi-omics analysis to identify genes associated with disease activity. The findings provide insights into potential biomarkers for disease activity monitoring and novel therapeutic targets for VEXAS syndrome.

S6-5

Pathophysiology and therapeutic development for systemic lupus erythematosus focusing on transcription factor IRF5

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is an intractable autoimmune disease that develops when antibodies against autoantigens such as DNA form immune complexes and deposit in tissues, causing inflammatory lesions throughout the body. Current therapies, including antibodies that inhibit the type I interferon (IFN) receptor (IFNAR1), which has been considered central to the pathogenesis of the disease, have been associated with relapse and side effects; therefore, novel therapies are desired. Using a mouse model of SLE, we have shown that hyperactivation of IFN regu-

latory factor 5 (IRF5), a transcription factor that regulates innate immune responses, forms the exacerbation cycle in SLE and that suppressing IRF5 expression only by half can prevent the onset of SLE; thus, IRF5 is a promising therapeutic target for SLE (Ban et al., *Immunity* 2016). Subsequently, a high-throughput screening (HTS) of approximately 100,000 compounds was conducted to find inhibitors of IRF5 activity, resulting in a prototype IRF5 inhibitor that selectively inhibits IRF5 activation. In addition, the fact that abnormal activation of IRF5 continues in human SLE even during remission, that even halving the expression level of IRF5 in a mouse SLE model suppresses disease onset much more strongly than complete inhibition of type I IFN, and that IRF5 inhibition is particularly effective in maintaining remission, show the possibility that IRF5 inhibition is a novel therapy that can overcome the limitations of current treatments (Ban et al., *Nat Commun* 2021). The results of our previous studies have confirmed that IRF5 is essential for type I IFN induction in SLE but that IRF5 also regulates the expression of genes other than type I IFNs, thereby causing SLE pathogenesis. However, not all of the various actions of IRF5 are important for SLE pathogenesis. Although IRF5 has been reported to be involved in SLE pathogenesis in various cell types, including dendritic cells, monocytes, B cells, and follicular dendritic cells, the target genes of IRF5 in each cell type are largely unknown. In this presentation, we will describe our previous research to understand the pathogenesis and to develop therapeutic strategies for SLE focusing on the transcription factor IRF5, and introduce our recent findings.

S6-6

Prevention of recurrence of congenital heart block in pregnancies of anti-SS-A-positive women using hydroxychloroquine (AMED-BIRTHDAY)

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Conflict of interest: Yes

Anti-SS-A antibodies are autoantibodies found in about 1% of healthy individuals, and congenital atrioventricular block (CHB) is complicated in about 2% of children of anti-SS-A antibody-positive mothers. Anti-SS-A antibody-positive pregnancies with previous CHB have a high recurrence rate of 16-18%. The overseas clinical trial PATCH demonstrated that hydroxychloroquine (HCQ) 400 mg/day significantly reduces the recurrence of CHB below the historical rate (18%) by >50% (7.4% (4/54)). In Japan, glucocorticoids are often used to prevent CHB, but the CHB recurrence rate was 10.6% (3/28). Twenty-eight patients have been enrolled in J-PATCH for prevention of CHB recurrence, and the results are awaited. In J-PATCH II, the first remote (decentralized) clinical trial in this field, the research group developed a protocol for J-PATCH II with the goal of expanding the indications for HCQ. After discussions with MHLW, it was decided that J-PATCH II could not be conducted as a follow-up study to J-PATCH under Advanced Medical Treatment B. Since the guidelines for anti-SS-A antibody-positive pregnancies are expected to mention the usefulness of the HCQ in 2025, we decided to choose the scheme of the Review Committee for Unapproved Drugs and Off-label Drugs for approval. PMDA and MHLW jointly held discussions on the scheme up to regulatory approval in the case of an application. The manufacturing and marketing companies reported the status of reimbursement overseas, and both PMDA and MHLW instructed us to conduct a survey on the actual status of drug use. Therefore, we conducted an analysis using the JMDC database, and a survey of physician members of the JCR. Based on the results of the actual usage, we believe that it is in the best interest of patients who desire a preventive drug to expand the indication of HCQ to prevention of recurrence of CHB through a public knowledge application.

S7-1

A case of D2TPsA mimicking rheumatoid arthritis and requiring frequent treatment switching

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Conflict of interest: None

A 50-year-old woman presented to our hospital with a complaint of finger and wrist pain from five months ago. She also had an episode of erythema that appeared on her lower legs which dermatologists suspected psoriasis four months before, but it disappeared spontaneously. On physical examination, she had depressed nails, but no rashes. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (ACPA) were both negative. Musculoskeletal ultrasound showed slight Power doppler signals around the MCP, PIP joints and extensor tendons. Radiologically, there were no pencil-in-cup deformity or bone erosion. And also there were no signs of interstitial pneumonia. We started treatment with prednisolone (PSL) 10 mg and cyclosporine (CsA) 100 mg and her symptoms relieved. However, her rashes flared up a year later. The skin biopsy revealed isometric extension of epidermal protrusions and neutrophilic infiltration within the epidermis which are findings consistent with psoriasis. Considering psoriatic arthritis refractory to CsA, we discontinued CsA and introduced adalimumab 40 mg. We subsequently increased the dose of adalimumab to 80 mg, but the patient did not respond to the treatment, so we switched it to infliximab, and her arthritis improved. Yet, during the course, her rashes gradually exacerbated and we considered the paradoxical reaction to TNF inhibitors. We changed infliximab to ixekizumab and the rashes improved. Both skin and joint symptoms were stable and ixekizumab was continued. However, her joint symptoms became to get worse so, we introduced upadacitinib 15 mg and the pain relieved. We experienced a case of difficult-to-treat PsA that required frequent treatment changes due to difficulty in differentiating from rheumatoid arthritis. In this session, we would mainly discuss about the diagnosis and treatment options.

S7-2

Difficult to treat Psoriatic Arthritis

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Conflict of interest: None

Psoriatic arthritis (PsA) is a chronic, inflammatory musculoskeletal disorder associated with psoriasis, characterized by a heterogeneous presentation that can include peripheral arthritis, axial disease, enthesitis, dactylitis, and skin and nail involvement. While advances in therapeutic options have improved outcomes for many patients, a subset of individuals remains refractory to treatment, referred to as “difficult-to-treat PsA” (D2T PsA). This term describes patients who fail to achieve adequate disease control despite multiple treatment strategies, leading to significant functional impairment and reduced quality of life. Understanding the underlying mechanisms, identifying predictive factors, and optimizing management approaches are critical to addressing the unmet needs of these patients. D2T PsA lacks a universally accepted definition, but it generally refers to cases where disease activity persists despite the use of multiple conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic DMARDs (bDMARDs), or targeted synthetic DMARDs (ts DMARDs). Persistent inflammation, radiographic progression, and high patient-reported symptom burden are hallmarks of D2T PsA. Factors such as comorbidities, treatment intolerance, drug resistance, and nonadherence may contribute to the complexity of these cases. Emerging evidence suggests that D2T PsA may involve distinct immunological and molecular mechanisms. Chronic activation of the IL-23/IL-17 axis, TNF-α signaling, and JAK-STAT pathways has been implicated in refractory inflammation. Additionally, genetic polymorphisms in genes such as HLA-B27 and PTPN22 have been associated with severe disease. Dysbiosis of the gut microbiome may also contribute to persistent inflammation by modulating systemic immune responses. The management of difficult-to-treat PsA presents several challenges. First, PsA encompasses a wide spectrum of clinical features, and patients may present with overlapping or shifting domains of involvement. This variability complicates the assessment of disease activity and the selection of optimal therapies. Second, conditions such as obesity, metabolic syndrome, cardiovascular disease, depression, and fibromyalgia are prevalent in PsA and can exacerbate symptoms or limit therapeutic responses. Additionally, comorbidities may pose safety concerns when using certain DMARDs or biologics. Third, some patients demonstrate inadequate responses to DMARDs or biologics despite appropriate dosing and duration. Mechanisms underlying treatment resis-

tance include genetic variability, immune system dysregulation, and pharmacokinetic factors. Lastly, medication nonadherence, often driven by side effects, fear of long-term toxicity, or psychological distress, can undermine treatment efficacy. Addressing these barriers requires a multidisciplinary approach. Effective management of D2T PsA involves several strategies. A thorough evaluation of disease domains, comorbidities, and patient-reported outcomes is essential to guide treatment decisions. Tools such as the Disease Activity in Psoriatic Arthritis (DAPSA) score or Psoriatic Arthritis Impact of Disease (PsAID) questionnaire can aid in monitoring. Sequential or combination use of bDMARDs and tsDMARDs targeting different pathways such as TNF-α, IL-12/23, IL-17, and JAK may overcome resistance. Dual inhibition strategies are an area of ongoing research. Pharmacogenomic profiling and biomarker-driven approaches could help tailor treatments to individual patient profiles. Effective management of obesity, metabolic syndrome, and mental health conditions can enhance overall treatment outcomes. Multidisciplinary care involving rheumatologists, dermatologists, and psychologists is particularly valuable. Regular exercise and physical therapy can improve functional capacity and reduce pain. Anti-inflammatory diets, weight loss, and smoking cessation may attenuate disease activity. IL-17 and IL-23 inhibitors such as secukinumab, ixekizumab, and guselkumab have shown promise in patients with refractory PsA. Targeting intracellular signaling pathways, JAK inhibitors such as tofacitinib and upadacitinib offer alternative mechanisms of action. The availability of biosimilars may improve accessibility and adherence by reducing costs. Further research is needed to elucidate the pathogenesis of D2T PsA and identify predictive biomarkers for treatment response. Long-term studies on the safety and efficacy of combination therapies and real-world data from patient registries will provide valuable insights. Advances in artificial intelligence and machine learning could facilitate precision medicine by integrating clinical, genetic, and imaging data. In conclusión, D2T PsA remains a significant clinical challenge, requiring a multifaceted approach that addresses both disease-specific and patient-related factors. By leveraging emerging therapies, adopting a personalized medicine paradigm, and promoting multidisciplinary care, clinicians can improve outcomes for this challenging patient population.

S7-3

A Case of Axial Spondyloarthritis with Response to NSAIDs but Radiographic Progression: Challenges in Monitoring and Treatment Approaches

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Conflict of interest: None

A 32-year-old man presented with morning stiffness and back pain on standing which began at the age of 22, lasted for several days and resolved spontaneously. He has a history of anterior uveitis, which improved with steroid eye drops. There is no significant family history, including collagen disease or inflammatory bowel disease. He has a desk job. At the age of 26, family members noticed poor posture. At the age of 32, the patient visited a local orthopaedic clinic, where x-rays revealed ankylosis of the spine. He was then referred to our hospital. X-rays showed syndesmophytes in the spine and ankylosis of the sacroiliac joints. The HLA-B27 test was positive, leading to the diagnosis of radiographic axial spondyloarthritis (r-axSpA). Initial assessment showed BASDAI 3.5, ASDAS 2.6 (CRP 1.1 mg/dL). Treatment with celecoxib was initiated and resulted in symptomatic improvement. Celecoxib was continued as needed. After eight years of follow-up, recent assessments showed BASDAI 2.3, ASDAS 1.0 (CRP 0.22 mg/dL), indicating improved disease activity. The ASDAS score ranged from inactive disease to moderate disease activity. Despite symptom control with intermittent NSAID use and minimal elevation of inflammatory markers, radiographic progression of syndesmophytes in the spine has been observed, including new syndesmophytes in the cervical spine. This raises the question of how to monitor and manage such cases where symptoms are controlled but radiographic progression continues.

S7-4

Clinical Characteristics and Predictors of Difficult-to-Manage Axial Spondyloarthritis: Insights from a Single-Center Retrospective Study

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Conflict of interest: None

Objective: The term "Difficult-to-Manage Axial Spondyloarthritis (D2M-ax-SpA)" was recently introduced by the Assessment of Spondyloarthritis International Society (ASAS) at the 2024 American College of Rheumatology Convergence. D2M-ax-SpA is defined by (a) failure of morer than 2 b/ts DMARDs with different mechanisms of action, (b) inadequate control of axSpA symptoms, and (c) problematic signs/symptoms as perceived by clinicians or patients. This study evaluated the prevalence and predictors of D2M-ax-SpA in a single-center cohort. **Methods:** A retrospective analysis was conducted on 560 patients with ax-SpA diagnosed per ASAS criteria at Taipei Veterans General Hospital (2009-2021) with a follow-up of more than 6 months. Patients were classified into three groups: D2M-ax-SpA, those using biologic/targeted synthetic (b/ts) DMARDs with one mechanism of action, and those without b/ts DMARDs. Statistical analysis included Kruskal-Wallis test, Fisher's tests, logistic regression, and ROC curve analysis. **Results:** Of the 560 patients (all B27 positive), 20 (3.6%) met the criteria for D2M-ax-SpA. D2M-ax-SpA patients had longer disease duration (median 3890 vs. 3292/2034 days, $p<0.001$), more peripheral arthritis ($p<0.001$), higher sacroiliitis grades ($p<0.001$), and elevated ESR/CRP ($p<0.001$). Multivariate analysis identified peripheral arthritis as a significant factor of D2M (OR: 4.68, 95% CI: 1.74-12.60, $p=0.002$). ROC analysis highlighted ESR and CRP as robust predictors, with an AUC of 0.785 for both markers ($p<0.001$), and optimal thresholds identified as >20 mm/Hr for ESR and >0.99 mg/dl for CRP. **Conclusion:** This study underscores the importance of peripheral arthritis and inflammatory markers in predicting D2M-ax-SpA. These findings can guide early identification and intervention strategies, potentially improving outcomes for patients at risk of difficult-to-treat disease. Further research is warranted to validate these predictors in larger cohorts and diverse populations.

S7-5

A Comprehensive overview of basic research in Spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis (SpA) is a chronic inflammatory disease involving complex interactions among genetic, environmental, and immunologic factors. It primarily affects the axial skeleton, entheses, and peripheral joints. The enthesis, where tendons and ligaments attach to bone, is a key site of inflammation. Genetic predispositions such as HLA-B27 and ERAP-1 drive immune dysregulation through mechanisms like ER stress and altered antigen presentation. Environmental triggers including mechanical stress via Piezo-1, p-Erk, p-p38, and gut inflammation or dysbiosis amplify immune activation. Dysregulated cytokines like TNF-α, IL-23, and IL-17 play central roles, with contributions from innate-like lymphocytes including MAIT, iNKT, and γδ-T cells and adaptive Th17 cells driven by CCL20, pSTAT3, and pathogenic subsets expressing OX40 and GITR. Card9+ neutrophils also play a role in driving inflammation. Pathological bone formation is fueled by fatty bone marrow lesions, IL-23 and IL-22 signaling in entheseal cells, and interactions between neutrophils and mesenchymal stem cells. Abnormal BMP and Wnt pathways further promote osteogenic differentiation. This blend of chronic inflammation and bone remodeling defines SpA as a distinct and challenging condition. Advances in research and targeted therapies provide hope for improved outcomes.

S8-1

Transcriptional control of human B cell activation and antibody production

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Conflict of interest: None

Long-lived memory B cells arise from the differentiation of naive B cells. Antigen-experienced memory B cells are geared towards enhanced effector functions compared to their naive counterpart and provide long-term humoral immunity. To investigate the differences in responsiveness of naive and memory B cells, we profiled the transcriptome at the single cell level of human naive (CD20+CD27-IgG-IgA-) and unswitched memory B cells (CD20+CD27+IgG-IgA-) of four healthy donors. Cells were profiled in a resting state as well as at early and late stages upon *in vitro* stimulation. Although both cell types underwent rapid proliferation and isotype switching, memory B cells proliferated more compared to naive cells. However, isotype switching was more frequent in naive B cells. Already at a resting state as well as shortly after stimulation, naive and memory B cells had considerably different transcriptional signatures suggesting that they were two cell states poised to differentiate differently upon activation. At later time points, both naive and memory B cells acquired multiple and divergent cell states thus recapitulating the highly dynamic process of immune response. Moreover, the machinery required to sustain the high biosynthetic requirements such as genes involved in unfolded protein response, was highly expressed in memory B cells compared to naive. Furthermore, naive and memory B cells activated two opposite gene regulatory networks upon differentiation. IRF4-regulon promoted differentiation towards plasma cells and it opposed SPI1-regulon which in turn promoted the germinal cell fate and isotype switching. Finally, we validated these TF networks using CRISPR-Cas9 technology. Taken together, our data highlights differences in activation dynamics between naive and memory B cells and illustrates how distinct and opposite gene programs regulate B cell fate selection and antibody transcription.

S8-2

Single cell multiomics across diverse humanpopulations reveals novel genetic determinants andmechanisms of immune-related complex diseases

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Conflict of interest: Yes

Understanding the gene regulatory mechanisms by which non-coding GWAS variants influence complex traits remains a key challenge in human genetics, motivating extensive efforts to map quantitative trait loci (QTLs) associated with molecular phenotypes such as gene expression (eQTLs). However, three major challenges complicate the identification of trait-relevant QTLs: (1) many trait-associated variants exert effects only in specific cell types or states, making it difficult to detect these variants in bulk studies; (2) a lack of population diversity in past studies, which have largely focused on individuals of European descent, may limit the generalizability of findings; and (3) GWAS and eQTL studies may be systematically biased towards identifying different types of variants, with eQTL studies potentially lacking power to discover the most trait-relevant genes. To address these challenges, we present the Human Immune Cell Census (HICC), a cross-sectional cohort comprising approximately 400 donors of African, East Asian, European, and Latinx descent. This study simultaneously profiles gene expression and chromatin accessibility across more than 1 million single immune cells, paired with dense genotyping data. We identify cell type-specific expression and chromatin accessibility QTLs and demonstrate the value of cell type-specific chromatin accessibility data in annotating trait-relevant genetic variation. Our findings highlight the importance of single-cell multi-omic approaches in advancing the discovery of genetic regulatory mechanisms underlying complex traits across diverse populations.

S8-3

Projecting human disease omics into single cell resolution

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Conflict of interest: None

The remarkable development of human omics analysis technology has ushered in an era of enormous data availability. However, there is a growing need for disciplines to interpret large-scale omics data in a cross-sectional manner to elucidate disease pathology and pathological stratification. By utilizing statistical genetics, our group has shown that the integration of large-scale human disease genetics, such as genome-wide association study (GWAS), with multilayered human omics information from diverse biological and medical disciplines can contribute to the stratification of disease pathologies. The human omics information to be obtained could be categorized into population, individual, or single-cell resolution. In addition to population-resolution omics information represented by GWAS and individual-resolution omics information such as immunophenotype, metabolome, and proteome, single-cell-resolution omics information by single-cell analysis is becoming increasingly popular. By projecting the omics information obtained at population/individual resolution to single-cell resolution, disease pathology can be observed in individual cells, and is expected to be applied to clarification of pathology and patient stratification (e.g., involvement of innate immune cells in COVID-19 severity, dynamic single cell eQTL effects reflecting cell trajectory, endogenous herpesvirus infection and autoimmune disease development). The development of new bioinformatics technology will also make it possible to observe changes in immune profiles at single-cell resolution through the projection of single-cell information on biological phenomena directly related to disease pathology, such as somatically acquired gene mutations along with aging and X chromosome inactivation escape. In this talk, we introduce our resources that utilize single-cell analysis techniques.

S8-4

Single cell analysis reveals Asian diversity and immune disease markers

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Genome Institute of Singapore, A *STAR

Conflict of interest: Yes

Single cell omics provides a powerful tool for discovering disease markers, characterizing tissue heterogeneity and stratifying patients. Using examples from chronic myeloid leukaemia (CML) and type 1 diabetes (T1D), I will show how single cell RNA-seq (scRNA-seq) can help us achieve these objectives in relatively small cohorts, far smaller than one would need for genetic association studies. We can also investigate the diversity of healthy humans by the same methods. To understand how ethnicity and genetic ancestry influenced human physiology we profiled 1,265,624 peripheral blood mononuclear cells from 619 individuals from 7 population groups in 5 Asian countries. We uncovered profound molecular and cellular differences between these 7 groups, including cell populations and genes with diagnostic and prognostic relevance. These results indicate that, from the perspective of immune phenotypes, “Asians” are a heterogeneous group. It is likely that other continental groups may also be similarly heterogeneous, and thus ethnicity-specific or ancestry-specific diagnostic and therapeutic strategies may be needed to fulfil the promise of Precision Medicine across the globe.

S8-5

Single-cell multi-omics analysis in rheumatic and allergic diseases

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Conflict of interest: Yes

Rheumatic and allergic diseases involve multiple organs and are driven by inappropriate activation of the immune system. Exploring immune dysregulation underlying the clinical symptoms through single-cell diversity in patient samples can significantly improve our understanding of disease mechanisms. Single-cell analysis of peripheral blood mononuclear cells (PBMCs) from patients with newly diagnosed microscopic polyangiitis (MPA) and healthy controls identified two distinct PBMC profiles: one exhibiting monocyte activation signature gene expression (MPA-MONO) and the other characterized by interferon-stimulated gene (ISG) expression (MPA-IFN). Patients in the MPA-MONO group had increased monocyte proportions in PBMCs, elevated C-reactive protein levels and a significantly higher rate of disease relapse. Conversely, the MPA-IFN group was characterized by high serum interferon-alpha levels, renal involvement and elevated MPO-ANCA levels, but showed a favorable response to immunosuppressive therapy. Building on these findings, our current focus is expanding beyond PBMCs to analyze total peripheral blood leukocyte populations in conditions such as vasculitis and systemic sclerosis. This presentation will highlight our recent work and the potential of single-cell analysis to address unmet needs in rheumatic and allergic diseases. In addition, I would like to discuss the challenges and opportunities of using this technology to develop future therapeutic strategies to improve patient outcomes.

S9-1

Future perspective of molecular targeted therapies in systemic sclerosis: Overview

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Conflict of interest: Yes

Systemic sclerosis (SSc) remains a challenging systemic autoimmune rheumatic disease with complex pathogenesis, clinical and molecular heterogeneity, and lack of effective disease-modifying treatments, leading to high morbidity and mortality. The mechanisms underlying interrelationships between microvascular dysfunction, autoimmunity, and tissue fibrosis in SSc still remain unclear. Recent advances in molecular and cell biology, coupled with technological breakthroughs such as omics analysis techniques, single-cell RNA sequencing, and artificial intelligence, are providing new avenues to understand the complex pathogenesis of SSc. These comprehensive approaches are essential to improve our understanding of pathogenic mechanisms and enable personalized treatment. Current major challenges include predicting, defining and classifying the disease, overcoming clinical heterogeneity, and establishing robust biomarkers for disease activity and progression. In addition, innovative clinical trial designs and patient-centered approaches are essential for development of effective treatments. Emerging therapies, including cell-based therapies, show promise. Integrating these advanced research technologies holds the potential for significant advances in the management of SSc patients.

S9-2

Genome-wide association study (GWAS) for systemic sclerosis (SSc) ~ from the genomics to precision medicine ~

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Conflict of interest: None

While previous GWASs for SSc have told us multiple genetic risks, the Euro-centric nature has been a long-standing obstacle to implementing the GWAS findings in East Asian populations. In addition, the lack of extensive functional annotation of the risk SNPs hinders us from understanding how genetic variations impact SSc pathology. We conducted the largest Asian SSc GWAS, by enrolling 1,428 cases and 112,599 controls throughout Japan. We identified three novel risk loci, one of which resides in the *FCGR/FCRL* region and shows a penetrating association in the Asian population. The SNP, rs10917688, is in complete LD with the lead SNP and found in a cis-regulatory element, which is predicted to be bound by IRF8. *IRF8* is one of the risk loci in European GWAS, and rs10917688 shows a significant association only in the presence of the risk allele of *IRF8* in Japanese. Furthermore, rs10917688 is marked with H3K4me1 in B cells, highlighting one of the cell type-specific impacts of this risk locus. The meta-analysis with the largest European meta-GWAS further identified additional three novel risk loci. The SNP-based heritability was relatively low, but significant both in Japanese and Europeans, confirming a polygenicity of SSc. We observed a moderate fitness of polygenic risk score (PRS) constructed from the meta-analysis effect sizes, indicating the potential portability of genetic associations beyond populations. Moreover, prioritizing the top 5% of SNPs of IRF8 binding sites in B cells improves the fitting of the PRS, underscoring the roles of B cells and IRF8 in SSc development. We recently updated the French GWAS and European meta-analysis and identified a novel risk locus in the gene encoding a protein necessary for antigen presentation. We further conducted the trans-ancestry meta-analysis with our Japanese GWAS and identified two more novel loci in intergenic regions. Our large-scale GWAS provides novel insights into the genetic basis of SSc pathology.

S9-3

Single-cell analysis of systemic sclerosis

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Conflict of interest: Yes

Advancements in single-cell omics analysis, especially single-cell (sc) RNA-seq, have significantly enhanced our understanding of systemic sclerosis (SSc). Through scRNA-seq analysis of SSc, we and others have identified distinct cell types and gene signatures associated with the disease, its subgroups, and various stages. These include dysregulated immune cells, such as inflammatory monocytes/macrophages and activated T cells, pro- and anti-fibrotic fibroblast subsets, and aberrant endothelial cells. In both the peripheral blood and affected skin of SSc patients, inflammatory monocytes are increased and are thought to contribute to chronic inflammation and fibrosis. Additionally, regulatory T cell (Treg) activation in peripheral blood was a characteristic feature of early-phase SSc patients, suggesting a role in disease initiation. Within SSc skin, CXCL13+ T cells exhibit a T follicular helper-like gene expression profile, which may promote local B-cell responses and contribute to autoimmunity. Notably, LGR5+ fibroblasts, which are potentially crucial for normal skin homeostasis, are significantly reduced in diffuse cutaneous SSc, implying a disruption in tissue maintenance. Skin endothelial cells in SSc patients show enhanced pro-angiogenic and proliferative activities, which could be connected to the clinical vasculopathy observed in SSc. Altogether, these findings emphasize the importance of identifying key cell types involved in SSc progression, which could lead to a better understanding of the disease and facilitate the development of novel therapeutic targets.

S9-4

SSc-PAH-specific induced pluripotent stem cells

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Conflict of interest: Yes

Despite recent advances in pulmonary vasodilator therapy, the prognosis of pulmonary arterial hypertension associated with systemic sclerosis (SSc-PAH) remains unsatisfactory, therefore needing further development of treatments. However, several factors hinder the development, such as the difficulties in obtaining pulmonary artery tissue and in collecting a sufficient number of cases. Disease-specific induced pluripotent stem (iPS) cells would be one of the solutions for these problems. We have recently established SSc-PAH-specific iPS cells from patient's peripheral blood mononuclear cells and differentiated them into endothelial cells. By functional and molecular studies on the differentiated cells, we found several abnormalities in the endothelial cells of SSc-PAH, including facilitated cell proliferation, impaired vasculogenesis, reduced expression of endothelial markers, and increased expression of mesenchymal markers. In this symposium, we would like to introduce our recent data and discuss

how we would develop novel treatment strategies for SSc-PAH.

S9-5

Personalized Medicine in Systemic Sclerosis: Current Status and the Road Ahead

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Conflict of interest: Yes

While interstitial lung disease (ILD) and skin fibrosis are key manifestations of systemic sclerosis (SSc), their course is highly heterogeneous. Moreover, response to the currently utilized treatments such as mycophenolate mofetil (MMF) is highly variable. Therefore, there is an unmet clinical need for prognostic/predictive biomarkers for informing the timely initiation of the most effective treatment, in order to prevent irreversible damage in SSc patients. Contrary to lung tissue, serum and peripheral blood cell (PBC) RNA can be obtained during routine clinical care and used for biomarker development. Several studies have shown that high serum c-reactive protein levels can prognosticate worse ILD course, including in those treated with MMF. Moreover, serum pneumoproteins are attractive biomarker candidates, because they are lung-specific and can be informative in a systemic disease, in which the course of skin and lung can be divergent. The pneumoprotein KL-6 is used clinically in Japan. Several international studies have confirmed the prognostic value of KL-6 in various clinical settings. There are also emerging data from clinical trials indicating that peripheral blood cell (PBC) RNA gene expression profiling can aid in identifying MMF likely responders. Skin is a prominently affected endorgan in SSc and can be biopsied during routine clinical care. Paralleling the clinical course, skin gene expression profiling shows a trend toward normalization over time. While some studies have indicated that an inflammatory skin transcriptomic profile can aid in identifying responders to immunosuppression, the predictive value of this molecular profile in patients who are on stable-dose MMF background treatment has not been investigated. Skin transcript profiling might also aid in identifying responders to targeted molecular therapies. In summary, peripheral blood, serum, and skin molecular profiling holds the promise to individualize monitoring and treatment decisions in SSc.

S10-1

Perioperative management of glucocorticoids in patients with rheumatoid arthritis having orthopedic joint surgery

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Conflict of interest: Yes

With recent advances in medications, treatment strategies for rheumatoid arthritis (RA) have greatly improved and the proportion of patients using glucocorticoids (GCs) has decreased. However, the number of patients with late-onset RA is increasing with the aging of the population, and there are concerns that an increasing number of patients will have to rely on GCs due to limited treatment options such as methotrexate and biological DMARDs because of various complications. In addition, the 2020 update of the JCR clinical practice guideline did not include any recommendations regarding perioperative management of GCs in patients with RA having orthopedic joint surgery. Therefore, it is a critical issue to consider the perioperative management of GCs in patients with RA on GC use. We conducted a systematic review of PubMed, Embase, Cochrane Central, and Igaku Chuo Zasshi published from 2004 to 2024 that focused on outcomes of complications (surgical site infection, death, postoperative infection, delayed wound healing, venous thrombosis, etc.) in patients with RA on GC use undergoing joint surgery, and four articles (guidelines or review articles) were ultimately extracted. Most of the reports indicated that perioperative GC management should be performed depending on the invasiveness of the surgery, the GC dose at the time of surgery, and the cumulative amount of GC dose, and no articles were found that suggested that perioperative GC management should not be performed. On the other hand, some articles emphasized that an individualized approach should be adopted based on the surgical risk level and the patient's adrenal functional status in order to reduce unnecessary GC use and the risk of postoperative complications. However, all of the reports were based on the results of observational studies which were low-quality levels of evidence, and were not based on randomized controlled trials (RCTs).

S10-2

Perioperative management of conventional synthetic anti-rheumatic drugs

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Conflict of interest: Yes

Rapid advances in drug therapies in recent years have markedly improved the disease activity of rheumatoid arthritis (RA). However, the progression of joint destruction cannot be completely inhibited in some cases. In addition, the number of elderly RA patients with osteoarthritis is increasing. Because surgery is sometimes necessary for these patients, perioperative anti-rheumatic drug management is important to reduce postoperative complications. Prospective studies compared perioperative complications in patients with RA undergoing surgery using MTX, and divided them into two groups: those who were stopped MTX and those who continued MTX during perioperative period. These results confirmed that complications did not increase when surgery was performed with continued MTX (Sany J 1993, Grenna DM 2001). Based on these evidences, the Japanese guideline for rheumatoid arthritis treatment 2024 includes a recommendation that "MTX should not be withdrawn during the perioperative period of orthopedic surgery (conditional)" (strength of recommendation: weak, level of evidence: very low, agreement: 7.11 out of 9). On the other hand, although papers examining the perioperative management of conventional synthetic anti-rheumatic drugs other than MTX are limited and the level of evidence is very low, there is no evidence that complications increase with continued use of conventional synthetic anti-rheumatic drugs during the perioperative period. The American College of Rheumatology guidelines for perioperative drug management recommend that leflunomide, sulfasalazine, and tacrolimus be continued in the perioperative period (Goodman SM. 2022). In this session, I will discuss the perioperative management of conventional synthetic anti-rheumatic drugs, with a focus on MTX.

S10-3

Development of Perioperative Antirheumatic Drug Management Guidelines: Management of TNF Inhibitors During the Perioperative Period

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Conflict of interest: Yes

The use of biologics in clinical practice in Japan has exceeded 20 years, with TNF inhibitors being the most commonly used. Biologics are associated with an increased infection risk, and the Japanese College of Rheumatology (JCR) guidelines recommend a temporary drug withdrawal during the perioperative period of orthopedic joint surgeries. Similarly, international guidelines address perioperative management of antirheumatic drugs. While clear evidence on the optimal withdrawal period is lacking, decisions are typically based on the dosing intervals of each drug, balancing risks and benefits. Risk factors for infections include glucocorticoid use, diabetes, and malnutrition. Patient backgrounds today differ significantly from those 10-20 years ago, suggesting the need to reexamine current evidence. When disease activity is well-controlled over time, many patients maintain good physical function, nutritional status, and are not on glucocorticoids, reducing their infection risk. In such cases, perioperative drug withdrawal is unlikely to cause significant disease flares or hinder rehabilitation, making it generally acceptable. However, surgical candidates often represent a more severe disease population, and RA remains a risk factor for infection, warranting careful consideration of drug withdrawal for safety. Additionally, the aging population of RA patients presents unique challenges. Advancements in cancer therapies have also introduced new treatment options, improving prognosis and increasing surgeries for bone metastasis-related fractures in daily practice. Experience with perioperative drug management in RA may offer valuable insights for these situations. This symposium aims to revisit these topics and explore them further.

S10-4

Perioperative management of DMARDs -non-TNF inhibitors-

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Conflict of interest: Yes

There is no established consensus between rheumatologists and orthopaedic surgeons over the ways of how anti-rheumatic drugs should be dealt when a patient with rheumatoid arthritis undergoes an operation such as orthopaedic surgery. Since the introduction of biological DMARDs, many had had concerns of increase of perioperative complications. A total of 20 years has past since the introduction, and accumulating practical evidence shows that the drugs have not increased the complications so much that most had feared. Based on the experience, many recommendations have proposed the perioperative management of MTX and biological DMARDs. However, the sum of the body of evidence is still shallow, and the recommendations are unfortunately not beyond expert opinions. Therefore, JCR aims to suggest more practical recommendations based on more precise, wider range of evidence and systematic reviews. On the other hand, the recommendations will be supported by the pharmaceutical mechanisms of the drugs in the light of the shallow body of evidence. This lecture will suggest the perioperative management of non-TNF inhibitors based on, hopefully, deep analysis of the shallow evidence supported by drug profiles with personal opinions.

S10-5

Perioperative management of JAK inhibitors of rheumaorthopaedic surgery

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Conflict of interest: Yes

Janus kinase inhibitors (JAKi) are small molecules used as oral tsDMARDs. Currently tofacitinib, baricitinib, peficitinib, filgotinib, and upadacitinib are commercially available in Japan for the treatment of RA. There has been concern that JAKi may increase the rate of postoperative complications in patients with RA who undergo orthopaedic surgery; however, there is little evidence to support this. Theoretically, longer discontinuation of immunosuppressive drugs should reduce incidence of surgical site infection (SSI) and delayed wound healing (DWH) but may increase the risk of flare-up of the disease. The Japan College of Rheumatology for post-marketing surveillance of JAKi suggested that careful management including discontinuation of tofacitinib should be performed during the perioperative period, and efforts should be made to detect SSI early by close attention to local symptoms. We identified articles indexed in PubMed, Embase, Cochrane Central and Japana Centra Revuo Medicina published from 2013 to 2024 and other articles. Articles fulfilling the predefined inclusion criteria were reviewed systematically and their quality was appraised. Almost statements on perioperative use of JAKi from guidelines and review papers were not based on the published evidence. After inclusion and exclusion by full-text review, 6 articles were analyzed. Pre-operative discontinuation period varied from none to 14 days, and four of 6 studies pointed out the concern about the disease flare-up due to longer perioperative discontinuation of JAKi. Most studies did not report SSI, and the incidence of DWH and SSI were not associated with the duration of JAKi withdrawal.

S11-1

Problems with the medical insurance system in Japan's rheumatism treatment -Compared to other countries-

Yoshitaka Shintoh
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Conflict of interest: None

In rheumatoid arthritis, biological agents are particularly expensive, and if you pay 30% of the cost, you will have to pay more than 30,000 yen a month. The average self-pay amount per person for diagnosis and treatment of the disease is high, at 264,000 yen per year. From the perspective of cost-effectiveness, while biological agents themselves are expensive, they are excellent in terms of therapeutic effect, and by controlling the

disease, other drug prescription fees and surgery fees can be reduced, and life prognosis can be improved. In the Japanese medical system, there are cases where rheumatoid arthritis patients in their 20s and 30s, who are of productive age and have a large impact on economic activity, give up on the use of biological agents due to low income, and their joint destruction progresses to the point where they can no longer work. There is great concern that Japan, with its declining birthrate and aging population, is leaving this situation unattended. In addition, according to a report by Matsuno et al., in European countries, except for the United States, which does not have a public medical insurance system, there is almost no self-payment of medical expenses. This is because public medical insurance is supported by taxes, and most of it is covered by consumption tax. However, there is a limit to the financial resources of the funded social insurance adopted in Japan. As part of the cost is paid out of pocket, patients must pay 30% (up to 10%) of medical expenses at the counter. Germany and France also have a similar system to Japan, but the out-of-pocket expenses are subsidized through consumption tax, so patients have to pay less out of pocket. South Korea also requires patients to pay 30% out of pocket, but rheumatoid factor-positive RA patients are treated as a specified disease and their out-of-pocket expenses are limited to 10%. It is said that the issue of high out-of-pocket medical expenses is an issue that Japan must give the most thought to. We will consider the medical insurance system that Japan should move towards in the future.

S11-2

Consider the current situation and future of rheumatic disease medical care from the patient's point of view

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Conflict of interest: None

As a representative rheumatic disease, we will consider medical treatment for rheumatoid arthritis. In Japan, rheumatoid arthritis is a relatively common disease affecting 0.5~1% of the population, and as it progresses, it causes joint inflammation, deformation, and functional impairment. Previously, treatment was to suppress arthritis, but since the approval of methotrexate in 1999 and infliximab in 2003, rheumatoid arthritis medical care has made great strides, and at the same time, rising medical costs have become a problem. In this article, we will consider the current state and future of rheumatoid arthritis medical care. For those who are not covered by the copayment, the initial consultation for a diagnosis of rheumatoid arthritis will cost around 6,000 to 8,000 yen for X-rays, blood tests, ultrasound, etc. As a treatment, the anchor drug methotrexate is 6~10 mg per week, costing about 600 yen per month, but biological drugs cost about 10,000~30,000 yen per month, and JAK inhibitors cost about 40,000 yen per month, which is expensive. Since rheumatoid arthritis is a chronic disease, treatment will continue forever. To cope with this expensive treatment, there are medical expense deductions, high medical expense systems, additional benefits, sickness and injury benefits, disability certificates for disability welfare, and designated intractable diseases as a specific medical expense subsidy system, and currently, treatment is being carried out using these support systems. The current situation is that patients refuse treatment because they cannot afford it. From the patient's point of view, it seems that the cost of treatment with the current highly effective treatment should be reduced, and if the price cannot be reduced, it is necessary to expand the welfare system.

S11-3

Proposals for Improving Insurance Medical Practice

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Conflict of interest: None

Treatment in the field of rheumatology and collagen diseases is advancing rapidly with the emergence of highly effective medications. However, administering these treatments safely requires utmost caution. Initially, treatment for rheumatology and collagen diseases is challenging and unique, and it presents distinct issues compared to diseases such as hypertension and diabetes. Rheumatology and collagen disease treatments that use biological agents and immunosuppressants can lead to serious side effects, and instances of claims and medical errors are not uncommon. Although some diseases in this treatment category qualify for additional fees such as guidance charges for rare disease outpatient care, the current situation is that these add-ons are less frequent compared to those for managing chronic lifestyle diseases like diabetes, including charges for home self-injection guidance and management. Within the field of rheumatology and collagen diseases, although there are additional payments for outpatient chemotherapy and home self-injection guidance for the administration of biological agents, there is an imbalance as no such add-ons exist for the administration of immunosuppressants, such as methotrexate, and JAK inhibitors, which require equally careful management. This not only undermines the economic viability of providing high-quality rheumatology care but may also impact patient outcomes by limiting access to necessary treatments. In this lecture, recognizing the inherent difficulties, complexities, and risks of rheumatology and collagen disease treatment, I will propose specific insurance reforms aimed at fostering a safer and more effective treatment environment for patients. Furthermore, guidance from health bureaus during insurance medical practice is a concern. Drawing from my experience managing four rheumatology and collagen disease clinics and one health screening center, and having participated in nine guidance sessions, "Setagaya Rheumatology" will present trends and measures for both collective individual guidance and individual guidance.

S11-4

Reformation of health insurance system to safeguard pharmaceutical industries

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Conflict of interest: None

We are facing shortages in drug supplies. Although the direct causes are the administrative disposition of some companies due to manufacturing fraud and difficulties in securing raw materials, the primary cause is the government's policy for suppressing health care costs. If a medicament becomes unprofitable despite its clinical usefulness, the manufacturer can only help by applying for its deletion from the National Health Insurance Drug Price Standard. Realizing the importance of reliable supplies and the underpinning profitability of clinically required therapeutic options, the Ministry of Health, Labor and Welfare belatedly set forth an unprofitable article re-calculation policy for 2025. The situation is more challenging for rheumatologists. Injectable gold will be unavailable starting May 2025. Anti-rheumatic drugs of decreasing demand are anticipated to be deleted from the Standard in the immediate future. When a deletion is applied without providing an alternative product, the Ministry ascertains related academic societies if it is acceptable. It is time for rheumatologists to assess and make a consensus on the necessity of anti-rheumatic drugs, especially csDMARDs that are already in shortage. The combination of bucillamine and salazosulfapyridine with MTX can be as effective as biological DMARDs in managing RA. However, the usefulness of these csDMARDs is often overlooked as treatment initiation with MTX and switching to biologicals or JAK inhibitors when MTX turns ineffective are widely accepted as a standard regimen. Even more overlooked is the importance of early diagnosis. As it is hard for primary care physicians to pick up possible pre-RA cases, they are not referred to specialists in core hospitals, and the necessity of csDMARDs for pre-RA management is largely ignored. Management strategies taking the continuum of RA development into consideration will eventually safeguard pharmaceutical industries.

S12-1

Management of infectious diseases under the treatment of glucocorticoids

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Conflict of interest: None

Autoimmune diseases treated with glucocorticoids are often complicated with airway barrier failure, as represented by interstitial lung diseases, therefore pulmonary infections comprise about half of all infections in

this population. These patients do not increase the risk of infection only with a certain specific pathogen. This is because glucocorticoids significantly suppress both innate and acquired immunity, and this action is due to multiple complex mechanisms, such as suppression of cytokine, inhibition of macrophage and neutrophil phagocytosis, opsonization impairment, inactivation of T or NK cells, reduction of antibody production, dysfunction of B cells, etc. However, cellular immunity is mainly affected, opportunistic pathogens such as viruses or fungi are common clinical problems. Half of the pulmonary infections are also opportunistic pathogens such as pneumocystis or aspergillus. Therefore, we must recognize to require reliable microbial diagnosis to ensure a successful outcome. The opportunistic infections for which primary prevention has been established in patients treated with glucocorticoid pneumocystis, hepatitis B virus, tuberculosis, and shingles. All these infections that can occur frequently if not prevented and are potentially fatal. The appropriate indication for prevention should be judged, and primary prevention must be provided if necessary. A wide range of opportunistic pathogens, for which there is no established prevention and early detection is essential, including aspergillus, nocardia, or cryptococcus. Although these pathogens are not common, they are often difficult to diagnose, so it is important to thoroughly understand the clinical characteristics of each pathogen and remember them as differential diagnosis. In this lecture, I will focus on the prevention and diagnosis of these opportunistic infections, and outline the practical management in daily clinical practice, while also covering the pitfalls to be aware of.

S12-2

Prevention and Treatment for Glucocorticoid-induced osteoporosis (GIOP)

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Conflict of interest: Yes

Glucocorticoids (GCs) are endogenous hormones with strong anti-inflammatory effects and broad metabolic functions. Even small doses can quickly induce bone fragility. Synthetic GCs are widely used for immune and inflammatory disorders, with an estimated 0.7-1.2% of adults in Japan (730,000-1,260,000 people) using oral GCs for over three months. Since GCs are a leading cause of iatrogenic osteoporosis, prescribing physicians must manage osteoporosis effectively. Risk factors for glucocorticoid-induced osteoporosis (GIOP) include advanced age, high GC dosage, low lumbar bone mineral density, prior fractures, and lack of bisphosphonate treatment. To minimize risks, GCs should be started at the lowest dose and tapered quickly. For unavoidable long-term use, early initiation of osteoporosis treatment is crucial. Available treatments in Japan include active vitamin D for bone formation, bisphosphonates and anti-RANKL antibodies to inhibit bone resorption, PTH analogues and anti-sclerostin antibodies to promote bone formation, and selective estrogen receptor modulators for postmenopausal osteoporosis. In 2014, the Japanese Society for Bone and Mineral Research (JSBMR) established criteria for GIOP treatment based on weighted risk factors for patients requiring GCs for over three months. However, a study by Soen et al. showed only 50% of eligible patients received osteoporosis treatment, and bone density tests were performed in just 6-7% of cases. To address this, the JSBMR released the 2023 Guidelines for the Management and Treatment of GIOP to promote appropriate care. In this symposium, I will provide rheumatologists with essential knowledge on GIOP prevention and treatment and share strategies to reduce fractures caused by GC-induced bone fragility.

S12-3

Glucocorticoid-induced diabetes

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Conflict of interest: Yes

The goal of diabetes treatment is to prevent the onset and progression of diabetic complications and to achieve a life expectancy and quality of daily life similar to that of people without diabetes. The same is true for glucocorticoid-induced diabetes. For example, elevated blood glucose from glucocorticoid therapy increases the risk of infections, and hyperosmotic hyperglycemia state has been reported in some cases. These infections and hyperosmotic hyperglycemia state are included in the acute complications of diabetes. Mechanisms of blood glucose elevation with glucocorticoid treatment include increased gluconeogenesis in the liver, decreased glucose uptake in skeletal muscle, and hyperglucagonemia. In response to these, pancreatic beta cells secrete more insulin, which has a blood glucose lowering effect, to maintain homeostasis and prevent blood glucose levels from rising. However, pancreatic beta cells that produce insulin are vulnerable to overload, and if the chronic hyperglycemic state caused by the above continues, both the quality and quantity of pancreatic beta cells will progressively decline. As a result, the secretion of insulin, the only hormone with a blood glucose lowering effect, is reduced, which in turn induces further hyperglycemia, forming a vicious cycle. This is the essence of the pathophysiology of type 2 diabetes, and the same pathophysiology can be assumed for elevated blood glucose caused by glucocorticoid therapy. Therefore, as in type 2 diabetes, prolonged hyperglycemia can lead to not only acute complications but also chronic complications. From the above, it goes without saying that proper glycemic management is important for people with glucocorticoid-induced diabetes. However, a characteristic of glucocorticoid-induced diabetes is that there is a lack of clinical data on treatment, and evidence has not been fully established. Therefore, actual treatment strategy must be addressed on a case-by-case basis.

S12-4

Rheumatic disease and atherosclerosis

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Conflict of interest: None

Rheumatic diseases are associated with a high risk of atherosclerotic disease. Recent studies have shown that atherosclerosis is partly driven by the hyperactivity of immune cells such as monocytes and macrophages. It is essential to understand not only the major risk factors for atherosclerosis but also the vascular damage associated with inflammation and the impact of medications. In particular, glucocorticoids (GCs) are powerful anti-inflammatory agents effective for managing acute disease flares. However, long-term GC use is associated with multiple side effects, including an increased risk of atherosclerosis. The management of atherosclerosis in rheumatic diseases should consider the following: 1. Optimization of GC Dosage: Aim for the shortest possible use of GCs, with dose reduction or discontinuation. When low-dose maintenance is required, regular assessment and adjustment are essential to minimize side effects. 2. Use of Immunosuppressants and Molecular Targeted Drugs: To reduce GC usage, prioritize disease control with other medications. These drugs can suppress the underlying inflammation in rheumatic diseases, potentially slowing the progression of atherosclerosis. JAK inhibitors should follow the rheumatoid arthritis guidelines for risk assessment. 3. Lifestyle Modifications: In patients with rheumatic diseases, appropriate nutrition and regular exercise contribute to the management of lipids and blood glucose, which is important for reducing atherosclerotic risk. 4. Monitoring of Risk Factors: Regular blood tests, blood pressure checks, and smoking cessation counseling are critical for managing lipids, blood glucose, and hypertension. 5. Use of Anti-Atherosclerotic Medications: When necessary, consider the use of statins or antiplatelet agents. In conclusion, effective management of atherosclerosis requires careful control of GC dosage and duration, alongside the management of disease activity and other risk factors.

S12-5

Glucocorticoid tapering protocols for the treatment of SLE

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Conflict of interest: None

Recently, the treatment outcomes for SLE have improved, and the

goal of treatment is shifting from lifesaving to avoiding organ damage and minimizing side effects. In order to reduce the side effects of glucocorticoids (GCs), it has become recommended to introduce immunosuppressants early and to reduce the initial dose of GCs rapidly in the treatment of lupus nephritis (LN). However, these recommendations are not based on sufficient evidences. Therefore, we conducted a multi-center retrospective study on the speed of GC reduction and response to treatment. The subjects were patients who were classified as having proliferative LN by renal biopsy, were treated with GC for the first time, and had data on urinary protein/creatinine ratio (UPCR) both before and 52 weeks after GC treatment. Patients who reduced their prednisolone (PSL) equivalent dose to 7.5 mg/day or less within 6 months of starting GC treatment were defined as the rapid GC reduction group, and patients who did not reduce their dose to 7.5 mg/day or less were defined as the conventional GC reduction group. The rates of achieving partial renal response (PRR) after 12 months were compared using modified Poisson regression analysis adjusting for multiple confounding factors. As a result, a total of 344 patients were enrolled from 17 facilities, of which 50 were in the rapid GC reduction group and 294 in the conventional GC reduction group. The PRR achievement rate after 12 months was 43/50 (86%) and 248/294 (84.4%), respectively. Even after adjusting for possible background factors, there was no significant difference in the PRR achievement rate (risk ratio 0.92, p=0.760). The similar results were obtained for complete renal response (CRR) after 12 months and PRR and CRR after 24 months. This revealed that GC does not affect renal prognosis even if it is reduced relatively rapidly when used in combination with immunosuppressants. On the other hand, there is very little evidence regarding GC protocols for pathologies other than LN, and we must rely on empirical treatment.

S12-6

Glucocorticoid regimens for remission induction of ANCA-associated vasculitis

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Conflict of interest: None

ANCA-associated vasculitis is characterized by the presence of circulating autoantibodies and a pauci-immune type small vessel vasculitis. ANCA-associated vasculitis includes microscopic polyangiitis, granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis. Treatment strategies for eosinophilic granulomatosis with polyangiitis are different from other two subtypes of ANCA-associated vasculitis due to its unique character of eosinophilic inflammation. Regarding microscopic polyangiitis and granulomatosis with polyangiitis, the previous clinical trials have led to the 2010's standard remission induction regimen with the combination of high-dose glucocorticoids and cyclophosphamide or rituximab. Although those therapies have high remission rates of 80-90%, side effects of high-dose glucocorticoids such as infections, osteoporosis and atherosclerosis, were a big issue. In the context of the background as above, the results of three randomized controlled trials have been reported in 2020's: the PEXIVAS trial (NEJM, 2020), the LoVAS trial (JAMA, 2021), and the ADVOCATE trial (NEJM, 2021). Although patients background and treatment regimens were different among those three trials, they all showed the successful results of reducing glucocorticoid-dose during remission induction and less frequent adverse events. Based on those trial results, the 2023 revised Japanese clinical practice guideline for ANCA-associated vasculitis recommends the reduced-dose glucocorticoids regimen instead of the conventional high-dose glucocorticoids regimen for remission induction of ANCA-associated vasculitis. In this presentation, I will focus on update of the clinical practice guideline and evidences regarding glucocorticoid regimens for ANCA-associated vasculitis.

S13-1

Pathogenesis of rheumatoid arthritis driven by T cells -basic and clinical research-

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Conflict of interest: Yes

In rheumatoid arthritis (RA), much knowledge has been accumulated through GWAS, eQTL analysis, and analysis of synovium and synovial fluid, which are sites of inflammation, as well as peripheral blood cells and proteins. There has been a revolution in the treatment of RA with biological agents and JAK inhibitors, and animal models have played many roles in this treatment. However, there are many differences between humans and mice, including genetic differences, and no perfect animal model of RA exists. Many clinical questions remain, such as differences in pathology before and after disease onset, blood biomarkers common to all arthritis in humans and models, the qualitative significance of autoantibodies that can cause arthritis, and the mechanism of elderly onset of RA which is on the rise. However, analysis of human samples alone, which are somewhat heterogeneous, is thought to be insufficient, and we believe that translation from animal models with uniform genes and environments may provide clues to identify these changes. eQTL analysis in RA has pointed out changes in T cells, particularly regulatory T cells. Using as examples our research, which examined RNAseq analysis from untreated elderly RA patients and cell behavior and scRNAseq analysis in local lymph nodes in animal models, we would like to discuss the complementarity of current basic and clinical research.

S13-2

Novel therapeutic strategies based on understanding the pathogenesis of inflammatory bone destruction

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Conflict of interest: None

There are two types of difference between physiology and pathology: continuous "quantitative" and discontinuous "qualitative". In regard to bone-resorptive diseases, osteoporosis exhibits "quantitatively" excessive bone-resorbing function of normal osteoclasts, whereas we have recently shown that "qualitatively" different kinds of osteoclasts are generated and contribute to the pathogenesis in arthritic bone destruction. Further analysis has demonstrated that the tissue structure at the site of joint destruction represent characteristic properties different from normal ones, suggesting that not only anti-inflammatory treatment but also controlling pathological tissue transformation is necessary for treating against these diseases. In this presentation, I will introduce the latest findings on the inflammatory osteoclast precursor cells (AtoM) and the newly identified another pathogenic cell types inducing AtoM in vivo, and discuss new treatment strategies for refractory bone destruction.

S13-3

3D imaging of the synovium defines an intricate immunological defence system at the blood-joint barrier

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Conflict of interest: None

Joint pain or inflammation is a common and early feature of a variety of systemic diseases. These include autoimmune diseases, such as SLE and adult onset Still's disease, as well as infection in organs distant to the musculoskeletal system, including enteric or genitourinary infections, which manifest as reactive arthritis. However, why joints are highly responsive to systemic inflammation and where in the synovium the inflammation starts are unknown. We sought to address these questions by developing a whole mount imaging system of the entire synovium to profile the vascular, neuronal and immune microarchitecture. This revealed that highly permeable $PV1^{+}$ capillaries were specifically located at the lining-sublining interface, in the periphery of the synovium, enabling entry of circulating stimuli into the joint. This area of vulnerability was occupied by three subsets of macrophages that demonstrated distinct responses to systemic immune complex (IC) challenge and reciprocally interacted with nociceptor neurons, forming a blood-joint barrier (BJB) to defend joint tissue.

S13-4

Elucidation of the pathogenesis of rheumatoid arthritis through T-cell receptor repertoire analysis

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Conflict of interest: None

T cells are the central regulators of the immune system, recognizing antigens through their T cell receptors (TCRs) and orchestrating antigen-specific immune responses. At the core of the TCR is the complementary determining region 3 (CDR3), which directly recognizes antigens. CDR3 exhibits highly diverse sequence patterns and plays a crucial role in distinguishing between self and non-self. Dysregulation in this self/non-self recognition by CDR3 is a fundamental pathological feature of autoimmune diseases. For instance, in rheumatoid arthritis (RA), abnormalities in the TCR-CDR3 repertoire are thought to promote immune responses against pathogenic antigens, such as citrullinated proteins. The advent of next-generation sequencing has made it easier to comprehensively analyze CDR3 sequences. Our team has been conducting large-scale studies to identify TCR sequence patterns associated with disease pathogenesis using both genetic analyses and case-control studies based on patient samples. In genetic analyses, we leverage HLA gene risk variants, the strongest genetic risk factors for autoimmune diseases, to detect TCR sequence pattern abnormalities present even before disease onset in healthy individuals at high risk. For example, we have observed an increased frequency of negatively charged amino acids in TCR-CDR3 sequences. In case-control studies using patient samples, we aim to identify persistent TCR sequence abnormalities that remain after disease onset. Simultaneously, we are developing experimental systems to efficiently process large-scale samples. These efforts are expected to shed light on the fundamental mechanisms of antigen-specific immune responses in RA and facilitate the identification of biomarkers useful for diagnosis and disease activity assessment. In this presentation, we will discuss the recent findings from our large-scale TCR analysis studies.

S13-5

Immunophenotypic profiles in autoimmune diseases

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Conflict of interest: Yes

In autoimmune diseases, molecular targeted therapies, which focus on specific molecules such as cytokines, have gained prominence. These therapies are the culmination of extensive research that spans from fundamental studies to clinical trials. Conversely, the outcomes of clinical trials and their associated basic analyses contribute to understanding human immune disorders, often drawing upon insights from mouse models in immunology. A limitation of mouse models is their inability to fully elucidate the diversity inherent in human diseases and the value of translational research is unquestionable. Even within the same disease, individual cases exhibit varied responses to molecular targeted therapies, highlighting the inherent diversity of disease states. This variation underscores the complexity of treating autoimmune disorders, where each patient may require a tailored therapeutic approach based on their unique clinical presentation. In addition to disease elucidation using mouse models, which have traditionally dominated research, the investigation of individual differences has also become a major focus. This shift is marked by the increasing use of various omics data to better understand the unique aspects of disease presentation and progression in different individuals. By accurately understanding the variations in disease states, we can selectively target only the molecules critical to the disease process. This precision in treatment not only enhances efficacy but also minimizes adverse events, significantly improving patient outcomes. I will present the analyses from various sources including our findings on the diversity observed across diseases and individual cases.

S14-1

Articular type juvenile idiopathic arthritis vs. rheumatoid arthritis: From the perspective of a pediatric rheumatologist

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Conflict of interest: None

Juvenile idiopathic arthritis (JIA) is any form of chronic arthritis of unknown etiology that begins before the age of 16 and continues for more than six weeks, and is diagnosed after thorough exclusion diagnosis. It is classified into seven types by the International Leagues of associations for Rheumatism (ILAR) and is also known as an umbrella name that includes diseases with different pathologies. On the other hand, rheumatoid arthritis (RA) is a single disease in which inflammation occurs in the joints due to immune abnormalities, resulting in joint pain and swelling. Currently, JIA is classified by the ILAR into systemic arthritis, oligoarthritis, rheumatoid factor (RF)-negative polyarthritis, RF-positive polyarthritis, psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis. They can be broadly divided into systemic and articular types, and the articular type can be further divided into oligoarthritis and polyarthritis. Some of these are quite homogeneous and appear to be present in both children and adults, while others are heterogeneous and specific to children. In recent years, the possibility of better defining these has emerged, and new, more appropriate classification criteria are being considered by the Paediatric Rheumatology International Trials Organization (PRINTO). Among the articular types, RF-positive polyarthritis is consistent with RA. In contrast, the RF-negative polyarthritis and oligoarthritis are heterogeneous, and both classifications include subsets of patients characterized by early onset and positivity for antinuclear antibodies. This is a more homogenous form that is only observed in childhood. As mentioned above, RF-positive polyarthritis is consistent with adult diseases, but children have unique symptoms and extra-articular symptoms not seen in adults, and in terms of prognosis, there are reports that adult (transitional cases aged 16 years or older) JIA has a better prognosis when compared with RA in patients with adult JIA who developed the disease at the same time, suggesting that the conditions are not completely consistent with adult diseases. This time, I would like to discuss the differences between articular type JIA and RA from the perspective of a pediatric rheumatologist.

S14-2

Articular JIA vs Rheumatoid Arthritis: From the Perspective of Adult Rheumatology

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Conflict of interest: Yes

Juvenile idiopathic arthritis (JIA) is a representative juvenile-onset collagen disease frequently encountered by adult rheumatologists. JIA is classified into seven subtypes, with oligoarthritis, RF-negative polyarthritis, and RF-positive polyarthritis grouped under the “articular types”. Notably, RF-positive Jpolyarthritis shares many features with rheumatoid arthritis (RA). However, adult rheumatologists often manage articular JIA post-transition as if it were equivalent to RA, without fully distinguishing between the characteristics of each JIA subtype and RA. Thus, it is important to clarify the specific features of articular JIA subtypes and delineate their differences and similarities with RA. In this presentation, I will address the following three aspects from the perspective of an adult rheumatologist: (1) differences among articular JIA subtypes, (2) differences between articular JIA and RA, and (3) distinctions between articular JIA and RA in patients after transitioning to adult care. In section (2), I will compare the two conditions regarding symptoms, notable complications, natural course and prognosis, treatment strategies, approved medications, disease activity assessment criteria, and medical assistance systems. I will also present findings from studies on prognosis comparisons between articular JIA and RA (Mod Rheumatol. 2020; 30: 78-84) and the validity of RA disease activity indices in articular JIA patients. In section (3), I will utilize data from the National Database of Rheumatic Diseases in Japan (NinJa) to compare treatment approaches and disease activity between young adult JIA and RA patients. Additionally, I will discuss the results of

a survey on adult rheumatologists' awareness of transitional care articular JIA (Mod Rheumatol 2018; 28: 981-985) and findings from a patient association survey (Mod Rheumatol 2021; 31: 691-696) to explore perspectives on transitional care for articular JIA patients in adult care.

S14-3

Childhood-onset systemic lupus erythematosus vs adult-onset systemic lupus erythematosus: a pediatric perspective

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is an autoimmune disease with a variety of clinical manifestations that predominantly affects young women. In Japan, childhood-onset SLE (cSLE) is defined as SLE that develops before the age of 16 years and accounts for 15%-17% of all SLE cases. The frequency of clinical manifestations of cSLE differs from that of adult-onset SLE (aSLE), with lupus nephritis being more frequently associated with cSLE, and renal histopathological findings being more severe. Cases of silent lupus nephritis without abnormal urinary findings at the initial presentation have been reported. Furthermore, discoid erythema, arthritis, and serositis are less common in cSLE than in aSLE. Given these clinical characteristics, the international classification criteria validated for aSLE lack precision, and the ACR-1997 classification criteria for cSLE have low sensitivity. The Japanese Ministry of Health and Welfare criteria, comprising 12 items with the addition of low complement level to the ACR-1997 criteria, are widely used in Japan because of their good sensitivity and specificity. Evidence for the treatment of cSLE is scarce and has been based on aSLE guidelines. Because of pediatric-specific side effects such as glucocorticoid-induced growth retardation, immunosuppressive drugs have been used in combination to reduce the glucocorticoid dose. A guide to cSLE based on the consensus of pediatric rheumatologists was published in 2018, and guidelines for the treatment of cSLE based on the GRADE system are currently being developed. Furthermore, recent genetic analyses have shown that monogenic SLE occurs in patients with young-onset SLE. The possibility of monogenic SLE should be considered for patients with early-onset disease, evidence of Mendelian inheritance or other strong family history, less typical manifestations, disease that is refractory to standard therapy, male sex, and consanguinity, even in the absence of a family history of SLE.

S14-4

Childhood-Onset vs. Adult-Onset SLE: The Role of Rheumatologists and Treatment Approaches in Adult Management

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Conflict of interest: Yes

Childhood-onset and adult-onset systemic lupus erythematosus (SLE) show distinct differences in clinical course, pathology, and treatment response, necessitating stage-appropriate management. Childhood-onset SLE often involves severe organ damage requiring early, intensive immunosuppressive therapy, whereas adult-onset SLE is influenced by chronic disease activity and comorbidities, which greatly affect long-term outcomes. These differences stem from factors such as immune system maturity at onset, genetics, environment, and hormonal changes. This presentation examines childhood-onset and adult-onset SLE from an adult care perspective, focusing on treatment and management challenges during the transition to adulthood. Childhood-onset SLE patients often require prolonged immunosuppressive therapy, bringing risks such as infections, drug-related side effects, and bone density loss. Extended disease activity also results in organ damage and reduced quality of life, making continuous support during transition essential. Distinct treatment strategies for childhood-onset and adult-onset SLE will also be discussed. In childhood-onset SLE, early intervention is crucial, especially in managing renal and central nervous system complications. For adult-onset cases, the focus is on stabilizing chronic disease activity and managing lifestyle-related risks. Treatment for adults emphasizes minimizing steroid use, optimizing immunosuppressive therapy, and patient education. The importance of multidisciplinary support in transitional care will be highlighted, with collaboration among healthcare providers, families, and patients to ensure a seamless shift to adult care. Given SLE's chronic nature, psychological support and patient education are vital to fostering patient independence. This presentation aims to deepen understanding of childhood-onset and adult-onset SLE differences, highlight the role of adult rheumatologists, and explore comprehensive support strategies in transitional care.

S14-5

Differences Between Juvenile Dermatomyositis and Adult Dermatomyositis -A pediatrician's perspective

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Conflict of interest: None

Juvenile dermatomyositis (JDM) is considered to belong to the same disease spectrum as adult dermatomyositis (DM), yet notable differences exist in onset age, clinical features, autoantibody profiles, complications, treatment responses, and prognosis. JDM accounts for 80-90% of juvenile idiopathic inflammatory myopathies (JIIM). Unlike adults, juvenile cases rarely present with polymyositis, inclusion body myositis, or immune-mediated necrotizing myopathy. The median age of illness onset for JDM is 7 years. Myositis-specific autoantibodies are frequently detected in JDM, though their patterns differ from adult DM. Anti-NXP2, anti-TIF-1, and anti-MDA5 antibodies are the most common, collectively representing 90% of JDM cases. Conversely, anti-ARS antibodies are rare in JDM, as are anti-NT5C1A and anti-HMGCR antibodies. Complications in JDM include a low malignancy incidence of around 1%. Interstitial lung disease is less common than in adults, with a prevalence of 27.5% according to a 2021 Japanese multicenter study. However, gastrointestinal and skin ulcers are more frequent in JDM than in adult DM. Treatment for moderate to severe JDM typically involves initial glucocorticoid pulse therapy, followed by maintenance therapy with early immunosuppressive agent use to mitigate side effects, such as growth impairment. Cyclophosphamide use is carefully considered due to its potential impact on ovarian function and fertility. JDM patients generally exhibit better therapeutic responses and survival outcomes compared to adults. Remission occurs within three years in about half of cases, with many achieving treatment discontinuation. However, long-term complications, such as subcutaneous calcinosis (20-30%) and functional disabilities (23-36%), remain challenges. Age-specific management strategies are essential, highlighting key differences between JDM and adult DM. This presentation will explore these distinctions in detail.

S14-6

Comparison of clinical characteristics between juvenile and adult-onset dermatomyositis from the adult rheumatologist's perspective

Takahisa Gono
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Conflict of interest: Yes

Dermatomyositis (DM) is an autoimmune disease characterized by skin rash and myositis. DM patients also present with joint, lung, cardiac, and esophageal gastrointestinal lesions. The etiology of DM involves genetic predisposition, mainly related to huma leukocyte antigen, and environmental factors such as ultraviolet light, infections, drugs, vaccinations, and cigarette smoking. The weighted balance of DM development between genetic and acquired factors differs between juvenile DM and adult-onset DM because the peak age of onset for juvenile DM (JDM) is between 5 and 14 years, whereas for adult-onset DM it is 50 to 64 years. Although anti-TIF1-γ-positive adult-onset DM patients often develop cancer, there is no association between the presence of anti-TIF1-γ antibody and cancer in JDM, suggesting that the pathogenesis of DM onset differs between JDM and adults. According to a proteomic and transcriptomic analysis, interferon-induced signaling and neutrophil degranulation are common to both JDM and adult-onset DM, although peripheral upstream and downstream components are differentially regulated between JDM and adult-onset DM. In terms of myositis autoantibody profiles and clinical characteristics, JDM patients and adult-onset DM patients have distinct

aspects: JDM patients often presents with subcutaneous calcification, leading to joint contracture; anti-synthetase autoantibody is the most common antibody in adult patients and are strongly associated with interstitial lung disease, whereas rarely detected in juvenile patients. In addition, treatment response is also different between juvenile and adult patients: corticosteroid discontinuation, complete clinical response and remission rates are higher in JDM than in adult-onset DM. The purpose of this symposium is to outline clinical characteristics of adult-onset DM, recognize its differences from JDM, and provide a comprehensive understanding of the disease as a whole, including juvenile and adult DM patients.

S14-7

Childhood-onset Sjögren's disease vs. adult-onset Sjögren's disease -from the perspective of pediatrics

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Conflict of interest: None

Sjögren's disease (SD) is a systemic inflammatory autoimmune disorder primarily characterized by the inflammation of the exocrine glands, such as the salivary and lacrimal glands, often accompanied by damage to various extra-glandular organs. Childhood-onset Sjögren's disease (cSD) differs from adult-onset SD, as it typically presents with fewer symptoms such as dry mouth and dry eyes due to damage to the salivary and lacrimal glands. However, a higher proportion of patients exhibit extraglandular symptoms such as fever, fatigue, and lymphadenopathy. Therefore, cSD is often misdiagnosed owing to the use of adult classification criteria. In a survey of 276 adult patients with SD conducted by the Japanese Sjögren's Syndrome Patients Association, approximately 10% reported having symptoms since childhood. The average time from the onset of SD symptoms to diagnosis was 10.5 years, indicating that diagnosis is often delayed. Although many factors regarding the continuity between cSD and adult-onset SD remain unknown, early treatment interventions based on appropriate diagnosis and activity assessment may improve the prognosis of SD if cSD is considered an early stage of SD. Currently, the cSD working group of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) and the SD interest group of the Pediatric Rheumatology European Society are leading efforts to create new classification criteria for childhood Sjögren's disease (CLassificAtion cRIteria for chIldhood on sjögRen: CLARIFIER), with the Sjögren's Disease working Group of the Pediatric Rheumatology Association of Japan participating as a representative of Asia. I also present the Sjögren's Syndrome Registry for All Ages (PRICURESOALA), which was established to elucidate the long-term prognosis of cSD, evaluate therapeutic interventions, and assess future prospects.

S14-8

Are juvenile-onset Sjögren's syndrome (SS) cases after transition to adulthood different from adult-onset SS cases?

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Conflict of interest: None

SS is an autoimmune disease that affects exocrine glands including salivary and lacrimal glands. In 2011, the MHLW Research Team conducted a nationwide epidemiological survey on SS (primary and secondary surveys), mainly focusing on adult cases. The primary survey estimated 68,483 of SS patients. In the secondary survey, clinical information of 2,195 cases diagnosed with SS by their attending physicians was collected, revealing that the average age was 60.8±15.2 years, including 14 cases under 20 years old, and the male-to-female ratio was 1:17.4. In the transitional care of juvenile-onset CTD, it is essential for physicians in adult departments to understand the pathophysiology and clinical characteristics of juvenile-onset CTD. In this lecture, based on the results of a post-hoc analysis of the aforementioned-nationwide epidemiological survey on SS (secondary survey), we will compare between juvenile-onset SS after transition to adulthood and adult-onset SS in terms of; 1) patient background and disease types, 2) fulfillment of diagnostic criteria items, and 3) treatment, to understand the characteristics of juvenile-onset SS after transition to adulthood. 1) Out of the 2,195 cases, the age of SS onset was reported in 1,625 cases. There were 50 juvenile-onset (under 16 years old) cases, and 1,575 adult-onset (aged 16 or older) cases. Compared to adult-onset cases, juvenile-onset cases were significantly younger at the time of the survey (35.7±11.3 vs 61.1±14.5 years) and had a significantly longer disease duration. 2) Compared to adult-onset cases, juvenile-onset cases had significantly lower frequencies of dry eyes and dry mouth, and significantly higher positive rates for anti-SS-A/SS-B antibodies, and a higher fulfillment rate of the 1999 Japanese diagnostic criteria for SS. 3) Compared to adult-onset cases, the usage of glucocorticoids was significantly higher, while that of secretagogues and local oral therapies was significantly lower in juvenile-onset cases.

S15-1

Best Use of Glucocorticoids from the Perspective of Disease Activity and Flare in SLE

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Conflict of interest: None

The treatment goal for systemic lupus erythematosus (SLE) is remission or low disease activity. In the EULAR recommendations for the management of SLE, glucocorticoids (GCs) are considered to be initiated with pulse therapy for patients with moderate-to-severe disease to control disease activity, and continuing hydroxychloroquine, using immunosuppressive drugs, and adding biologic agents are recommended to reduce the GC dosage. From the viewpoint of adverse events, minimizing and preferably discontinuing GCs during maintenance therapy are desirable. However, although up to 17% of patients with SLE may successfully stop all medications for a while, only 1% of patients will successfully continue without all medications for ≧5 years and have no disease activity. In a 12-month randomized controlled trial comparing prednisone maintenance with discontinuation in patients with SLE in clinical remission on prednisone 5 mg/day, the proportion of patients experiencing a flare was significantly lower in the maintenance group compared with the withdrawal group (risk ratio 0.2), but the SLICC/ACR damage index (SDI) increase and GC toxicity index were similar in the two treatment groups. A meta-analysis examining the risk of flare and SDI increase after discontinuation of low-dose GCs in SLE also showed an increased risk of flare with discontinuation but no significant protection against SDI increase. Thus, discontinuing low-dose GCs is associated with a significant risk of flare in patients with stable SLE, whereas it is not significantly associated with protection against damage accrual. An international survey of 130 clinicians reported that >60% of the clinicians preferred to continue low-dose GC (prednisolone 5 mg/day) in patients with SLE, even when the duration of complete remission was 5 years. This abstract will outline the evidence to discuss the best use of GCs from the perspective of disease activity and flare in SLE.

S15-2

New Treatment Strategies for Lupus Nephritis

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Conflict of interest: Yes

In the treatment of lupus nephritis, it is important to maintain long-term renal function while minimizing treatment-related side effects. This requires implementing an appropriate induction therapy tailored to the disease state to achieve remission, followed by maintenance therapy to prevent relapse over the long term. For proliferative lupus nephritis (Class III/IV±V), the ALMS trial demonstrated that the efficacy of mycophenolate mofetil (MMF) and intravenous cyclophosphamide (IVCY) were nearly equivalent, establishing both as first-line treatment options. Subsequent clinical trials for various drugs have mostly failed; however, the utility of MMF combined with calcineurin inhibitors (CNI, including tacrolimus

and voclosporin), MMF with belimumab (BLM), and IVCY-AZA combined with BLM has been demonstrated. Based on these findings, the 2023 European Alliance of Associations for Rheumatology (EULAR) recommendations for SLE and the 2024 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for lupus nephritis have included MMF, IVCY, MMF+CNI, and MMF/IVCY-AZA+BLM as first-line therapies. Moreover, the recently released 2024 American College of Rheumatology (ACR) guidelines for lupus nephritis no longer list MMF and IVCY as first-line treatments but instead prioritize combination therapies such as MMF+BLM or MMF+CNI as new first-line options. An important recent trend in induction therapy is the reduction of glucocorticoid (GC) use, aiming to minimize GC-related side effects. While GC pulse therapy remains recommended at the initiation of treatment, subsequent dosing begins at lower levels than traditionally used, with early tapering prioritized. Eventually, maintaining a dose equivalent to prednisone ≦5 mg/day or <5 mg/day is recommended. This symposium will provide a comprehensive overview of these novel therapeutic strategies for lupus nephritis, offering insights into optimal treatment selection based on the latest data. This symposium will provide a comprehensive overview of these novel therapeutic strategies for lupus nephritis, offering insights into optimal treatment selection based on the latest data.

S15-3

Optimizing Management of Disease Activity and Recurrence in Neuropsychiatric Systemic Lupus Erythematosus

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Conflict of interest: None

Patients with systemic lupus erythematosus (SLE) can develop neuropsychiatric SLE (NPSLE), a potentially life-threatening complication. In Japan, treatment guidelines for NPSLE, particularly for inflammatory manifestations, are outlined separately as major organ damage like lupus nephritis. Research using murine models has elucidated the mechanisms underlying inflammatory central nervous system lesions in NPSLE, highlighting the roles of autoantibodies, cytokines, microglial activation, and blood-brain barrier (BBB) disruption. Based on these findings, we demonstrated the utility of the autoantibody against the N-methyl-D-aspartate receptor subunit GluN2A/B (anti-GluN2) as a diagnostic marker for psychiatric manifestations in SLE patients. Additionally, interleukin-6 has been identified as a significant biomarker for detecting psychiatric symptoms in the retrospective study. We also observed that soluble triggering receptor expressed on myeloid cells 2, a marker of microglial activation, is elevated in cerebrospinal fluid alongside anti-GluN2. Besides, we demonstrated the crucial role of BBB disruption in the development of psychiatric symptoms in NPSLE. To reduce NPSLE recurrence, it is essential to monitor disease activity through biomarkers and perform regular evaluations of mental and cognitive function. Given the immunological similarities between systemic and central nervous system inflammation in SLE, novel molecular-targeted therapies are expected to be effective for inflammatory NPSLE. However, a definitive diagnostic standard and therapies with strong evidence are still lacking due to the rarity and heterogeneity of NPSLE, which present significant unmet needs in its evaluation and treatment. To establish reliable diagnostic methods, identify robust disease biomarkers, and validate the utility of existing ones, a multidisciplinary consortium involving experts from various medical fields and a sufficiently large cohort of NPSLE patients must be developed.

S15-4

Strategies for controlling disease activity and flare in SLE using molecular-targeted drugs

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Conflict of interest: Yes

For more than half a century, the treatment of systemic lupus erythematosus (SLE) has centred on glucocorticoids (GC) and immunosuppressants. Although these are necessary for controlling disease activity, they are non-specific treatments, and the accumulation of organ damage caused by the drugs can reduce patient quality of life. Therefore, there has been a drive to develop disease-specific molecular target drugs that can control disease activity and suppress relapses over the long term. As many of the SLE disease susceptibility genes are related to signal transduction in dendritic cells and lymphocytes, multiple molecules that bridge the innate and adaptive immune systems are promising therapeutic targets. Currently, the anti-BAFF antibody belimumab and the anti-type I interferon receptor antibody anifrolumab are approved for use in active SLE where standard treatment is ineffective, and the anti-CD20 antibody rituximab is approved for use in lupus nephritis in Japan. In addition, phase 2 and 3 trials are underway for multiple molecular targeted drugs that target JAK, TYK2, CD19, CD20, CD38, CD40, CD40L, BDCA2, BAFF receptors, TLR7/TLR8, etc. SLE is a clinically and immunologically diverse autoimmune disease, and the cells or molecules targeted for treatment are diverse. This is why nonspecific immunosuppressants such as GC are effective, but it is necessary to clarify when and for which patients to use molecular targeted therapy. Theoretically, the challenge for the future is to implement precision medicine, in which molecular targeted drugs are selected according to the heterogeneity of SLE and the pathology of each patient group.

S15-5

The Potential of CAR-T Cell Therapy for Controlling Disease Activity and Relapse in SLE

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Conflict of interest: Yes

CAR-T cell therapy uses the patient's own T cells, modified through genetic engineering to express a chimeric antigen receptor (CAR). A CAR consists of an extracellular domain based on a single-chain antibody targeting specific antigens, an intracellular signaling domain, and a hinge and transmembrane structure linking these components. Advances in CAR-T therapy have been driven by enhancements to the intracellular signaling domains, which have improved therapeutic efficacy. Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by diverse autoantibodies, and rituximab, a CD20-targeted therapy, has shown efficacy in some patients, though it failed to demonstrate consistent effectiveness in randomized controlled trials. In this context, Mackensen et al. conducted a single-arm clinical trial using CD19-targeted CAR-T cells in five patients with refractory, treatment-resistant active SLE. Three months after CAR-T cell infusion, these patients showed significant improvement in both clinical symptoms and laboratory results. During a follow-up period of 4 to 16 months, disease activity remained in remission, and patients were able to achieve a steroid-free state. Safety concerns associated with CAR-T therapy for tumors, particularly the risk of severe cytokine release syndrome (CRS) and immune cell-associated neurotoxicity syndrome (ICANS), were not prominent in this study. Only mild CRS occurred, and no cases of ICANS were observed. While this study presents promising results, several critical issues must be addressed for further clinical application. These include optimizing preconditioning methods, selecting appropriate cells for CAR introduction, refining criteria for patient selection, and evaluating the need for maintenance therapy. Despite these challenges, CD19-targeted CAR-T therapy shows great promise as a treatment for refractory SLE, with the potential to achieve a steroid-free state.

S15-6

Elucidation of immunological pathways associated with disease activity and flare in SLE

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Conflict of interest: Yes

Key factors influencing the prognosis of systemic lupus erythematosus (SLE) include organ damage at onset and relapse, as well as the cumulative organ damage associated with glucocorticoid-based treatments. To improve long-term outcomes in SLE, it is essential to understand the mechanisms underlying disease activity and flares and to develop treatment

strategies accordingly. The most characteristic immune abnormality in SLE is the overactivation of type I interferon (IFN), an antiviral cytokine. Recent advancements in the accurate measurement of type I IFN activity have shown that it correlates with disease activity and is associated with flares. The next critical question is how specific effects of type I IFN are linked to disease activity and flares. Recent transcriptomic and spatial molecular analyses, particularly single-cell RNA sequencing (scRNAseq), have begun to elucidate the target cells of type I IFN. One relatively clear pathway is its effect on the adaptive immune system, especially its involvement in extrafollicular pathways. B cells crucial to extrafollicular responses include atypical B cells (ABCs), which are supported by peripheral helper T cells and ThA cells. These helper T cells proliferate and activate under the influence of type I IFN, producing IL-21 and CXCL13. In a study of 63 SLE patients meeting LLDAS criteria over approximately five years, we investigated the relationship between flares and 27 immune cell subsets, focusing on type I IFN-related signaling pathways. The mitochondrial and cell cycle pathways in ThA cells, Tfh cells, and Th17 cells were associated with flares. In B cells, type I IFN signaling was linked to the differentiation of memory B cells expressing IGHV4-34, a component of autoreactive B cell receptors. Interestingly, patients with a high frequency of IGHV4-34-expressing memory B cells (IGHV4-34 high) exhibited higher disease activity and treatment resistance, despite receiving comparable glucocorticoid doses to those with lower frequencies. Additionally, the IGHV4-34 high group demonstrated an increased risk of flares. These findings suggest that type I IFN and the adaptive immune responses it influences are closely associated with disease activity and flares in SLE. Moving forward, an important challenge will be the identification of patients at high risk for flares based on these immune parameters and the integration of these insights into clinical practice.

S16-1

Positioning TNF Inhibitors for Peripheral Arthritis and Enthesitis Treatment

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Conflict of interest: None

TNF inhibitors are a well-established primary treatment option for managing arthritis and enthesitis in axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA). With the advent of IL-17, IL-23, and JAK inhibitors, discussions are ongoing about their optimal use. Treatment selection now requires a personalized approach, considering each patient's disease characteristics and risk profile. Recent large-scale trials have confirmed the efficacy of IL-17 inhibitors for arthritis and enthesitis in axSpA and PsA, with especially high effectiveness for skin lesions. Consequently, EULAR recommends TNF and IL-17 inhibitors equally for treating arthritis and enthesitis in PsA, while favoring IL-17 and IL-23 inhibitors for cases with psoriatic skin involvement. For patients with uveitis, TNF inhibitors are preferred, and for those with inflammatory bowel disease, TNF, IL-23, or JAK inhibitors may be suitable. While TNF inhibitors have extensive long-term safety data, IL-17 and IL-23 inhibitors are also known for their safety. Thus, selecting based on individual safety profiles is essential. In practice, however, many patients present mainly with arthritis and enthesitis, without significant skin lesions, uveitis, or inflammatory bowel disease, making the timing of TNF inhibitor selection challenging in such cases. The accumulation of real-world data and advances in predictive biomarker research for TNF inhibitor responsiveness in axSpA and PsA are anticipated to enable more precise treatment approaches. This presentation will discuss the latest evidence and challenges regarding TNF inhibitors for arthritis and enthesitis in axSpA and PsA, and explore patient profiles for whom TNF inhibitors may be most suitable.

S16-2

Positioning of IL-17 Inhibitors for Peripheral Arthritis and Enthesitis: Challenges to minimal disease activity (MDA)

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Conflict of interest: Yes

Psoriatic arthritis (PsA) has six domains: peripheral arthritis, axis involvement, enthesitis, dactilitis, nail lesions, and psoriatic skin plaque. IL-17 inhibitors are known to be highly effective for each domain. In peripheral arthritis of PsA, some RCTs have shown same efficacy comparable to that of TNF inhibitors, but when evaluation of skin lesions is added, IL-17 inhibitors show higher efficacy. In addition, the role of IL-17 in enthesitis is very important, and there is a lot of evidence demonstrating the efficacy of IL-17 inhibitors. The EULAR recommendation 2023 update in PsA recommends the use of IL-17 inhibitors in patients with PsA with severe skin lesion. In addition, the AXIS study reported that approximately 30% of PsA patients have axial involvement. IL-17 inhibitors are recommended for a wide range of patients but are first-line agents especially in patients with severe skin rash and peripheral arthritis or enthesitis as well as axial involvement. Moreover, IL-17 inhibitors play quite important role for the PsA treatment toword minimal disease activity (MDA). Currently, there are four types of IL-17 inhibitors available for PsA include secukinumab and ixekizumab, monoclonal antibodies against IL-17A; brodalumab, a monoclonal antibody against IL-17 receptor A; and a dual monoclonal antibody acting on both IL-17A and IL-17F; bimekizumab. This presentation will focus on the molecular mechanisms and therapeutic effects of IL-17 inhibitors and discuss their positioning in the treatment of peripheral arthritis and enthesitis. In addition, treatment strategies based on disease activity, site of involvement, and presence of complications will be presented, and the role of IL-17 inhibitors and their use to maximize therapeutic efficacy will be discussed. In addition, adverse events and safety in the indications for IL-17 inhibitors will be discussed, as well as key points for continuation of treatment and patient management.

S16-3

JAK inhibitors for the treatment of peripheral arthritis and enthesitis

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Conflict of interest: None

Spondyloarthritis (SpA) is a highly heterogeneous systemic autoimmune disease. It is broadly classified into axial and peripheral SpA, which include radiographic axial SpA (r-axSpA) and psoriatic arthritis (PsA), respectively. The main pathology is enthesitis, which leads to a variety of clinical symptoms such as spinal and sacroiliac joint involvement, and peripheral arthritis. The activation of the IL-23/Th17 axis plays a central role in the pathogenesis of enthesitis and various molecular targeted drugs have become available. However, as shown by many phase 3 trials targeting PsA, the achievement rate of minimal disease activity, the treatment target is about one-third, even when treated with these molecular targeted drugs. In other words, simultaneous improvement of various symptoms in SpA has not been fully achieved. To overcome such issues, the emergence of novel molecular-targeted drugs has been expected. Recently, JAK inhibitors (only upadacitinib in Japan) have become available for SpA (PsA, r-axSpA and non-radiographic axial SpA (nr-axSpA)) in Japan. Upadacitinib is a JAK inhibitor that inhibits the Janus kinase family JAK1/JAK2/JAK3/TYK2 and exerts an antirheumatic effect by suppressing the transmission of multiple cytokine signals and exerting an immunosuppressive effect. In fact, the high efficacy and safety profile have been shown in several large-scale clinical trials and its use is recommended in the PsA EULAR recommendation 2023 update. On the other hand, due to the experience with RA and the high rate of lifestyle-related diseases as a risk factor for cardiovascular events in PsA/SpA, its use with the consideration for safety is emphasized. JAK inhibitors are expected to be a useful treatment option that contributes to improving patient outcomes. On the other hand, further accumulation of safety profiles is essential.

S16-4

Role of TNF Inhibitors in the Treatment of Axial Spondyloarthritis

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Conflict of interest: Yes

In axial spondyloarthritis (axSpA), including ankylosing spondylitis

(AS), TNF inhibitors are pivotal in treatment due to their ability to target TNF, a key inflammatory mediator implicated in disease pathogenesis. These drugs are particularly considered when NSAIDs or csDMARDs fail to provide adequate relief. For axial lesions, where csDMARDs have limited efficacy, TNF inhibitors, IL-17 inhibitors, or JAK inhibitors are recommended for NSAID-refractory cases. Clinical trials have demonstrated the effectiveness of TNF inhibitors such as etanercept, infliximab, adalimumab, and golimumab, with approximately 60% of AS patients achieving ASAS20 responses and 40% achieving ASAS40 responses. Similar benefits have been observed for certolizumab pegol in both AS and non-radiographic axSpA (nr-axSpA). TNF inhibitors effectively reduce symptoms like enthesitis and dactylitis and inflammation in sacroiliac joints and the spine, as evidenced by improved CRP levels and MRI findings. During 12-28 weeks of treatment, TNF inhibitors achieve partial remission in 16-62% of patients and inactive disease (ASDAS <1.3) in about 40%. Predictors of better outcomes include younger age, male gender, high baseline disease activity, short disease duration, absence of enthesitis, and presence of HLA-B27. Patients with shorter disease duration show better responses than those with disease lasting over two years. While 60-75% of AS patients respond well to the first TNF inhibitor, 15-25% exhibit primary non-response. Secondary non-response or intolerance necessitates switching to alternative biologics, with the first TNF inhibitor showing a one-year retention rate of about 77%. This lecture provides an overview of the usefulness of TNF inhibitors in the treatment of spondyloarthritis.

S16-5

Positioning of IL-17 inhibitors in spondylitis

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Conflict of interest: None

ASAS/EULAR recommendations for the management of axial spondyloarthritis (axSpA) were updated in 2022. Patients suffering from pain and stiffness should use an NSAID as first-line drug treatment (Phase 1). TNFi, IL-17i or JAKi should be considered in patients with high disease activities despite conventional treatments (Phase 2). If there is a history of recurrent uveitis or active inflammatory bowel disease (IBD), preference should be given to TNFi. In patients with significant psoriasis, an IL-17i may be preferred. Absence of response to treatment should prompt re-evaluation of the diagnosis of consideration of the presence of comorbidities (Phase 3). Following a first b/ts DMARD failure, switching to another bDMARD (TNFi or IL-17i) or a JAKi should be considered. Ankylosing spondylitis (AS) patients have often elevated inflammatory reactions such as CRP. However, AS patients even with high disease activities occasionally have negative CRP. AS patients with negative CRP are less responsive to TNFi treatment compared to positive CRP. Ixekizumab, one of IL-17i, was shown in a clinical trial for AS to be effective in patients with low CRP and poor inflammation of the spine and sacroiliac joints on MRI. The use of IL-17i should be considered for AS with poor inflammatory findings on blood tests and MRI. Psoriatic arthritis (PsA) patients have often axial disease. EULAR recommendations for the management of PsA with pharmacological therapies were updated in 2023. In patients with clinically relevant axial disease with an insufficient response to NSAIDs, therapy with IL-17i, TNFi and JAKi should be considered. When there is relevant skin involvement, IL-17i or IL-12/23i may be preferred for patients with peripheral arthritis and inadequate response to csDMARDs. This session will discuss the position of IL-17i in the treatment for SpA spondylitis, including examples from our own experience.

S16-6

The Role of JAK Inhibitors in the Treatment of Spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis (SpA) is a group of disorders that cause chronic inflammation in axial joints, such as the sacroiliac joints and spine, as well as in peripheral joints, tendons, and entheses. SpA includes axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA), both of which can lead to joint pain, stiffness, and functional impairment, significantly affecting patients' quality of life. Traditionally, the treatment of axSpA has started with nonsteroidal anti-inflammatory drugs (NSAIDs) as the first-line therapy. If the response is insufficient, biologic disease-modifying anti-rheumatic drugs (bDMARDs), such as TNF inhibitors and IL-17 inhibitors, are introduced. Similarly, in PsA, NSAIDs, conventional synthetic DMARDs (csDMARDs), and bDMARDs are widely used in treatment. However, a significant proportion of patients still experience suboptimal outcomes, underscoring the need for additional treatment options. In this context, Janus kinase (JAK) inhibitors have emerged as a promising new therapeutic option. In Japan, the JAK inhibitor upadacitinib was approved for PsA in 2021, with further approvals for ankylosing spondylitis and non-radiographic axSpA in 2022. These new approvals have notably expanded the range of therapeutic options for SpA. As the concept of "difficult-to-treat" SpA becomes increasingly recognized, similar to that in rheumatoid arthritis, a broader array of treatment choices may offer greater opportunities to effectively treat more patients. Additionally, there is growing interest in the pain-relieving effects of JAK inhibitors and in potential differences in efficacy based on gender. This presentation will provide an overview of the efficacy and safety of JAK inhibitors in patients with SpA, as well as discuss the current positioning of JAK inhibitors in the latest treatment guidelines and their role in clinical practice amidst an expanding array of therapeutic options.

S17-1

What is Team-Based Care to Support Future Rheumatoid Arthritis Patients?From the Physician's Perspective

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Conflict of interest: Yes

Data from the National Database of Rheumatic Diseases in Japan (NinJa) show that the aging population of RA patients and the increase in late-onset cases are becoming evident, with the average age at death also rising annually. It is anticipated that there will be a growing number of elderly RA patients with various comorbidities, such as malignancies and dementia, as well as an increase in patients transitioning to home healthcare. Additionally, the birth rate among young female RA patients is lower than that of the general population, and the support system for transitioning juvenile patients to adult healthcare is insufficient. According to the report from the Health Sciences Council's Rheumatism and Related Diseases Committee, although disease activity in RA patients is decreasing, there is a need for support tailored to each life stage. The report highlights the lack of adequate support for patients and their families and stresses the need for promoting team-based medical care through collaboration between physicians and medical staff. To address these issues, we established research groups under the Ministry of Health, Labour and Welfare's Science Research Project. These groups are working to understand the current state of RA patient support, identify unmet needs, and tackle existing challenges. In this presentation, we will demonstrate the trends over time for RA patients using NinJa data, and share the results of a survey conducted by our research groups on RA patient support, targeting medical staff, caregiving and welfare professionals, and physicians. We will clarify the current situation and challenges in RA patient support. Furthermore, based on these survey findings, we will explore the optimal approach for team-based care for future RA patients, the roles expected of physicians, and the responsibilities they should assume. We will also introduce the RA patient support materials developed by our research groups.

S17-2

The role of nurses in team medical care to support patients with rheumatoid arthritis for the future

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Conflict of interest: None

The remarkable progress in pharmacotherapy for rheumatoid arthritis (RA) brought about a major change in the role of nurses, who were the coordinators of team medical care. When methotrexate (MTX) was approved in 1999, the role of nurses was to provide guidance on oral administration and infection prevention, to receive telephone consultations and to explain about drug suspension. In 2003, biological agents appeared, and nurses played a major role in infusion of injectable agents, subcutaneous injection, and especially self-injection guidance. In 2013, JAK inhibitors became available, increasing the number of treatment options, and nurses' roles also included to support share decision making (SDM) and to increase self-efficacy. Nurses are also required to provide detailed support according to each life stage, such as providing support to women who are financially and mentally unstable during pregnancy and childbirth, and to the adolescent and young adult (AYA) generation, as well as advising the patients with comorbidities such as age-related musculoskeletal degenerative diseases, lung, heart, and kidney diseases, dementia, and D2T RA that is resistant to pharmacotherapy. Looking back at the dramatic progress made in medicine over the past quarter century, we can expect a further paradigm shift to occur in the future. However, behind this, there is a possibility that new issues and problems that cannot be solved by pharmacotherapy alone will emerge. In that sense, I believe that the role of nurses will expand.

S17-3

Conviviality in rehabilitation for rheumatoid arthritis

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National Rehabilitation Center for Persons with Disabilities

Conflict of interest: None

The etymology of the word "rehabilitation" comes from the Latin words, re "again" + habilis "humanlike". Rehabilitation is the process of restoring a person to a human-like state when he or she has fallen into an inhuman state, in other words, "restoration of honor and dignity". In the field of rheumatology, advances in pharmacotherapy and surgical treatment have enabled thorough control of disease activity, and have created an environment in which patients actively engage in rehabilitation to improve their quality of life. In the total management of rheumatoid arthritis, rehabilitation is one of the four pillars along with pharmacotherapy, surgical therapy, and care. The cornerstone of rehabilitation medicine is multidisciplinary cooperation. Starting with the multidisciplinary team model, there is the inter-relational team model, which emphasizes information sharing and conferences, and the cross-professional team model, which actively covers other professions beyond one's own area of expertise. The important thing is for medical staff to "think together" and "co-create" the lives of patients with illnesses and disabilities. Meanwhile, the environment surrounding rehabilitation medicine is becoming increasingly severe. The number of convalescent beds in Japan has almost quintupled over the past 20 years to approximately 94,000 beds. Competition for patients is fierce. In addition, the fiscal 2024 revision of reimbursement abolished the additional fee for system reinforcement, limiting the number of units per day for rehabilitation of locomotory organs to 6 units. In the future, even more intense "competition" is expected for the survival of convalescent rehabilitation wards. In the rehabilitation of rheumatoid arthritis, orthopedic surgeons often play the role of physiatrists. In a multidisciplinary orchestra, how to organize the orchestra members and what kind of music to play together require the talent and effort not only as a performer but also as a conductor.

S17-4

What is team medical care supporting Rheumatoid Arthritis Patients in the Near Future? -in the case of pharmacist-

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Conflict of interest: None

Because of many therapeutic drugs, treatment guidelines and diagnostic methods for rheumatoid arthritis (RA) have been developed, many patients can complete their treatment through outpatient care. While outside prescriptions are a well-established healthcare system, hospitals often face challenges in tracking patients' adherence to their medications without establishing various collaborative systems. Pharmacists must understand not only RA medications but also complication treatment drug. Moreover, pharmacists are expected to engage in region-based activities, such as supporting health maintenance, assisting patients who can't visit hospital, connecting financially distressed patients with welfare systems to ensure continued treatment, and encouraging medical consultations. These efforts aim to help the public maintain their health. I have experienced two patients needed support. One had just been diagnosed with RA, and the other was considering treatment with biologic agents. It was a valuable experienced as a certified RA pharmacist, However, not all pharmacists are equipped to provide similar support. Additionally, opportunities for community pharmacists to gain advanced expertise are limited. In fact, surveys of pharmacists have revealed frequent struggles with providing day-to-day medication guidance. Although there are more pharmacies than convenience stores, their potential to support patients effectively remains underutilized. To integrate RA care into regional team-based healthcare, the first priority is to increase community pharmacists to specialize in RA. Certified RA pharmacists should take the lead in establishing networks of pharmacists capable of providing support from both medical and welfare perspectives, facilitating information sharing among professionals. If such a network is realized, patients across the country could receive consistent support and maintain a high quality of life, enjoying "Good Days" wherever they live. Now we build the system.

S17-5

Practicing Team Medicine in the Community -From the Perspective of a Medical Social Worker-

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Conflict of interest: None

Recently, team-based healthcare is emphasized in all medical specialties, but in rheumatology, the importance of such care has been recognized early on, making interdisciplinary collaboration essential. The 2024 revision of medical reimbursement clarified the roles of "curative care" and "care that heals and supports". Acute conditions and injuries are treated with "curative care", while rheumatic diseases, as autoimmune disorders, require long-term care even in remission, falling under "care that heals and supports". In 2025, making one in five individuals 75 or older. With an aging population, it is necessary to continue rheumatic treatment while addressing comorbidities, emphasizing the importance of "care that heals and supports". Thus, future team-based healthcare will require stronger collaboration with caregiving and welfare services. While medical care focuses on treatment, patients continue their lives while receiving care. To support home life, it is vital to collaborate with nursing and welfare services, sharing information and addressing challenges. Medical Social Workers (MSW) play a key role in linking healthcare with nursing and welfare, understanding what is important in both treatment and care. For example, as rheumatic patients age, cognitive decline may make managing medications or self-injections difficult. MSWs work with family members, care managers, pharmacies, and nursing care providers to continue treatment. The welfare sector, being closer to patients' daily lives, can identify abilities that may still be maintained despite cognitive decline. By evaluating these and fostering collaboration, necessary services and care can be determined, helping patients live the life they desire. There are differences between healthcare and welfare perspectives, and to promote effective team-based care, a facilitator is needed to ensure smooth collaboration. Understanding that supporting the patient's desired life is the ultimate goal is crucial. Professionals must clarify their roles, demonstrate expertise, and recognize that "the patient is also a member of the team". This approach will support future rheumatic patients. This symposium will share the current status and challenges of collaboration from the MSW perspective and offer an opportunity to discuss the future of team-based care.

S18-1

Microscopic and molecular perspectives on pathogenesis of vasculitis

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Conflict of interest: Yes

Vasculitis is classified into large-vessel vasculitis, medium-vessel vasculitis, small-vessel vasculitis, variable-vessel vasculitis, single-organ vasculitis, vasculitis associated with systemic disease, and vasculitis associated with probable etiology based on the discussion at the Chapel Hill Consensus Conference 2012 (CHCC2012). The CHCC2012 classification organizes vasculitis from a clinical perspective that focuses on the size and distribution of blood vessels affected, and the underlying disease. Although the CHCC classification is useful for understanding vasculitis comprehensively, diseases should be classified based on etiology and pathophysiology. Accoeding to histopathological findings, vasculitis is classified into granulomatous vasculitis, necrotizing vasculitis, and leukocytoclastic vasculitis, and this session will review their etiology and pathophysiology. Granulomatous vasculitis includes Takayasu arteritis and giant cell arteritis. In both diseases, immune cells such as CD4 T cells, CD8 T cells, and macrophages are thought to play an important role in pathogenesis. Recently, autoantibodies that are presumed to contribute to the development of Takayasu arteritis have also been identified. Necrotizing vasculitis is divided into those caused by anti-neutrophil cytoplasmic antibody (ANCA) and those that are not associated with ANCA, and the elucidation of pathogenesis of the former has progressed dramatically in recent years. IgA vasculitis is a disease that exhibits leukocytoclastic vasculitis. Complement activation is thought to be involved in pathogenesis, but the involvement of neutrophil extracellular traps is also attracting attention. Elucidation of etiology and pathophysiology of each disease is important for the development of molecular-targeting therapies for vasculitis.

S18-2

Vasculitis from the viewpoint of a cardiologist: focusing on Takayasu arteritis

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Conflict of interest: Yes

Takayasu arteritis (TAK) is a large vessel vasculitis, mainly affecting the aorta and its major branches. The diagnosis is based on subjective symptoms and imaging findings, which include multiple or diffuse wall thickening, stenosis/obstruction, dilation/aneurysms in the aorta and branch vessels. The mainstay of treatment for TAK is steroid. However, more than half of patients relapse upon tapering the dose of steroids. Conventional immunosuppressive therapy has shown inadequate results in patients with TAK refractory to steroid therapy, but a clinical trial of tocilizumab (TCZ), an anti-IL-6 receptor antibody, was conducted in Japan and TCZ received regulatory approval for TAK in 2017 (Nakaoka et al. Ann. Rheum Dis 2018, Rheumatology 2020). TCZ has been widely used in Japan for refractory TAK, and its efficacy and safety have been demonstrated (Harigai et al. Mod Rheumatol 2023). On the other hand, blood tests no longer function as relapse markers because acute phase proteins (e.g., CRP) become negative under TCZ administration. Therefore, in the follow-up of patients with TAK on TCZ, it is necessary to conduct a detailed interview of symptoms in an outpatient setting, along with regular imaging tests to check the worsening of wall thickening, stenosis/obstruction, and dilatation/aneurysm formation (Nakaoka et al. Rheumatology 2022). We investigated the association between aortic aneurysm formation events and gut microbiota in patients with TAK, and reported that aortic aneurysm events were significantly more common in TAK patients whose gut microbiota contained the commensal oral bacterium Campylobacter gracilis than in negative patients (ART 2023). We have established a collaborative research system with the JPVAS study group to collect stool and saliva samples from the patients with TAK on a larger scale. In addition, patients with TAK often require catheterization, endovascular treatment, or cardiovascular surgery, and postoperative complications such as delayed wound healing, systemic infection, and surgical site infection are usually increased in patients receiving steroids or TCZ. However, there are no guidelines or solid evidence that clearly define the optimal perioperative treatment strategy for hypertensive patients requiring cardiovascular surgery. Therefore, we review the evidence and recent experience supporting the perioperative use of TCZ and would like to propose a protocol to reduce complications in TAK patients undergoing invasive cardiovascular procedures (Arita et al. Circ J in press).

S18-3

Pathophysiology of Vasculitis from a Neurological Perspective

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Conflict of interest: None

Neurological involvement, particularly peripheral neuropathy, is a common manifestation of ANCA-associated vasculitis, especially Eosinophilic granulomatosis with polyangiitis (EGPA). While nerve biopsies are infrequently performed due to their invasive nature, they can be indicated when neurological symptoms are the presenting feature. Given the unique structure of nerves with long axons, even a single focal injury can lead to distal degeneration and nerve conduction interruption. Although recovery often takes years, early treatment can shorten this time. In ANCA-associated vasculitis, inflammation typically affects small arteries, capillaries, and venules. Characteristic vasculitic changes are often observed in peripheral nerves, where these vessels are closely packed. While ischemia due to vasculitis has been considered the primary cause of nerve damage, other mechanisms are also involved. Recent studies have shown that ANCA-positive and ANCA-negative EGPA have distinct clinical features. However, the high prevalence of polyneuropathy in both groups prompted a re-examination of nerve biopsy specimens. These studies revealed necrotizing vasculitis in the ANCA-positive group, while eosinophilic infiltration and degranulation predominated in the ANCA-negative group (Mod Rheumatol. 2011). Although inflammatory cells rarely directly invade nerve fibers, eosinophilic degranulation inside the endoneurium was observed in the ANCA-negative group and was associated with severe nerve degeneration. Furthermore, neutrophil extracellular traps were detected in the nutrient vessels of nerves in microscopic polyangiitis, while eosinophil-mediated direct damage to nerves (ETosis) was observed in EGPA. Charcot-Leyden crystals, formed from galectin-10 released by eosinophils, were also identified. These findings suggest that both ischemia due to vasculitis and direct injury by eosinophils contribute to the pathogenesis of neurological complications in EGPA.

S18-4

Pathogenesis and evaluation of ANCA-associated glomerulonephritis from the perspective of nephrology

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Conflict of interest: Yes

Renal damage caused by ANCA-associated vasculitis (AAV) is collectively called ANCA-associated glomerulonephritis (AAV-GN), and clinically presents as rapidly progressive glomerulonephritis and pathologically as crescentic glomerulonephritis. Recently, the prognosis of patients has improved due to early diagnosis and treatment protocols that have been established through the widespread use of ANCA measurement. However, AAV-GN still causes end-stage renal failure and is a serious complication that affects prognosis of AAV-patients in Japan, where the incidence rate is high among elderly people. The diagnosis of AAV-GN, the degree of tissue damage, and renal prognosis are evaluated by tissue diagnosis by renal biopsy. The glomerular damage observed in renal tissue is mainly caused by locally accumulated leukocytes, therefore complement-targeting drugs that have been used in recent years also exert an anti-inflammatory effect by suppressing neutrophil activation. On the other hand, the remission induction therapy is often started without a histological diagnosis in patients with poor general condition, serious comorbidities, or concomitant medications increaseing bleeding risk. In addition, because renal tissue diagnosis is not suitable for periodic disease assessment after therapeutic intervention, biomarkers are being developed both in Japan and overseas as an alternative disease assessment method to renal biopsy. In this symposium, I will outline the mechanism of leukocyte accumulation into the glomerulus and crescent formation in AAV-GN, and the possibility of non-invasive diagnostic methods focusing on leuko-

cyte-expressed proteins, based on research results from Japan and overseas. We hope that young nephrologists will deepen their understanding of the purpose of leukocytes introduced into the glomerulus and the process from leukocyte activation to tissue damage, and obtain hints for new therapeutic targets and diagnostic methods in the future.

S18-5

The Pathophysiology of Systemic Vasculitis from the Perspective of Rheumatology

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Conflict of interest: None

Systemic vasculitis is a group of diseases characterized by inflammation of blood vessels involving multiple organs, requiring collaboration across various medical specialties such as cardiology, nephrology, neurology, and pulmonology. Personalized multidisciplinary medicine is crucial due to the variability in affected organs and clinical symptoms among patients. This presentation explores the pathophysiology, clinical management, and treatment advancements in vasculitis from the rheumatology perspective. Rheumatologists specialize in diagnosing and treating vasculitis based on immunological mechanisms. For ANCA-associated vasculitis, such as microscopic polyangiitis and granulomatosis with polyangiitis, differences in the use of cyclophosphamide and rituximab among specialties have been observed. Similarly, the varying effectiveness of tocilizumab and TNF inhibitors in Takayasu arteritis and giant cell arteritis highlights distinct disease mechanisms. Rheumatologists also manage diverse vasculitis subtypes, including large-, medium-, and small-vessel vasculitis, and secondary vasculitis. With extensive experience in biologic therapies for systemic vasculitis and other autoimmune diseases e.g. rheumatoid arthritis, rheumatologists are well-equipped to introduce molecularly targeted treatments. These therapies are integral to multidisciplinary care, emphasizing the vital role of rheumatology. Research indicates interdepartmental differences in diagnostic practices, such as fundoscopy or echocardiographic examinations, for large-vessel vasculitis. Rheumatologists often integrate these findings to establish comprehensive management strategies tailored to individual patients. This presentation underscores the unique role of rheumatology in systemic vasculitis management and the importance of interdepartmental collaboration for improved patient outcomes.

S19-1

AI Applications in Medical Imaging: Integration of Large Language Models and Causal Inference

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Conflict of interest: Yes

The development of large language models (LLMs), such as ChatGPT, is driving significant changes in image AI research. Medical AI applications, including chest X-ray imaging and endoscopy, are now used in clinical practice; however, they are primarily designed as single-task AI systems, limited to specific tasks. In contrast, LLMs can learn multiple tasks simultaneously. While early LLMs focused solely on language-based tasks, such as summarizing medical histories, recent advancements have introduced multimodal LLMs (MMLLMs), capable of processing not only text but also images and videos. This has enabled applications like training models on radiology reports that integrate text and images. Cloud-based LLMs, such as ChatGPT, pose potential risks of data breaches, but the emergence of open-source LLMs that can operate within hospitals now facilitates secure research. The mechanisms behind the exceptional capabilities of LLMs remain unclear; however, it is hypothesized that they incorporate causal analysis principles. Causal analysis, a growing field at the intersection of AI and statistics, comprises two key domains: causal discovery and causal inference. Causal discovery involves estimating causal diagrams from observational data, while causal inference assesses the consistency between diagrams and data to analyze causal relationships. These techniques are now being applied to image data and multimodal datasets, such as electronic medical records that combine text and images. This presentation will highlight advancements in language and image AI, with a focus on the current state of medical imaging research, particularly in applications related to rheumatoid arthritis.

S19-2

AI-based functional genetics elucidates the pathogenesis of autoimmune diseases

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Conflict of interest: None

The biology of humans and mice shares many commonalities, and research using mice has significantly advanced the field of immunology. However, the pathogenesis of autoimmune diseases remains insufficiently understood, making it challenging to accurately replicate the pathological immune phenomena occurring in patients within mouse models. While studies using disease model mice are highly valuable for elucidating disease mechanisms, they have inherent limitations. Consequently, increasing emphasis has been placed on human immunology using patient-derived samples in recent years. Risk polymorphisms identified through genome-wide association studies (GWAS) are valuable analytical tools for investigating the causes of human diseases. Advances in functional genetics have facilitated the analysis of these risk polymorphisms, revealing that many contribute to disease onset through abnormalities such as cell-type-specific transcription factor activity, gene expression regulation, and cytokine pathway activity. These findings have progressively clarified the pathogenesis of autoimmune diseases. Currently, most functional evaluations of risk polymorphisms rely on classical statistical approaches. However, recent years have seen numerous attempts to apply AI to this field. This presentation will explore these research efforts and their significance.

S19-3

Transformer-based AI Technology Outlook: Acceleration by NVIDIA, Experience with XR, and Market Environment

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Conflict of interest: Yes

The use of artificial intelligence (AI) is rapidly expanding in the domain. The “Transformer” architecture, proposed in 2017, is attracting attention as a central technology. It is equipped with parallel processing power and an “attention mechanism” that outperforms RNN-type models, and is capable of efficiently and accurately extracting knowledge from complex and diverse data sets. As a result, support for integrated clinical decision making and data-driven medicine have become even clearer. NVIDIA’s GPU technology is indispensable to the computational infrastructure that supports the Transformer, and through optimizations such as the Transformer Engine, NVIDIA has dramatically accelerated model learning and inference processes that require enormous amounts of computation, resulting in a market capitalization of over $1 trillion. The company’s market capitalization has grown to over $1 trillion, putting it on par with FANG (Facebook=Meta, Amazon, Netflix, and Google) in terms of market value. The author himself has worked on the application of XR (Mixed Reality including Augmented Reality and Virtual Reality) technology using NVIDIA’s GPUs in the past, and he feels that the parallel processing performance and hardware optimization provided by NVIDIA were of great benefit in that case as well. NVIDIA’s technological foundation, which has been cultivated in fields that require large-scale data and real-time performance, such as XR, will also play an important role in the field of medical AI. However, there are many issues to be overcome in the use of Transformer, including bias, ethical issues, and interpretability. By addressing these issues, AI should evolve into a safer and more reliable method. This symposium will examine the new prospects that Transformer could bring and the challenges we face in the future, based on NVIDIA’s acceleration of the computational environment and the author’s involvement in the XR field.

S19-4

The reality and expectations of remote medicine using DX in isolated islands and rural areas

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Conflict of interest: None

In remote islands and rural areas with aging populations, medical access is limited due to reduced transportation options and cognitive or physical decline. Specialist shortages further hinder equitable care. Although telemedicine has high demand, barriers like low ICT literacy and concerns about online consultation quality have slowed its adoption. To address these challenges, we implemented models like the Nagasaki University RA Remote Medical System (NURAS) and the Mobile Clinic in Goto City. Additionally, drone delivery of medications following online pharmacy guidance has been trialed to address the lack of insurance pharmacies. 1) NURAS Developed in collaboration with Nagasaki University and partners, NURAS uses Mixed Reality (MR) technology to connect RA patients on remote islands with specialists. Patients scan affected areas with 3D cameras, and specialists review detailed holograms using HoloLens 2. This Doctor to Patient with Doctor (D to P with D) model also provides guidance for local doctors. After 12 months, all six trial patients achieved clinical remission. 2) Mobile Clinic The Mobile Clinic, a vehicle equipped with medical devices and staffed by nurses, visits patients' homes to enable online consultations. This Doctor to Patient with Nurse (D to P with N) model supports chronic disease patients and facilitates better communication during consultations. By October 2024, it had served 68 patients over 438 consultations. This symposium will focus on NURAS and explore expectations and challenges of initiatives like mobile clinics and drone-based medication delivery.

S19-5

The forefront of AI - Utilization and future of AI in the medical field

Shinji Chiba
National Technology Office, Microsoft Japan

Conflict of interest: None

AI has evolved significantly over the past few years and is still continuing to develop. In order to take on-site operations, especially various operations in clinical sites and laboratories, to the next stage and perform digital transformation in the true sense, it is necessary to accurately grasp the trends in technology. In this session, we will mainly touch on the current state of AI proposed by Microsoft and what it will look like in the future.

S20-1

Identification of Novel Age-Associated Helper T (ThA) Cells and Their Role in the Pathogenesis of Autoimmune Disorders

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Conflict of interest: Yes

Aging is one of the risk factors for developing autoimmune diseases. Autoimmune disorders, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), often occur in middle or older ages. However, the precise role of immune senescence in the pathogenesis of autoimmune disorders remains poorly understood. Among immune cell types, T cells are particularly susceptible to the effects of aging due to their differentiation and maturation in the thymus, an organ that atrophies with age. Through the construction of a functional genome database of peripheral immune cells, "ImmuNexUT (Immune Cell Gene Expression Atlas from the University of Tokyo)", we have identified a novel $CD4^+$ T cell subset, termed "Age-associated helper T (ThA)" cells, which increased with age and in autoimmune diseases. Analysis of 354 flow cytometric data and 1562 RNA-seq datasets obtained from healthy controls (HC) and patients with autoimmune diseases, including RA, SLE, and idiopathic inflammatory myopathy (IIM), along with *in vitro* studies, revealed that ThA cells correspond to cytotoxic $CD4^+$ T cells. Moreover, these cells exhibited a unique capacity to assist B cells in producing antibodies in autoimmune diseases. Our study identified the transcription factor ZEB2 as a key regulator of the gene expression of ThA cells, including the expression of *GZMA* and *CXCL13*. Intriguingly, integrated analysis of gene expression and clinical parameters demonstrated that the gene expression variations of ThA cells significantly reflected disease exacerbations in SLE and were associated with autoantibody production. Furthermore, we observed the infiltration of ThA cells in the lungs and muscles affected in IIM, implying their involvement in the organ damage associated with IIM. This talk outlines the characteristics and involvements of ThA cells in the pathogenesis of autoimmune disorders and the possibility of applications for new therapies.

S20-2

Understanding the Pathogenesis of ANCA-Associated Vasculitis through Single-Cell Analysis

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Conflict of interest: Yes

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic autoimmune disease characterized by inflammation of small blood vessels, caused by autoantibodies targeting neutrophil cytoplasmic proteins such as myeloperoxidase and proteinase 3. Clinically, patients display diverse organ-specific symptoms, with glomerulonephritis being a hallmark feature. In our study, peripheral blood mononuclear cells (PBMCs) and neutrophils from newly diagnosed microscopic polyangiitis (MPA) patients were analyzed. A notable increase in activated CD14-positive monocytes and type-I interferon-associated CD14-positive monocytes was identified as a key feature of MPA. Further stratification revealed two distinct patient subgroups within MPA: the MPA-MONO group, characterized by a higher risk of relapse, and the MPA-IFN group, characterized by a favorable response to immunosuppressive therapy. Neutrophils were classified into seven subsets. Two subsets showed significant expansion in MPA patients, including one prominently associated with enhanced ANCA-induced neutrophil extracellular trap (NET) formation. These findings suggest the cellular and molecular mechanisms underlying the clinical variability of AAV and highlight the potential for therapeutic approaches based on single-cell analysis.

S20-3

Translational research on Sjögren's syndrome (SS) focusing on T cell dysregulation

Hiroto Tsuboi, Saori Abe, Hirofumi Toko, Ayako Kitada, Toshiki Sugita, Masaru Shimizu, Ayako Ohyama, Hiromitsu Asashima, Haruka Miki, Yuya Kondo, Isao Matsumoto
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Conflict of interest: None

In SS, salivary glands infiltrating T cells could induce activation and proliferation of B cells, and differentiation into plasmacytes, as well as contribute to apoptosis of glands cells. In this symposium, we will discuss 1) detection and pathogenic roles of autoantigens specific T cells, 2) pathogenic association of $CD8^+$memory T cells and $CD8^+$Treg, and 3) development of novel therapeutic strategy targeted on dysregulated T cells in SS. 1) We detected M3 muscarinic acetylcholine receptor (M3R) reactive Th1 and Th17 in peripheral blood, and M3R reactive Th17 associated with disease activity and anti-M3R antibody in SS. Moreover, we confirmed

that M3R reactive T cells could develop autoimmune sialadenitis in mice. We recently revealed that peripheral Tfh significantly increased in SS compared with healthy control (HC), and peripheral Tfh1 and Tfh2 frequently shared TCR repertoire with LSG infiltrating T cells. The genome-scale platform to identify the epitopes recognized by $CD4^+$T cells has been newly developed, reporting the novel autoantigens in SS. 2) scRNA-Seq of LSG in SS revealed that $CD8^+$T cells exhibit greater clonal expansion compared to $CD4^+$T cells, the presence of $CD69^+CD103^-CD8^+$ $GZMK^+$tissue-resident memory T cells was identified, and this subset showed a significant positive correlation with focus score of LSG. We found that peripheral $CD8^+$Tregs were significantly reduced in SS than in HC. Moreover, we demonstrated that CDK8/19 inhibitor had the potential to convert $CD8^+$memory T cells into $CD8^+$Tregs, and this conversion could contribute to regulation of SS. 3) Iscalimab (anti-CD40 antibody) significantly improved the placebo-adjusted ESSDAI in a dose-dependent manner in one phase II RCT. Dazodalibep (CD40L antagonist) also significantly improved ESSDAI and ESSPRI compared to placebo in one phase II RCT. Furthermore, low-dose IL-2, which induces an increase in Treg, significantly improved ESSDAI and VAS for dryness compared to placebo in one phase II RCT.

S20-4

Pathological analysis using animal models; SLE model mice in COVID-19

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Conflict of interest: Yes

The molecular targeted agents dramatically changed the treatment of several rheumatic diseases, such as rheumatoid arthritis. These agents were developed largely based on the plausible findings from animal disease models. However, such findings were sometimes not replicated in human diseases due to the diversity of immune reactions among the species. Disease models also have advantages in evaluating the effects of scoping genes or developing agents in living organisms under complex immune systems. Namely, animal models are still useful to validate the pathological concepts derived from the well-established omics analysis using human samples. Here, I describe our findings from our SARS-CoV-2 infection experiments using various disease mouse models. COVID-19 is a quite unique infection complicated with a high frequency of cytokine storm and thrombosis in the acute phase and sometimes results in a post-infection condition, Long COVID. We hypothesized early in the pandemic that the pathological mechanisms of COVID-19 complications might resemble those of rheumatic diseases. Therefore, we conducted SARS-CoV-2 infection experiments using several mouse models of SLE, and those of atherosclerosis and obesity, risk factors in COVID-19. Using several SLE models, we demonstrated the pathological mechanism of lung inflammation caused by alveolar epithelial cell death during SARS-CoV-2 infection and the development of multiple organ thrombosis after SARS-CoV-2 infection. In the obese mice, we elucidated that the visceral fat accumulation resulted in the cytokine storm under SARS-CoV-2 infection and that anti-inflammatory treatment could prolong their survival. Additionally, using animal models, we revealed the potential mechanisms of disease progression caused by the genetic risk region identified in the patients with severe COVID-19. Although COVID-19 is still a novel and largely unknown disease for human beings, we have elucidated the pathogenesis through animal model analyses, at least in part. There is no doubt about the usefulness of disease animal models in pathological analysis. However, we need to focus on alternative technologies that could replace animal experiments in the future.

S20-5

Pathogenesis and autoantibody production in systemic autoimmune diesase-associated interstitial lung disease

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Conflict of interest: None

Interstitial lung disease (ILD) is one of the common complication of systemic autoimmune diseases such as rheumatoid arthritis (RA), inflammatory myopathy, and mixed connective tissue diseases (MCTD). ILD associated with autoimmune diseases is characterized by lymphocyte infiltration and sometimes ectopic germinal center formation, however, the details of the immune response in the lung lesions have not been fully understood. Among these, RA-ILD has been relatively well studied, and it has been speculated that lung lesions are involved in the production of autoantibodies, since post-translational modification of proteins by smoking can be an antigen for anti-CCP antibodies, anti-CCP antibodies are detected in bronchoalveolar lavage fluid (BALF), and a common citrullinated antigen is found in the lung and synovial membranes. We have been focusing on the antigen specificity of lymphocytes infiltrating the lesion site, and we analyzed the antigen specificity of B cells in ILD associated with RA, MCTD, Sjogren's syndrome, and inflammatory myopathy. The sequences of antibodies of individual B cells in the BALF of each disease were analyzed, and recombinant monoclonal antibodies were produced in vitro. The reactivity of these antibodies was analyzed. Notably, from 10% to a maximum of 60% of the antibodies produced in the lungs were disease-specific autoantibodies, such as anti-CCP antibodies, anti-RNP antibodies, and anti-ARS antibodies. When the somatic hypermutations of these autoantibodies was converted to germline sequences, many of them showed attenuated reactivity to self-antigens, and some of them recognized diverse epitopes including conformational epitopes, suggesting that these autoantibodies underwent antigen-driven affinity maturation. Therefore, we hypothesize that disease-specific autoantibody production by infiltrating lymphocytes may be common pathophysiology of ILD associated with systemic autoimmune diseases.

S21-1

New Frontiers in Autoinflammation: Dispatch from Bethesda

Dan Kastner
Inflammatory Disease Section, National Human Genome Research Institute, USA

Conflict of interest: None

During the last year our research group has focused on a number of new initiatives. During my talk I will concentrate on three topics. First, I will summarize our work on patients with *STAT4* gain-of-function germline mutations underlying the syndrome of disabling pansclerotic morphea. Second, I will summarize the our work on patients with biallelic loss-of-function mutations in *SHARPIN* as the cause of sharpenia, an inborn error of cell death. And thirdly, I will discuss unpublished work on the role of cofilin-1 as a negative regulator of the NLRP3 inflammasome, and the possible development of cofilin-1 peptides as novel inhibitors of the spectrum of NLRP3-driven inflammation.

S21-2

Recent advancement of inflammasomopathy

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Conflict of interest: Yes

The autoinflammatory syndromes are mainly hereditary and its main pathophysiological condition is inflammation. The concept of "autoinflammation" was first proposed by Dr. Kastner in NIH in 1999, and 20 years have passed since then. At that time, the diseases caused by inflammasome activation, or inflammasomopathy, such as familial Mediterranean fever, cryopyrin-associated periodic syndrome, and mevalonate kinase deficiency were reported. Now, we have more than 50 causative genes for autoinflammatory syndromes, including type I interferonopathy involving the overproduction of type 1 interferon and diseases related to the regulation of NF-κ B signaling. The autoinflammatory syndrome is included in inborn errors of immunity, and the number of the identified new genes in the category of the autoinflammatory syndrome is the most among inborn errors of immunity and is increasing. In recent years, the existence of adult-onset autoinflammatory syndromes such as VEXAS syndrome and late-onset cryopyrin-associated periodic syndrome has been reported, and their importance from the clinical point of view is increasing

for adult rheumatologists as well as pediatric rheumatologist. In this lecture, I will explain the latest topics and the current situation in Japan regarding inflammasomopathy.

S21-3

Type 1 Interferonopathy

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Conflict of interest: None

Interferons (IFNs) are a group of cytokines that play an important role in the host defense against viruses. Although IFNs are important for host defense, excessive production of IFNs is halmful and is involved in autoinflammatory diseases, the so-called type I interferonopathy. The term "type I interferonopathy" was proposed by Dr Yanick Crow in 2011. More than 50 diseases have been categorized as type I interferonopathies. In this symposium, I briefly review the history of type I interferonopathy. In addition, I present our recent data on type I interferonopathy.

S21-4

Sources and effects of excess IL-18 in Auto- and Hyperinflammatory Diseases

Scott Canna
Children's Hospital of Philadelphia and University of Pennsylvania Perelman School of Medicine, USA

Conflict of interest: Yes

Several new discoveries have revived interest in the pathogenic potential and possible clinical roles of IL-18. IL-18 is an IL-1 family cytokine with potent ability to induce IFNgamma production. However, basic investigations and now clinical observations suggest a more complex picture. Unique aspects of IL-18 biology at the levels of transcription, activation, secretion, neutralization, receptor distribution and signalling help to explain its pleiotropic roles in mucosal and systemic inflammation. Blood biomarker studies reveal a cytokine for which profound elevation, associated with detectable 'free IL-18', defines a group of autoinflammatory diseases in which IL-18 dysregulation can be a primary driving feature, the so-called 'IL-18 opathies'. This impressive specificity might accelerate diagnoses and identify patients amenable to therapeutic IL-18 blockade. Pathogenically, human and animal studies identify a preferential activation of CD8 (+) T cells over other IL-18-responsive lymphocytes. IL-18 agonist treatments that leverage the site of production or subversion of endogenous IL-18 inhibition show promise in augmenting immune responses to cancer. Thus, the unique aspects of IL-18 biology are finally beginning to have clinical impact in precision diagnostics, disease monitoring and targeted treatment of inflammatory and malignant diseases.

S21-5

Current Status and Issues of Adult-Onset Still's Disease in Japan

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Conflict of interest: Yes

Adult-onset Still's disease (AOSD) is an idiopathic systemic inflammatory disorder characterized by symptoms such as fever, arthritis, rash, and sore throat. Blood tests typically reveal neutrophil-predominant leukocytosis and liver function abnormalities, while autoantibodies are absent, and hyperferritinemia is a distinguishing feature. Recently, based on recommendations from EULAR/PReS, the potential unification of AOSD and systemic juvenile idiopathic arthritis (sJIA) has come under consideration. These two diseases are suggested to share common pathophysiological mechanisms, evidenced by elevated levels of inflammasome-related molecules such as serum IL-18 and gasdermin D, as well as high levels of M2 macrophage markers, including CD163 and heme oxygenase-1 (HO-1). In addition to these serum profile similarities, both diseases display weak genetic predisposition. Meanwhile, emerging attention has been directed toward acquired autoinflammatory disorders that mimics AOSD clinically and serologically that are caused by genetic mutations. Notably, newly identified conditions such as aquired NLRC4-associated disorders and VEXAS syndrome play critical roles in the differential diagnosis and understanding of AOSD pathogenesis. Given that these disorders can present with clinical manifestations similar to AOSD, genetic testing may become essential for definitive diagnosis in similar conditions. In this presentation, I will provide an overview of the latest insights on the diagnosis, pathogenesis, and treatment of AOSD in Japan, discussing both similarities and differences with sJIA. Additionally, I will address the challenges of transition care for patients entering adulthood, aiming to foster discussions on establishing improved healthcare systems.

Educational Lecture

EL1

Year in review, clinical

Yoshiya Tanaka
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Conflict of interest: Yes

Systemic autoimmune rheumatic diseases (SARDs) have been considered intractable and refractory to treatments, but the elucidation of cell surface antigens, cytokines, receptors, and signaling molecules that play a central role in the pathological process, and the identification of disease susceptibility genes through genome-wide association studies, have clarified which molecules to target for therapy. In addition, molecular-targeted therapies are moving away from glucocorticoid-based therapies, which have multiple side effects and are nonspecific, to highly selective immunosuppressive drugs and molecular-targeted therapies, which are becoming the mainstream. Based on the background, guidelines and treatment recommendations are rapidly being revised for many diseases, including rheumatoid arthritis and systemic lupus erythematosus. On the other hand, new developments are being brought to address many unmet needs that remain in systemic autoimmune rheumatic diseases, including long-term safety, economic burdens, coronary disruption, difficult-to-treat patients, response to organ damage, drug withdrawal after remission, and differential use of different therapeutic agents. Furthermore, CAR-T therapy and T-cell engager (TCE) therapy for systemic lupus erythematosus and other diseases are expected to have the potential to induce immune system restructuring and even cure the disease.

EL2

Year in review (Basic)

Keishi Fujio
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Conflict of interest: Yes

Rheumatic diseases, including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), are characterized by organ damage driven by excessive immune cell responses. Recent advancements in biological agents and molecular-targeted therapies have significantly improved the management of rheumatic diseases. However, these therapeutic developments have also highlighted the heterogeneity of patient populations, such as variability in treatment responsiveness. To further enhance treatment outcomes, it is crucial to stratify patient populations, select optimal therapies based on this stratification, and pursue novel drug development strategies. The recent progress in technologies such as flow cytometry, mass cytometry, single-cell RNA sequencing, and spatial molecular analysis has accelerated the understanding of disease pathogenesis, which underpins these approaches. A key factor driving this deeper understanding is the identification of novel cell populations in inflamed tissues. For example, the discovery of peripheral helper T (TPH) cells in 2017 significantly advanced the understanding of the pathogenesis of rheumatic diseases such as RA, SLE, and IgG4-related diseases. In 2024, several new cell populations in RA synovium have been reported. DKK3+CD200+ fibroblasts, for instance, are found not only in the synovium but also at entheses, where they suppress inflammation and increase following molecular-targeted therapies. DC3, a dendritic cell population, is enriched in active RA synovium, is in close proximity to TPH cells, and is associated with disease flares. Additionally, GZMK+CD8+ T cells are elevated in RA synovium, where they activate the complement pathway by cleaving C2 and C4 via GZMK. In SLE, ThA cells, which increase with age, possess both cytotoxic activity and B cell helper functions. These cells are associated with disease activity and are reported to be targets of calcineurin inhibitors. The differentiation mechanisms of atypical B cells (ABC), which are critical for autoantibody production, are also being elucidated. The identification of such novel cell populations functions as a guide to understanding pathogenesis, unveiling previously unknown immune networks. The elucidation of these networks has started to reveal multidimensional links between the immune system and disease prognosis. In this lecture, I aim to introduce foundational findings published in the past year that contribute to our understanding of rheumatic disease pathogenesis.

EL3

Frontiers in knee osteoarthritis treatment

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Conflict of interest: None

The number of patients with knee osteoarthritis has been increasing in recent years. It is estimated that there are approximately 25 million radiological degenerative changes in Japan, with approximately 8 million being painful. Knee joint disorders, as weight-bearing joints of the lower limb, are one of the major obstacles to extending healthy life expectancy. Accurate diagnosis is the first and most important step in treatment, and conservative therapy is the rule. Surgical treatment is chosen when the knee is refractory to conservative treatment, when the pathology is accurately understood and when surgical treatment can be expected to be effective. Peripheral nerve radiofrequency ablation has recently been covered by insurance as an intermediate treatment between conservative and surgical treatment. It targets knee OA patients who are refractory to conventional conservative treatment and do not wish to undergo surgical treatment, and uses radiofrequency ablation to target the three knee nerves. It targets the superior medial, superior lateral and inferior medial knee nerves under local anesthesia using joint echo. It can be performed on a daily basis in 30 minutes. It is advisable to fully explain that this is not a treatment that completely eliminates basic knee pain, and to confirm the effectiveness of the nerve block prior to the procedure. In addition, an increasing number of patients are requesting regenerative medicine. Currently, regenerative medicine for knee OA can be broadly classified into platelet rich plasma (PRP) therapy and adipose-derived stem cell transplantation. The target range is wide from early to end-stage OA, but it is difficult to regenerate the articular cartilage of the weight-bearing area in end-stage OA, and the mechanism of action is still unclear in many respects. At present, it is thought to be effective against knee pain through its anti-inflammatory action. Surgical treatment has been also advancing, with tibial high osteotomy having been performed using two-dimensional surgical planning based on simple frontal X-ray images, but attempts are now being made to perform accurate surgery based on three-dimensional preoperative planning using CT images and to stabilize the degenerated and dislocated medial meniscus at the same time. In arthroplasty, based on three-dimensional surgical planning, intraoperative navigation and robotic technology are being used to enable more accurate surgery tailored to individual knee joints and to provide a higher level of knee joint function.

EL4

Perspectives and Challenges of Telemedicine in Rheumatic Diseases: Insights from 'Recommendations for Establishing Online Medical Care for RA, JIA with Oligoarthritis or Polyarthritis, and SLE'

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Conflict of interest: None

Approximately half of rheumatoid arthritis (RA) patients are elderly and have low consultation rates at specialized medical institutions. Meanwhile, the declining number of pediatricians due to a decreasing birthrate limits access to specialized care for juvenile idiopathic arthritis (JIA). Ongoing reforms in physicians' work styles highlight the demand for efficient healthcare delivery systems, raising expectations for telemedicine, including online consultations. In Nagasaki Prefecture, where specialists are scarce and remote islands are numerous, Nagasaki University has developed "NURAS", a mixed reality-based telemedicine system, and begun pilot testing with RA patients. In March 2024, the Japanese Medical Science Federation issued recommendations advocating a hybrid model combining online consultations with in-person visits at least once every six months for RA and systemic lupus erythematosus (SLE), provided disease activity is stable. A research group funded by the Ministry of Health, Labour and Welfare expanded on these recommendations, incorporating Points to Consider proposed by the European League Against Rheumatism

(EULAR). Our study targeted RA, JIA oligoarthritis/polyarthritis, and SLE, conducting surveys with rheumatology societies and patient groups to identify telemedicine needs and challenges. The findings addressed patient and provider concerns by specialty (e.g., internal medicine, orthopedics, pediatrics) and context (e.g., home care, rural healthcare). The recommendations emphasized economic considerations, such as medical fee adjustments and barriers to telemedicine implementation. Collaboration with the Japanese Telemedicine and Telecare Association and international case studies enriched the proposal. Based on these insights, this presentation explores the prospects and challenges of telemedicine for rheumatic diseases.

EL5

Abnormal Bone Metabolism and Its Management in Rheumatic Diseases: Essential Knowledge for Rheumatologists

Kosuke Ebina[1,2], Yuki Etani[2], Takaaki Noguchi[1], Seiji Okada[1]
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Conflict of interest: Yes

In patients with rheumatic diseases such as rheumatoid arthritis (RA), increased bone resorption and suppressed bone formation, driven by inflammatory cytokines from the early stages of disease, along with systemic bone loss, have been reported to correlate with both elevated fracture risk and progression of joint destruction. Inflammatory cytokines such as interleukin-17 (IL-17), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6), produced by inflammatory cells in the joint lesions, stimulate mesenchymal cells like synovial fibroblasts to express receptor activator of nuclear factor κB ligand (RANKL), a key inducer of osteoclastogenesis. This leads not only to systemic bone loss but also to localized bone erosion around the joints. Furthermore, anti-citrullinated peptide antibodies (ACPA), an autoantibody specific to RA, have been found to enhance osteoclast differentiation. Factors such as menopause and immobilization due to joint destruction also promote RANKL expression by osteocytes and osteoblasts. On the other hand, TNF-α and glucocorticoids inhibit Wnt signaling, which is crucial for bone formation. Consequently, RA patients often exhibit a weakened, porous bone microarchitecture characterized by increased cortical bone resorption from the inner cortex due to osteoclast induction related to menopause and inflammation, along with reduced periosteal apposition from glucocorticoid and inflammation effects. To prevent the progression of bone and joint destruction associated with systemic and periarticular bone loss, it is essential to control inflammation and prevent joint destruction from the early stages, maintain physical function, avoid glucocorticoids whenever possible, and select medications based on the patient's bone metabolism status. In this presentation, I will review the mechanisms underlying bone and joint destruction and osteoporosis progression in RA, as well as discuss management strategies, including new therapeutic agents.

EL7-1

Overview of the clinical practice guideline for juvenile idiopathic arthritis

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Conflict of interest: Yes

The 2024 edition of the "Juvenile Idiopathic Arthritis (JIA) Clinical Practice Guideline" was compiled by the Japan Rheumatology Society Juvenile Idiopathic Arthritis Clinical Practice Guidelines Subcommittee. It is the first JIA guideline in Japan to cover both systemic and articular types. Until now, pediatric rare diseases have generally lacked clinical research papers that serve as evidence, and have often been composed of expert opinions, but JIA has not been able to go beyond the realm of a "guide". However, this time, we asked the systematic review (SR) staff to thoroughly collect current papers, and the general committee will review them and present the evidence level and recommendation statement. The target disease types of this guideline are systemic, oligoarthritis, and polyarthritis, the target age is all ages, and the clinical questions (CQs) are mainly set to treatment. The members who created the guideline were pediatric rheumatologists, internal medicine rheumatologists, ophthalmologists, patients/families, and guideline creation instructors, and the items of particular interest were macrophage activation syndrome (MAS) and uveitis, which are common complications of JIA. The first half of the guideline is a narrative part that summarizes the classification, diagnosis, and management of JIA, which also serves as a revision of the "Juvenile Idiopathic Arthritis Initial Care Guide 2015", and the second half is an SR part that provides detailed information on a total of 23 CQs, including 8 systemic types, 4 MAS, 6 articular types, and 5 uveitis, for which SR was conducted as much as possible. In this lecture, we will provide an overview of this guideline, dividing it into a narrative part and an SR part. It is our sincere hope that these guidelines will be useful in a variety of ways not only to pediatric rheumatologists, but also to adult rheumatologists, ophthalmologists, medical staff, and patients and their families. Finally, we would like to express our deepest gratitude to all those who participated in the creation of these guidelines and to everyone who provided their cooperation.

EL7-2

Development of clinical guideline for the management of pediatric onset systemic lupus erythematosus in Japan

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Conflict of interest: Yes

Pediatric onset systemic lupus erythematosus (SLE) accounts for 15-17% of all cases. Clinical course of pediatric onset systemic lupus erythematosus (SLE) is more severe compared to that of adult onset SLE, including the frequency and severity of lupus nephritis. For treatment, steroid pulse therapy and mycophenolate mofetil are used frequently, and as for biologics, only belimumab (div) is currently covered by insurance for children aged 5 years and older in Japan. Most children with childhood-onset SLE are necessary to continue treatment even after they reach adulthood. However, the clinical features and treatment plans are different between children and adults. In order to successfully transition from childhood to adulthood, it is necessary to understand the differences and similarities between pediatric-onset and adult-onset SLE. Regarding the development of treatment guidelines, a clinical guide for the management of pediatric SLE was published in 2018 based on the results of a nationwide survey and the consensus of specialists. In conjunction with the revision of this clinical guide, the production works of first treatment guidelines for pediatric SLE in Japan has begun in collaboration with the Japan Rheumatology Association, Japan Pediatric Rheumatology Society, Japanese Society of Pediatric Nephrology, Japanese Society of Pediatric Dermatology, Japanese Society of Pediatric Neurology, Japanese Society of Pediatric Ophthalmology, and Japanese Society of Pediatric Hematology. In this lecture, I will present the clinical features and treatment status of childhood-onset SLE based on Japan's national database, comparing it with SLE onset in the AYA generation, and present the latest treatment strategies based on evidences obtained through the production of the guideline.

EL8

Immune-Related Adverse Events: The Role of the Rheumatologist

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Conflict of interest: None

In recent years, the indications of immune checkpoint inhibitors (ICIs) have expanded, with increasing combination therapies using anti-PD-1 and anti-CTLA-4 antibodies. As a result, the incidence of immune-related adverse events (irAEs) has also risen, particularly rheumatic irAEs. Oncology departments frequently consult rheumatologists regarding the diagnosis and management of these events, as well as ICI eligibility for patients with a history of autoimmune diseases. ICI-induced arthritis (ICI-IA) is one of the most common organ-specific irAEs. Although its manage-

ment strategy is becoming clearer, challenges remain. Some patients develop joint destruction within months of ICI initiation, making it difficult to distinguish ICI-IA from subclinical rheumatoid arthritis (RA). Glucocorticoids (GC) are the first-line treatment for ICI-IA, but concerns exist about GC's potential to reduce ICI efficacy. The differences between ICI-IA and ICI-induced polymyalgia rheumatica (ICI-PMR), in terms of pathology and treatment, are still not well-defined. Inflammatory myopathies are another important consideration among rheumatic irAEs. These conditions can affect not only skeletal muscle but also the myocardium, sometimes presenting with myasthenia gravis-like symptoms, which differ from typical dermatomyositis. In 2023, tocilizumab was approved for the treatment of cytokine release syndrome (CRS) associated with cancer treatments, that highlights the growing role of rheumatologists in managing ICI-related complications. On the other hand, lupus-like symptoms in patients receiving ICI treatment, or issues in existing systemic lupus erythematosus (SLE) patients, are rarely encountered in clinical practice. The impact of immune checkpoint blockade on autoimmune diseases likely varies by each disease entitiy. This lecture will discuss the rheumatologist's role in managing irAEs, focusing on ICI administration in patients with pre-existing autoimmune diseases and the development of new autoimmune conditions following ICI therapy.

EL9

Management strategies for pregnancy in patients with rheumatic diseases

Yu Funakubo Asanuma
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Conflict of interest: Yes

Among rheumatic diseases, systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are particularly common in women of childbearing age. In Japan, the average age of marriage and childbirth has been increasing. However, fertility generally declines with age, and the risks of miscarriage and fetal abnormalities rise. Additionally, the prevalence of lifestyle-related diseases and uterine disorders increases, further elevating the risks associated with pregnancy and delivery. It is anticipated that more women will plan pregnancies after being diagnosed with connective tissue diseases in the future, making it essential to balance the treatment of the underlying disease with assisted reproductive technology. When considering pregnancy and childbirth in women with rheumatic diseases, it is crucial to plan pregnancies carefully while taking into account not only the maternal disease status and organ involvement but also the potential effects of treatment medications on the fetus. Furthermore, close collaboration among rheumatologists, obstetricians, and other healthcare professionals is vital for managing pregnancies. This lecture will focus on pregnancy management in cases frequently encountered by rheumatologists, including RA, SLE, antiphospholipid antibody positivity, and anti-SS-A/anti-SS-B antibody positivity. Topics will include the impact of rheumatic diseases on fertility and pregnancy progression, the effects of pregnancy on disease activity, conditions required for pregnancy, necessary diagnostic evaluations, and permissible drug therapies during pregnancy and lactation. This presentation aims to provide an opportunity to explore treatment and management strategies for pregnancy and childbirth in patients with rheumatic diseases.

EL10

New findings from the revised guidelines for the treatment of autoinflammatory diseases

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Conflict of interest: Yes

Although autoinflammatory diseases are rare, a definitive diagnosis can be made through genetic testing, which makes it possible to provide disease-specific treatment and more appropriate treatment for patients. On the other hand, due to their rarity, even doctors specializing in rheumatic diseases have limited experience with these diseases. In addition, there are diseases for which the molecular mechanism is not fully understood without standard treatment. From 2014, "Research on the establishment of clinical guidelines for autoinflammatory diseases" group funded by the Ministry of Health, Labor and Welfare (MHLW), with the cooperation of the Pediatric Rheumatology Association of Japan (PRAJ), the "Clinical Practice Guidelines for the Management of Autoinflammatory Diseases 2017" were published for Familial Mediterranean Fever, Cryopyrin-Associated Periodic Syndrome, TRAPS, Mevalonate Kinase Deficiency, Blau Syndrome, and PFAPA. Subsequently, in 2017, a system for genetic testing as part of health insurance was established on the Kazusa Genetic Testing Laboratory, and the Japanese Society for Immunodeficiency and Autoinflammatory Diseases was established. These changes have led to significant progress in the medical environment surrounding autoinflammatory diseases. On the other hand, there were expectations for more clarification of diagnostic criteria, such as the creation of treatment guidelines for diseases not covered by guidelines and for which standard treatments have not yet been established, and the interpretation of MEFV gene tests for familial Mediterranean fever. With the above background, the "Research on the development of a nationwide medical system for autoinflammatory diseases and related diseases, the establishment of a transition medical system, and the establishment of clinical practice guidelines" group funded by MHLW, started the revision of the guideline in 2020. In this revision, FMF and PFAPA were added to the list of diseases covered by the previous version, and new guidelines were created for A20 haploinsufficiency, Nakajo-Nishimura syndrome, and PAPA syndrome with the cooperation of the Japanese College of Rheumatology, PRAJ, and the Japanese Society for Immunodeficiency and Autoinflammatory Diseases. In this lecture, I will explain the new findings resulting from the revision. I hope that this guideline will help more people become aware of autoinflammatory diseases, improve the quality of autoinflammatory disease treatment, create new evidence, and contribute to improving patient QOL through shared decision making.

EL11

The Utility of Imaging in the Management of Inflammatory Arthritis

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Conflict of interest: Yes

Imaging diagnosis, mainly X-ray, ultrasound, and MRI, plays an essential role in the diagnosis and management of inflammatory arthritis, including rheumatoid arthritis (RA), spondyloarthritis (SpA), crystal-induced arthritis, infectious arthritis, and polymyalgia rheumatica. Each imaging technique has its own characteristics, with different sensitivity and specificity for detecting abnormal findings. Sensitivity and specificity are in a trade-off relationship, and the point to be emphasized depends on the purpose of the diagnosis. Findings with high specificity are important for definitive diagnosis, while those with high sensitivity and ease of evaluation are required for therapeutic monitoring. For example, in RA, bone erosion on X-ray and bone marrow edema on MRI are specific findings, and synovitis on ultrasound is a sensitive indicator. In addition, crystal deposits at cartilage sites detected by ultrasound have relatively high specificity and are useful for differentiating crystal-induced arthritis. Furthermore, consideration of not only the type of abnormal findings but also their severity and location contributes to the accuracy of diagnosis. In addition, pathological findings detected on imaging are closely related to disease-specific pathology and can help in understanding the pathogenesis and inferring the mode of disease progression. For example, findings of synovitis and adherence inflammation reflect the pathology of RA and SpA spectrums, respectively, and may be applied to treatment selection by considering the associated cells and cytokines. This lecture aims to explain how to effectively utilize the characteristics of various imaging modalities and to deepen understanding of the pathophysiology of each disease, leading to better management.

EL12

An Overview of JAK Inhibitors in Immune-Mediated Inflammatory Diseases

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Conflict of interest: Yes

JAK inhibitors have been on the market for more than a decade. Initially approved for myeloproliferative disorders and rheumatoid arthritis, indications have expanded to include inflammatory, allergic, and dermatologic diseases. Among biologics, TNF inhibitors are now approved for a wide range of inflammatory diseases, and the expansion of indications for JAK inhibitors is even more significant. Part of the reason for the expansion of indications for JAK inhibitors is their mechanism of action: JAK inhibitors work by inhibiting JAK downstream of cytokine receptors, and there are more than 50 cytokines that use JAK as a signaling pathway. These cytokines include EPO and IL-3 involved in hematopoiesis, IL-2 and IL-7 involved in lymphocyte survival and function, IL-6 and IFN involved in inflammation and immune response, IL-12 and IL-23 important for T cell differentiation, and IL-4 and IL-5 involved in allergy. The JAK pathway is essential for key immune responses and has therefore been shown to be effective against various diseases. In view of the fact that several biologics have been approved for various immune-mediated diseases, this lecture will discuss the role of cytokines in the pathogenesis of various diseases based on clinical evidence. Clinical issues related to JAK selectivity and side effects will also be discussed.

EL13

Pathophysiology, precise Diagnosis, and Treatment strategy for arthralgia and arthritis, guided by musculoskeltal ultrasound

Yasuhiro Tani
Orthopedics and Rheumatology, Nagato General Hospital

Conflict of interest: None

Recenly, Treatments of arthritis, espesially rheumatoid arthritis, have dramatically develoved. At the same time, imaging diagnosis of arhtralgia and arthritis have so dramatically developed. X-ray, CT, and MRI are gold standard before, but, recently efficiency of musculoskeltal ultrasound (MSUS) have reported on papers because of technology advancement of MSUS. The purpose of MSUS for arthralgia and arthritis are, 1 Diagnosis 2 Estimete for diesease actibity 3 Judgement of treatment response. Diagnosis: we can check the synovitis, tenosynovitis, enthesitis, bone erosion, and, skin edema, etc. Estimate for diesease ativity: we can check the Gray Scale (GS) for volume of synovitis, Power Dopplar (PD) for risk of bone erosion. Judgement of treat response: we can eisily compare with before treatment and after. As a result, we can strictly control for rheumatoid arthritis. Moreover, it is essential for us to use the MSUS for pain approach, for example, intervention asisted by ultrasound. That technique lead the pain releif because of accuracy. And we can shered condiotion of the joint and around joint, soft tissue with patients. So, MSUS is good comunication tool. Addiotionally, I think that visualizetion of physical condition will change the patient's emotion and motivation for theraphy. On the day of the lecture, we will share the efficient for arthritis and attraction of MSUS, and I hope that many audience will be facsineted by the MSUS after the lecture.

EL14

Best use of MTX - Based on the guidance for MTX use and RA management

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Conflict of interest: Yes

The American College of Rheumatology and the European Alliance of Associations for Rheumatology recommend that patients with rheumatoid arthritis (RA) should be started on conventional synthetic antirheumatic drugs (csDMARDs) as monotherapy. Methotrexate (MTX) is usually the first-line drug among csDMARDs because the choice of treatment should be based on an optimal balance of efficacy, safety, and cost burden, and it may be also used as a second-line drug in consideration of the risk-benefit balance for each individual patient in current super-aged society of Japan. Concomitant use of folic acid is now recommended for all patients starting MTX, regardless of the starting dose of MTX. This is in line with the international standard, as the advantages of non-use of folic acid are minimal and clearly outweighed by the disadvantages, now that MTX can be administered in sufficient doses. In Japan, a subcutaneous injection formulation of MTX was also approved in September 2022, and is expected to reduce gastrointestinal symptoms and liver dysfunction at the same dose compared to oral administration. However, the frequency of serious and potentially fatal adverse events, such as hematologic and lymphatic disorders and respiratory involvement, is not expected to decrease by subcutaneous MTX, and therefore, great care must be taken in the choice of patients and MTX doses for them. In this presentation, we will discuss the best use of MTX together, including how to increase the dose of MTX, including single and divided doses, and how to manage non-serious adverse events such as liver dysfunction, as well as serious events including severe infections, acute and diffuse lung injury, pancytopenia, and lymphoproliferative disorders.

EL15

Immunological Function and Infection Control in Patients with Rheumatic Diseases - Focusing on Vaccination

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Conflict of interest: None

Patients with rheumatic diseases are at higher risk of infections due to compromised immunity from disease activity and treatments. Glucocorticoids, immunosuppressants, biologics, and JAK inhibitors weaken immune function, increasing susceptibility to infections. Vaccination is a critical strategy to reduce these risks and improve both survival and quality of life. Influenza, pneumococcal infections, shingles, and COVID-19 are particularly severe in these patients, and vaccination against these diseases is strongly recommended globally. Live attenuated vaccines can cause vaccine-derived infections in immunosuppressed patients. As such, they are generally administered before starting immunosuppressive therapy and avoided during treatment. In contrast, inactivated and RNA vaccines are safer during immunosuppressive therapy. Examples include vaccines for influenza, pneumococcal infections, shingles, and COVID-19. However, their effectiveness may be reduced in heavily immunosuppressed individuals. Vaccination timing should be carefully planned, ideally, before immunosuppressive therapy begins. If urgent treatment is required or the disease is highly active, vaccination may need to be postponed. Clear communication between patients and physicians is essential for appropriate decision-making. Other measures to control infections include screening for tuberculosis and hepatitis B, prophylaxis for Pneumocystis pneumonia, and monitoring for cytomegalovirus. Patients should also receive education on basic infection prevention measures, and household members should be encouraged to get vaccinated to further reduce infection risks. Infection control is as vital as managing disease activity in rheumatic diseases. Infections complicate treatment and increase mortality risks. This lecture overviews the importance of comprehensive infection prevention strategies, with vaccination as a cornerstone in improving patient outcomes.

EL16

Current Status and Issues of VEXAS Syndrome in Japan

Yohei Kirino
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Conflict of interest: Yes

Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic (VEXAS) syndrome (VS) is a new disease concept proposed in 2020, characterized by older men, chondritis, skin rash, pulmonary infiltrates and macrocytic anemia. The cause has been shown to be an acquired loss-of-function mutation of the E1 ubiquitin-like modifier activating enzyme 1 (UBA1) gene in hematopoietic progenitor cells, and most VS patients have a loss of function mutation in exon 3 methionine 41 (Met41). Mutations at other sites have been reported, but are rare. Although the mechanism of inflam-

mation has not yet been fully elucidated, it is assumed that extracellular release of DAMPS due to enhanced cell death may contribute to the pathogenesis. The diagnosis criteria are currently under review by the Japan Ministry of Health, Labour and Welfare's Autoinflammatory Diseases Study Group. The consensus guidelines of the International Working Group on VS will be released soon. Despite these social improvements, real-world data on VS is still lacking. A nationwide prospective registry study of VEXAS syndrome is currently underway and recently published short-term 3-month results. The study developed and tracked VEXASCAF, a scoring of symptoms related to VS over the past month. Results showed a significant decrease in VEXASCAF after enrollment, but no change in glucocorticoid dosage. Only 7.4% of patients achieved the remission criteria proposed by the French registry study (FRENVEX) after only 3 months, indicating the limitations of the current treatment strategy for VS. In addition, 36.6% of patients had a incidence of adverse events such as malignancy, infection, and thrombosis; challenges in VS include the development of diagnostic criteria, optimization of genetic testing, development of disease activity indicators, and development of therapeutic agents. In this presentation, I would like to discuss the diagnosis and treatment of VS in light of the latest findings.

EL17

When and what type of surgery should be indicated?~modern rheumaorthopaedic surgery in total management~

Keiichiro Nishida
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Conflict of interest: None

Surgical treatment for rheumatoid arthritis (RA) is one of the four pillars of the total management strategy, together with drug therapy, patient education, and rehabilitation, and is positioned to compensate for the limitations of the other three pillars through pain relief and functional improvement. Many patients still require surgical treatment, including some with difficult-to-treat RA with multidrug-resistant RA. Joint destruction may also progress before disease activity is controlled by effective drugs, in cases with complications or side effects for DMARDs, who were not treated by effective medications early in the course of the disease, and whose financial circumstances preclude using expensive medicines. Small joints of the hands and feet are frequently affected in RA, and joint fusion and arthroplasty have traditionally been indicated for pain relief and functional impairments. Still, corrective osteotomy of the feet as a joint-sparing procedure has become more common during these two decades. Although the frequency of the reconstruction for tendon rupture and decompression for entrapment neuropathy is decreasing, surgical techniques for these conditions are still needed to master for rheumaorthopaedic surgeons. In addition, advances in medical technology and implant design have expanded the indications for shoulder and ankle joint arthroplasty, which were not performed very often in the past, contributing to improved patient quality of life. The accuracy of joint replacement surgery has also improved due to advances in navigation systems, preoperative 3D simulation, and robot-assisted surgery. Furthermore, with the aging of patients, the need for surgery for periprosthetic joint fractures and degenerative spine disease is also increasing. In this lecture for young rheumatologists, I will introduce the recent progress of rheumaorthopaedic surgery and explain its indications and importance.

EL18

Insights into the Diversity of Rheumatic Diseases through Single-Cell Analysis

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Conflict of interest: Yes

The human body is composed of nearly 30 trillion cells. Although some cell populations appear uniform, the genes expressed by individual cells can differ significantly. Single-cell RNA sequencing (scRNA-seq) has emerged as a tool to explore this gene expression variability at the single-cell level. Initially this technique applied in 2009 to analyze the transcriptomes of a single blastocyst and oocyte, there have been remarkable technical advancements over the past decade. Since the late 2010s, its application to patient samples has advanced our understanding of disease mechanisms through detailed single-cell analyses. Autoimmune rheumatic diseases arise from inappropriate immune activation, often resulting in a broad spectrum of multi-organ symptoms. These diverse clinical presentations complicate diagnosis and treatment. Single-cell analysis offers a promising approach to identify unique immune abnormalities responsible for these symptoms in individual cases. Here, I would like to summarize the latest findings from single-cell analyses of clinical samples in rheumatic diseases and highlight their implications for tailored strategies based on specific disease mechanisms.

EL19

Interstitial Lung Disease in Connective Tissue Diseases: Prognosis and Treatment

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Conflict of interest: Yes

Interstitial lung disease associated with connective tissue diseases (CTD-ILD) carries a poor prognosis, with pathogenesis and therapeutic strategies varying significantly among underlying diseases. ILD patterns influence treatment approaches across different CTDs. This lecture will first examine the significance of ILD patterns in CTD-ILD, particularly focusing on the usual interstitial pneumonia (UIP) pattern on high-resolution CT (HRCT) as a poor prognostic indicator. We will discuss management strategies for different ILD patterns and key radiological findings for differentiating between UIP, nonspecific interstitial pneumonia (NSIP), and organizing pneumonia (OP) patterns. We will analyze four major CTDs - rheumatoid arthritis (RA), systemic sclerosis (SSc), inflammatory myositis, and vasculitis - emphasizing their distinct characteristics. Key topics include disease activity control and UIP significance in RA, the role of inflammation and fibrosis in SSc, and autoantibody-based treatment strategies in myositis-associated ILD. Treatment discussions will focus on current international guidelines, covering both traditional immunosuppressive approaches and the emerging role of antifibrotic agents, particularly in SSc-ILD and RA-ILD. We will review monitoring methods, including respiratory symptoms, pulmonary function tests, and imaging studies, along with therapeutic outcome measures based on recent consensus. This presentation aims to enhance understanding of CTD-ILD's disease-specific characteristics while providing evidence-based strategies for clinical practice.

EL20

Practical use of autoantibodies in management of systemic autoimmune rheumatic diseases

Masataka Kuwana
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Conflict of interest: Yes

A variety of circulating autoantibodies are detected in patients with systemic autoimmune rheumatic diseases, and are widely used as convenient biomarkers for diagnosis, disease subclassification, and evaluation of disease activity. Since the discovery of LE cells by Hagraves in 1948, clinically meaningful autoantibodies have been reported one after another. Through identification of their corresponding antigens and the development of convenient assay systems, additional clinical significance has been reported by studies involving a large number of patients across regions and races. Autoantibodies that are detected with high specificity for specific diseases are adopted as items in the disease classification criteria. These autoantibodies are also useful for early diagnosis because they can be detected in patients' sera before the onset of disease. In addition, since these autoantibodies are associated with specific clinical subtypes, they can be used to predict the development, progression, and prognosis of various organ involvements, making them useful in the practice of precision medicine. However, it is important not to rely solely on autoantibody results when deciding on management plans, but to make a comprehensive judgment that includes medical history taking, physical examination, and physiologic and imaging test findings. In addition, false-positive and false-negative results can occur in assays used in our clinical practice. In

particular, unapproved assay systems that have not been verified by comparison with the gold-standard methods should not be used for medical purposes, as they may lead to incorrect clinical judgments. In this lecture, I will cover best ways to use autoantibodies in daily medical practice.

EL21

Night Tales from Clinical Immunology: A Rheumatologist's Perspective

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Conflict of interest: Yes

Recent advances in genetic analysis technology have enabled scientists to extract DNA from ancient human remains and understand the impact of natural selection on human evolution. This field, known as paleogenomics, has provided valuable insights into our genetic history and its implications for modern human health. For example, it is now well-established that present-day humans carry 1-2% of Neanderthal genes, which have been found to influence various aspects of human health, including the severity of COVID-19. Genes associated with autoimmune diseases have been strongly influenced by natural selection, particularly through exposure to infectious diseases. For instance, some of the SLE susceptible genes, such as Fcγ receptor 2b polymorphisms and BAFF promoter gene variants, have been positively selected for malaria resistance. Additionally, ERAP2 gene polymorphisms involved in spondyloarthritis or MEFV gene polymorphisms related to Mediterranean fever have been naturally selected due to resistance against the plague (Black Death) that struck Europe in the 14th century. By analyzing genetic information from human remains, researchers can now connect genetic changes to historical events such as famines and infectious disease outbreaks across various regions. This interdisciplinary approach combines insights from genetics, archaeology, and history to weave a new narrative of human evolution and adaptation. Rheumatologists, with their expertise in both basic immunology and human diseases, are uniquely positioned to contribute to this field of study. In this seminar, we will explore the origins of autoimmune diseases by examining the stories revealed through genetic natural selection, which we might call the "Night Tales from Clinical Immunology". Our journey will take us back 400 million years to the "acquisition of jaws" in vertebrates, a pivotal moment in evolutionary history.

EL22

Castleman disease and TAFRO syndrome

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Conflict of interest: None

Castleman disease (CD), first described in 1956, includes a range of conditions. Unicentric CD (UCD) with hyaline vascular histology is distinct because it lacks hyper-cytokine syndrome and is curable by surgical resection. In contrast, multicentric CD (MCD) is characterized by interleukin-6 (IL-6) overexpression, hyper-IL-6 syndrome, and polyclonal lymphadenopathy. MCD includes human herpesvirus-8 (HHV-8) related cases, idiopathic MCD (HHV-8 negative) cases, and conditions mimicking MCD associated with other diseases. CD remains incompletely understood due to its rarity and challenges in clinical and pathological diagnosis. TAFRO syndrome, reported in Japan in 2010, is characterized by thrombocytopenia, anasarca (edema, pleural effusion and ascites), fever, reticulin myelofibrosis (or renal insufficiency), and organomegaly (hepatosplenomegaly and lymphadenopathy). Because lymph node histology in TAFRO syndrome resembles that of CD, TAFRO syndrome is described as related to MCD. Clinically, however, these conditions differ markedly. While elevated interleukin-6 (IL-6) expression is a feature of MCD, it is not disease specific, rendering it unsuitable for differential diagnosis. Advancing the understanding of these disorders requires identifying novel disease-specific biomarkers. This review outlines the characteristics of CD and TAFRO syndrome.

EL23

Preclinical rheumatoid arthritis and its therapeutic interventions

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Conflict of interest: None

Rheumatoid arthritis (RA) is an inflammatory disease causing synovitis and bone destruction, primarily affecting synovial joints. It is marked by disease-specific autoantibodies such as anti-CCP antibodies and RFs, which can be detected before RA onset, highlighting the importance of the preclinical stage. This stage includes an asymptomatic period, a joint pain phase without arthritis, and "undifferentiated arthritis", where arthritis is present but does not meet RA classification criteria. RA is a multifactorial autoimmune disease influenced by genetic and environmental factors. The HLA-DRB1 gene polymorphism is the major genetic factor, but other susceptibility genes have been identified through genome-wide association studies. Environmental factors include the microbiome, smoking, and air pollutants, with mucosal tissues like the lungs, oral cavity, and intestines being potential autoimmunity sites, known as the "mucosal origin theory". Smoking is strongly associated with RA, evidenced by the correlation between smoking-induced bronchus-associated lymphoid tissue and anti-CCP antibody production. Predicting RA progression in the preclinical stage allows for preemptive or suppressive treatment. Imaging studies, such as HR-pQCT, US and MRI, have shown that bone loss and synovitis correlate with subsequent RA development. For instance, our MRI study found a significant correlation between symmetric MCP tenosynovitis and RA progression in undifferentiated arthritis patients. As understanding of preclinical RA improves, interest grows in preventing its development. Measures like smoking cessation and periodontal disease treatment may reduce RA risk, and pharmacologic interventions with MTX, abatacept, rituximab, and others have been explored to prevent RA onset. This presentation will discuss these prevention efforts and the pathogenesis of preclinical RA, representing true precision medicine in RA management.

EL24

Advancing patient safety beyond risk management

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Conflict of interest: None

Patient safety in Japan began around the year 2000, following a series of major medical accidents at some hospitals that became significant social issues. Until then, adverse events in healthcare were typically attributed to the knowledge and skills of healthcare professionals or to patient and medication-related factors. Safety managers in medical institutions began learning methods to analyze medical incidents and implement countermeasures. However, ensuring patient safety remains an ongoing challenge, both in Japan and globally. In Japan, the concept of patient safety has historically been associated with risk management efforts aimed at protecting hospital organizations from external threats, such as litigation. While risk management will continue to be an important aspect of healthcare, it is necessary to reconsider the actions required to provide safe, patient-centered care. Healthcare encompasses a wide range of contexts, including environments where high-risk drugs and materials must be handled carefully under specific conditions, settings where teams collaboratively provide treatment, and situations where diverse risks continuously emerge. No single approach can achieve safety. Traditionally, efforts have focused on enhancing individual expertise and relying on the skills of healthcare professionals to manage risks. However, moving forward, greater emphasis must be placed on organizational strategies, including improving teamwork, standardizing workflows, and strengthening management practices. The approach to achieving safety in healthcare, viewed as a system, is grounded in the principles of quality management, a methodology developed in Japan's manufacturing industry. Quality management involves organizational management concepts, data collection and analysis, and practical methods for implementing improvement activities at the workplace level. These are the essential competencies that physicians, as lead-

ers in clinical practice, must acquire.

EL25

Rheumatic diseases common in the elderly: Treatment and points to note

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Conflict of interest: None

Reflecting the recent aging society, patients with connective tissue rheumatic diseases (CTD) are becoming increasingly elderly. For example, rheumatoid arthritis (RA) patients are aging, and the number of patients with RA that develops at older ages is increasing. Elderly RA is classified into RA with onset at a young age and elderly onset RA (EORA) with onset at age 60 or older. In aging patients with RA, multifaceted treatments such as anti-rheumatic drugs, analgesics, surgery, and rehabilitation are required depending on bone destruction and ADL. On the other hand, in the early stages of EORA, treatment is based on T2T, but a treatment strategy that takes into account organ complications is realistic. In addition, it is often difficult to differentiate between seronegative EORA and polymyalgia rheumatica, and it is necessary to sort out the points of differentiation between similar pathologies. Focusing on other CTDs, ANCA-associated vasculitis tends to occur at an older age, and it goes without saying that the risk-benefit balance is important in recent immunological treatment strategies aimed at achieving remission. Giant cell arteritis (GCA) usually develops in people over 50 years of age, with the peak incidence occurring in the 60s and 70s. In the past, glucocorticoid (GC)-based treatment for GCA inevitably led to poor prognosis and reduced quality of life due to treatment-related complications. However, aggressive treatment with tocilizumab can now reduce the GC dosage and the occurrence of treatment-related complications. The common clinical features of elderly-onset CTD patients are that they often have a variety of complications and take multiple medications, that they are immunocompromised hosts, and that they can easily become frail. It is important to understand complications and concomitant medications, and promptly intervene with medical support, and it is necessary to practice and devise treatments that do not rely on GC.

EL26

Organ involvement and management of Sjögren's syndrome

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Conflict of interest: Yes

Sjögren's syndrome: SS causes immune abnormalities with anti-Ro/SS-A antibodies and sicca symptoms, which impair the quality of life of patients. SS presents a variety of extraglandular symptoms, and while the EULAR Sjögren's syndrome Disease Activity Index: ESSDAI is used for applications for designated intractable diseases, there are organ disorders that are not included in the ESSDAI. The types of organ disorders are divided into glandular symptoms and extraglandular symptoms that extend to the whole body and organ disorder evaluation is also important in pregnancy and delivery management for children and anti-Ro/SS-A antibody-positive cases. For glandular symptoms, muscarinic receptor agonists and diquafosol sodium are used, and for extraglandular symptoms, immunosuppressants are used, but the recommendation level is weak. No biological agents including rituximab have been approved in Japan. Nipocalimab, an anti-FcRn monoclonal antibody, has been shown to be effective in rheumatoid arthritis in which TNF inhibitors are ineffective, and in SS, a randomized controlled trial showed a significant improvement in the primary endpoint, ClinESSDAI. In a phase 2b trial of the anti-BAFF receptor antibody ianalumab: VAY-736 in SS, significant improvements were observed in stimulated salivary flow rate in addition to the primary endpoint, ESSDAI. The selective Tyk2 inhibitor deucravacitinib has been shown to be effective in psoriasis and psoriatic arthritis, and a phase 2 trial of lupus showed improvement in the primary endpoint. In a phase 2 trial of dazodalibep, a fusion protein targeting CD40 ligand, ESSDAI improvement was achieved in the ESSDAI $\geqq$ 5 group, and ESSPRI improvement was observed in the ESSDAI < 5/EULAR Sjögren's syndrome Patient Reported Index: ESSPRI $\geqq$ 5 group. In this presentation, in addition to organ damage evaluation and conventional treatment, we will introduce the current situation in which multiple clinical trials are underway for SS.

Meet the Expert

MTE1

Characteristics of juvenile idiopathic arthritis (JIA) that differ from rheumatoid arthritis -Focusing on synthetic antirheumatic drugs and biological agents available in Japan-

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Conflict of interest: Yes

As of December 2024, there are 25 synthetic antirheumatic drugs and biological agents available for rheumatoid arthritis in Japan, which is rare in the world. On the other hand, in juvenile idiopathic arthritis (JIA), the former is only one methotrexate drug and one JAK inhibitor, and the latter is only five drugs, so the disparity is extremely large. Some reports have proven that the common triggering factor for inflammatory pathology in arthritis is inflammatory cytokines, as monoclonal antibodies and specific receptors against individual inflammatory cytokines have recently been formulated as therapeutic drugs, and the fact that they inhibit the function of a single inflammatory cytokine leads to the end of inflammation. In JIA, various inflammatory cytokines are produced, and the mechanism by which they are mutually induced has also been revealed, but there is a leading cytokine specific to the disease, and it is believed that inflammation can be ended by blocking that cytokine. In systemic JIA, patients are forced to use large amounts of glucocorticoids for a long period of time to combat the strong systemic inflammation, which causes side effects such as obesity, growth retardation, osteoporosis, vertebral compression fractures, femoral head necrosis, and steroid-induced diabetes, making the lives of patients extremely restricted. As a treatment with biological agents, tocilizumab (TCZ) as an anti-IL-6 inhibitor was approved after clinical trials ahead of the rest of the world and has been found to be highly effective with minor side effects, making it an essential miracle drug. Canakinumab, which has anti-IL-1 inhibitory effects, has also been approved in Japan and has shown effectiveness in clinical settings in cases where TCZ is ineffective. In addition, anti-TNF drugs such as etanercept (ETN) and adalimumab (ADA) are used in cases where arthritis persists even after systemic symptoms have improved. Meanwhile, in arthritic JIA, in addition to the ETN, ADA, and TCZ, abatacept, which inhibits the costimulatory signal between antigen-presenting cells and T cells, which are located upstream of inflammation, has been approved in Japan. In this presentation, we will provide an overview of the drugs that can be used for JIA, their dosage forms, and how to use them in clinical practice, with a focus on the differences between JIA and RA. We will also provide an overview of the characteristics of JIA that are different from rheumatoid arthritis.

MTE2

SSc Quiz: Basic knowledge on SSc management

Masataka Kuwana
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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. Diagnosis, disease classification, evaluation of disease activity, and prediction of future outcomes cannot be properly judged without knowledge and experience unique to SSc. For example, a short disease duration (within 18 months) is widely used as a disease activity index for patients with diffuse cutaneous SSc and an inclusion criterion for clinical trials. However, the evaluation varies greatly depending on which time point is considered to be the onset of symptoms attributable to SSc. In addition, since pathological mechanisms of Raynaud's phenomenon and digital ulcers are different, the treatment approaches to these conditions should be different. Recently, a number of "therapeutics" have been approved for treatment of SSc based on the results of randomized controlled trials, but a correct understanding of the treatment evidence is necessary when applying them to clinical practice. In this session, I will introduce basic knowledge essential for the management of SSc patients using case-based quiz.

MTE3

Statistical Method for Analyzing Repeatedly Measured Data

Ayumi Shintani
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Conflict of interest: None

In clinical practice, it is common to collect repeated measurements within a single patient over time. This lecture will introduce statistical methods suitable for analyzing such paired data. First, the paired t-test will be discussed, starting with its fundamental concepts. The presentation will delve into how to address and compare within-subject variation and between-subject variation. The paired t-test examines changes within the same subject, making it more likely to detect statistical significance, which is particularly useful for evaluating treatment effects. However, this method has limitations. For pre-post designs, factors unrelated to the intervention itself-such as psychological influences or lifestyle changes-can bias the results. To mitigate these issues, randomized trials with control groups are essential. Additionally, approaches for handling missing data will be discussed, including methods such as mixed-effects models. These methods minimize bias caused by missing data and enhance the reliability of conclusions. The lecture will also explore statistical techniques for analyzing data measured three or more times, such as Repeated Measures ANOVA, fixed effects models, and mixed-effects models. These methods are effective in capturing the effects of time and treatment. With accounting for within-subject variation, the analyses can enhance statistical power. Using the free statistical software EZR, the lecture will provide practical examples, including data formatting and step-by-step procedures for applying these methods.

MTE4

Classification and treatment of chronic pain

Takahiro Ushida
Department of Pain Medicine, Aichi Medical University

Conflict of interest: Yes

Chronic pain, defined as pain lasting more than three months, significantly impacts patients' quality of life. The International Classification of Diseases, 11th Edition (ICD-11), divides chronic pain into "chronic primary pain" and "chronic secondary pain". Chronic primary pain includes conditions like irritable bowel syndrome, nonspecific chronic low back pain, and fibromyalgia, which cannot be explained by other pain classifications. It is defined from a phenomenological perspective, often addressing pain with unclear causes. Chronic secondary pain, by contrast, is associated with underlying diseases or physical conditions and generally includes nociceptive and neuropathic pain. Pain mechanisms are categorized into nociceptive, neuropathic, and nociplastic pain. Nociceptive pain arises from tissue damage or inflammation, with treatment focusing on controlling inflammation, appropriate medications, and physical therapy. Inflammatory pain, such as in rheumatic diseases, falls under this category and is managed based on the T2T (Treat to Target) principle. However, chronic cases often involve psychosocial factors, making their management essential for successful outcomes. Neuropathic pain stems from nerve damage or dysfunction, treated with antiepileptic drugs, antidepressants, or nerve block therapies. Nociplastic pain results from pain amplification and reduced inhibitory mechanisms, often linked to chronic primary pain. Many patients exhibit a combination of these mechanisms, necessitating comprehensive treatment plans involving medications, psychosocial approaches, exercise therapy, and rehabilitation. A biopsychosocial approach is vital for chronic pain management, requiring multidisciplinary collaboration. Exercise therapy plays a central role, improving physical function while positively influencing psychological and social factors. Integrating exercise with psychosocial support enhances outcomes and offers multifaceted improvements in chronic pain management.

MTE5

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

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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.

MTE6

Preparing for Rheumatology Treatment in Times of Disaster

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Conflict of interest: None

Every year disasters occur in various parts of Japan. 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. On the other hand, the issue is how to maintain the system to provide medical services when medical personnel or medical institutions are affected by the disaster. When patients themselves are affected by a disaster, they must consider how to respond depending on their situation. These include daily living conditions (whether they are living at home or in an evacuation shelter, whether they have access to electricity and water, etc.) and medical conditions (whether they have prescription drugs on hand, whether they are able to go to the hospital, etc.). 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

Precision medicine in rheumatic diseases: How to differentially select targeted therapies?

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Conflict of interest: Yes

The 21st century has marked a paradigm shift in the treatment of rheumatic diseases. Clinical remission has become a realistic therapeutic goal for most of patients with rheumatic diseases such as rheumatoid arthritis and psoriatic arthritis by the appropriate treatment using anti-rheumatic drugs. Among them, molecular targeted therapies are used for many immune and infectious diseases and it is necessary to establish new therapeutic systems and strategies based on their differential application. The establishment of precision medicine is considered particularly important in rheumatic diseases with clinical and molecular heterogeneity. We have reported that patients with psoriatic arthritis could be classified into four subgroups by differences in the peripheral lymphocyte phenotypes based on the expression of chemokine receptors and that differential use of biological DMARDs in different subgroups resulted in better effectiveness to each drug. Our results suggest that pathological stratification of diseases associated with characteristic cytokines by analyzing lymphocytes and other parameters might enable selection of optimal molecular target drugs based on the pathology and development of precision medicine.

MTE8

Management of the antiphospholipid syndrome: AtoZ

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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.

MTE9

Appropriate knowledge for management of axial spondyloarthritis

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Conflict of interest: Yes

Axial spondyloarthritis (axSpA) is a group of disorders characterized by predominant arthritis in axial joints, such as the sacroiliac joints and spine. It commonly presents with inflammatory back pain in young men and is strongly associated with the HLA-B27 gene across different populations. The inflammation originates at ligamentous entheses, extending to adjacent bone and causing bone erosion, which is subsequently repaired by adipose tissue, followed by new bone formation. These changes typically become apparent on X-rays over a span of two years. In advanced stages, syndesmophyte formation can lead to spinal ankylosis. AxSpA progresses from non-radiographic axial spondyloarthritis (nr-axSpA), where apparent X-ray changes in the sacroiliac joints are absent, to ankylosing

spondylitis (AS). However, not all cases of nr-axSpA progress to the radiographic axSpA. Despite this, the disease burden in nr-axSpA is similar to that in AS, underscoring the importance of early diagnosis and treatment intervention to improve patients' activities of daily living (ADL) and quality of life (QOL). However, diagnosing axSpA can be challenging. The most critical factor in diagnosing axSpA is the presence of sacroiliitis. The ASAS (Ankylosing SpondyloArthritis International Society) classification criteria for axSpA are intended for use in already diagnosed cases, and their application for diagnostic purposes is incorrect. Diagnosis should be based on a thorough understanding of axSpA features, clinical examination, and test findings, with differential and exclusion diagnoses carefully considered. Ongoing observation after initiating treatment is also essential for accurate diagnosis. In treating axSpA, patient education emphasizing smoking cessation and exercise is crucial. Pharmacotherapy primarily involves non-steroidal anti-inflammatory drugs (NSAIDs). Methotrexate lacks evidence for efficacy in axSpA, and systemic glucocorticoids are not typically used. If NSAIDs are insufficient, options include TNF inhibitors, IL-17 inhibitors, or JAK inhibitors. However, the effects of these treatments on inhibiting bone formation are not yet well understood. This MTE aims to outline accurate knowledge about axSpA, a condition with limited exposure and diagnostic challenges, to prevent overtreatment and ensure proper care.

MTE10

RA Hand Surgery

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Conflict of interest: Yes

In recent years, rheumatoid arthritis (RA) drug treatment has changed dramatically. 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. At this time, I would like to consider conservative and surgical treatments 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, intra-articular injections are first performed, and orthotics are also considered. If the effect of these conservative treatments is insufficient, synovectomy is considered before combined destruction appear. This is important from a joint protection perspective, and it can also prevent tendon rupture, so the timing of surgical intervention is important. 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 characteristic deformity has already occurred, the cause should be understood and surgical procedures will be considered depending on the situation. Surgery is considered according to the progression of joint destruction. Given the impact of joint repair, joint-protection surgery will be performed if possible. 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. 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.

MTE11

The basics of physical examination for skin thickening in scleroderma

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Conflict of interest: Yes

Scleroderma (SSc) is one of the connective tissue diseases (CTDs) characterized by excessive remodeling, microvascular abnormalities, and autoimmunity. CTDs have a common disease process, 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. Since SSc is difficult to find at an inflammatory phase clinically, the treatment approach must be different from other CTDs. For the development of new drugs, both identification of treatment targets and treatment-responsive measures are quite important. However, in SSc, it was difficult for us to develop new treatment agents that could regulate the fibrosis/remodeling steps directly. Also, the development of treatment-responsive measures has been delayed 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. 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 overview the significance of the evaluation of the Rodnan skin thickening score and the outline of the procedure, especially for beginners.

MTE12

Topics on synovial lesions and immune pathology in RA

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Department of Rheumatology, University of Tsukuba

Conflict of interest: Yes

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 from needle biopsies of the joints. In the primary joint, single-cell RNA sequencing of synovial cells has revealed what cell groups produce what cytokines, chemokines, and other proteins, as well as the connections between cells. In this session, we will summarize and discuss the latest theories on: 1) Joint cell groups obtained from human immunological analysis 2) Joint cells and biologics, changes and significance of JAK inhibitors 3) Pathological mechanisms of elderly-onset RA We will also discuss with participants the intersections and hints in the clinical pathological analysis of RA and its animal models, including our own studies.

MTE13

What you need to know about MTX: basics and clinical practice

Ayako Nakajima
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Conflict of interest: None

In the treatment of rheumatoid arthritis (RA), the usefulness of biologics and JAK inhibitors has been widely reported in recent years. At the same time, it has been noted that the use and dosage of methotrexate (MTX) in daily clinical practice have decreased compared to before. However, since the introduction of injectable MTX, the change in administration routes has mitigated gastrointestinal symptoms, allowing for higher tolerated doses of MTX, which contributes to better disease activity control. As a result, the value of MTX has been re-recognized. MTX remains the anchor drug in RA treatment because it balances efficacy and safety while offering excellent cost-effectiveness. To utilize MTX effectively, it is essential to have a solid understanding of its mechanisms of action. MTX, developed in the 1940s as a folate metabolism antagonist, is known not only for its strong antiproliferative effects but also for its diverse actions, such as increasing adenosine, producing reactive oxygen species, and suppressing inflammatory cytokines like IL-6, IL-1β, and TNFα. Additionally, recent studies have highlighted differences in efficacy and side effects depending on the degree of MTX polyglutamation. When using MTX, it is crucial to follow the *Guidelines for Methotrexate (MTX) Use and Clinical Practice, 2023 Edition*. Screening should be conducted thoroughly, and for eligible patients, the dosage should be increased promptly to achieve therapeutic goals. At the same time, patient education and rigorous monitoring are essential to detect adverse events early, such as bone marrow suppression, lymphoproliferative disorders, and interstitial pneumonia, to minimizing patient burden as much as possible. In this session, my aim is to provide an overview of the foundational knowledge and clinical utility of MTX, which plays a pivotal role in Phase I treatment for RA aiming at remission. Additionally, I will address participants' questions to

deepen their understanding of MTX.

MTE14

Antinuclear antibodies in systemic autoimmune rheumatic diseases: Up-to-date 2025

Takao Fujii
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Conflict of interest: None

Connective tissue diseases are described as systemic autoimmune rheumatic diseases (SARD), because high titer of antinuclear antibodies (ANA) can be frequently found in sera from patients. Currently, ANA includes not only antibodies (Abs) against nuclear components but also Abs against cytoplasm and cell membranes. It has been suggested that the production of many ANA involves autoreactive T cell, but not non-specific B cell activation. When SARD are suspected, ANA test should be performed. In the 2019 ACR/EULAR classification criteria for systemic lupus erythematosus (SLE), positive ANA (≧x80) is described as an entry criteria. In addition, in systemic sclerosis or idiopathic inflammatory myositis, the close associations between ANA and clinical manifestations are recognized in many cases. There are many methods for measuring ANA. In recent years, new methods have been developed for detecting disease-specific ANA. One is the line blot method, in which autoantigens are spotted on a membrane and then ANA is detected with an enzyme-labeled secondary Ab. The other is the protein array method, in which antigen proteins are prepared in a undenatured (non-dried) state by germ cell-free protein synthesis and the reaction with Abs is detected while maintaining the three-dimensional structure. Both systems can detect many ANA those cannot be measured in daily practice. Whereas it is confirmed that both methods have clinical utility, neither method is currently approved for insurance coverage in Japan. Even in cases where ANA has clinical significance, its pathogenesis is often unclear. We have shown that ANA in cerebrospinal fluid is associated with cytokines in neuropsychiatric SLE. It has also been reported that immunization of mice with human TIF1-γ protein induces anti-TIF1-γ Abs and develops myositis (*Ann Rheum Dis,* 2021). In this seminar, I would like to introduce the latest information on ANA.

MTE15

Rheumatic foot surgery: Commitment to functional reconstruction

Makoto Hirao
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Conflict of interest: None

With the development of drug treatment for rheumatoid arthritis (RA), orthopedic surgeons would like to provide lower limb function reconstructive surgery technology that will allow RA patients to regain more normal bipedal gait. Ultimately, if the problem of the foot in contact with the ground remains, it will not be possible to regain a comprehensively normal bipedal gait, so it is important to focus on the problem of the foot from the early stage when RA is being managed, to provide conservative treatment, and to build a mindset and a system of cooperation among medical professionals so that necessary surgical procedures can be performed at an appropriate stage. In order to maintain and improve the walking ability of RA patients, the current situation is that we are learning from cases every day and going through trial.

MTE16

Clinical epidemiology study in patients with rheumatic diseases using medical big data

Ryoko Sakai
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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 Japan, there are some kinds of claims data to be able to use for clinical epidemiological study. 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.

MTE17

Considering the relapse of rheumatic diseases

Keishi Fujio
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Conflict of interest: Yes

The advent of molecularly targeted drugs has significantly improved the treatment of rheumatic diseases. In rheumatoid arthritis (RA), recent data from Japanese registry studies indicate that approximately 50% of patients achieve DAS28-ESR remission, while 40% reach SDAI/CDAI remission. However, relapse after remission is not uncommon. Even with continued treatment, the relapse rate is reported to be 10-20% over 12 months. If bDMARDs are tapered, the relapse rate rises to approximately 40% within a year, and if discontinued, it reaches 50-60%. In clinical practice, attempts to taper glucocorticoids (GC) or DMARDs are often made following remission, highlighting that relapse remains a significant challenge even in remission cases. Specifically, in older adults classified as frail, relapse may lead to irreversible declines in physical function. In systemic lupus erythematosus (SLE), the advent of molecularly targeted drugs has also improved disease control. However, the DORIS remission rate under treatment remains around 30-50%. In SLE, treatment strategies prioritize tapering GC, with relapse rates reported to be around 10-20% annually. Both major and minor flares in SLE have been associated with approximately a twofold increase in the accumulation of organ damage. In SLE patients stabilized on prednisone (PSL) at 5 mg/day, discontinuation of PSL has been associated with a relapse rate of 27%, suggesting that GC discontinuation is feasible in many cases. However, considering the substantial impact of relapse, tapering must be approached cautiously. Thus, understanding the pathology of relapse in SLE and predicting high-risk cases is also expected to improve patient outcomes. In this session, we aim to discuss the current and future potential for predicting relapse in RA and SLE based on clinical and immunological parameters, building on the knowledge outlined above.

MTE18

Advances in the Management of Pregnancy Complicated by Collagen Diseases

Hiroaki Dobashi
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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. The treatment of rheumatic diseases has greatly progressed with the development of various therapeutic agents and the establishment of evidence for their efficacy and safety. 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 MTE, I would like to present the problems and solutions in each situation, including failed cases, based on our own experience, and discuss with you the pregnancy of a patient with collagen disease.

MTE19

Advances in treatment strategies for Large-vessel vasculitis

Masayoshi Harigai
Sanno Medical Center

Conflict of interest: Yes

Large-vessel vasculitis affects the aorta and its major branches and includes Takayasu arteritis and giant cell arteritis. Prevalence (per million) calculated from the number of patients registered with the designated intractable diseases are 42.6 for Takayasu arteritis and 25.6 for giant cell arteritis. Considering the prevalent age of the diseases and future changes in the population structure of Japan, the difference in the numbers of patients and the prevalence between the two diseases is expected to narrow in the near future. Takayasu arteritis shows intimal thickening, inflammation and fibrotic damage to the tunica media and fibrotic advantitial thickening, while giant cell arteritis shows changes in intimal and tunica media, but less advantitial changes, and granulomatous lesions with multinucleated giant cells. For many years, glucocorticoids (GCs) were the main stay of treatment, but rapid progress has been made in molecularly targeted therapies for both diseases. The efficacy and safety of TNF inhibitors, IL-6 inhibitors, IL-17 inhibitors, CTLA4-Ig, and JAK inhibitors have been reported in Takayasu arteritis, and IL-6 inhibitors, IL-17 inhibitors, GM-CSF inhibitors, CTLA4-Ig, and JAK inhibitors in giant cell arteritis. In parallel with these advances in therapeutic agents, treat-to-target strategies are being incorporated into the treatment of large-vessel vasculitis, although the definition of remission or low disease activity as a treatment target remains a challenge. This Meet the Expert will discuss current and future perspectives on treatment strategies for large-vessel vasculitis.

MTE20

How to diagnose and manage juvenile spondyloarthritis

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Conflict of interest: None

Juvenile Spondyloarthritis refers to spondyloarthritis that develops before puberty. Spondyloarthritis is a disease that develops in young people, and there are about 10% of cases that develop in childhood. There are many cases of peripheral spondyloarthritis in childhood onset cases, and even in axial spondyloarthritis, it takes time for axial lesions to appear. In addition, from the perspective of the healthcare system and health insurance, juvenile spondyloarthritis patients are diagnosed and managed using the classification criteria for juvenile idiopathic arthritis. In this situation, there are differences in the approved drugs and available medical subsidy systems compared to adults. As differences in the disease state, healthcare system and treatment are important themes in terms of transitional healthcare support, we would like to deepen our understanding of these points.

MTE21

Research Question Brush-up Workshop

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Conflict of interest: None

Are you feeling stuck, wanting to conduct clinical research but not knowing where to begin? We are organizing a group workshop focusing on creating and refining Research Questions (RQ) - the most fundamental aspect of research - for medical staff. You will experience the process of transforming clinical questions into actionable research projects. Furthermore, we are pleased to announce that professional researchers from various fields - including rehabilitation specialists, nurses, pharmacists, and physicians - will participate as facilitators and share their own research experiences. This is an excellent opportunity to learn about real-world research practices. The workshop is open to all conference participants, including physicians, rehabilitation specialists, nurses, pharmacists, and other medical staff members. We believe this workshop will provide an excellent opportunity to build research connections among participants. Through discussions, your research ideas can be refined and elevated, potentially providing significant momentum toward publication. Building a network of peers is crucial for advancing research. You are guaranteed to gain valuable experience by sharing research ideas and engaging in stimulating discussions. Don’t miss this valuable opportunity. We sincerely look forward to your participation. CopyRetryClaude can make mistakes. Please double-check responses.

MTE22

Hands-on seminar for systematic reviews using RevMan and GRADEpro

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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 were held as part of the revision process for guidelines on the treatment of rheumatoid arthritis and large vessel vasculitis; opportunities for clinicians to engage 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.

MTE23

Unraveling Sjögren's syndrome and IgG4-related disease through imaging

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Conflict of interest: None

Sjögren's syndrome (SS) and IgG4-retaled dacryoadenitis and sialadenitis (IgG4-DS) are both diseases of unknown cause that target the lacrimal and salivary glands, and in the past they were recognized as the same disease. Now, many researchers have clarified the differences between the two diseases, and the understanding of the differences has been improved. As a specialist in diagnostic imaging, I am concerned about the fact that imaging examinations are not yet fully utilized in the diagnosis of both diseases. Globally, the usefulness of ultrasonography in the diagnosis of SS and IgG4-DS is becoming widely known, and there has been steady progress towards its introduction into diagnostic and classification criteria. I strongly hope that imaging examinations, including MRI, which is also a non-invasive imaging method, will be officially introduced into the diagnosis and classification criteria in the future, and I will continue to promote their usefulness to the world. I would like to take this opportunity of this interactive educational program to share the appeal of salivary gland imaging with those doctors who are interested in this field. In doing so, they will be reminded that imaging examinations are a very effective item that can provide a variety of information that will bring us closer to the core of diseases such as SS and IgG4-DS. I also hope that you will take what you learn in this program back to your daily clinical practice and make use of it. In this program, we plan to teach basic salivary gland ultrasonography and MRI reading skills for SS and IgG4-DS, and to show clearly what we can learn from actual images and how we should apply them in our daily clinical practice, using specific examples. At the same time, we would like to interact with participants through various cases of SS and IgG4-DS.

MTE24

Assessment of disease activity in Large-vessel vasculitis

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

Conflict of interest: Yes

Giant cell arteritis (GCA) is characterized by vasculitis of the temporal, ophthalmic, subclavian to axillary arteries, and descending thoracic to abdominal aorta, and is accompanied by polymyalgia rheumatica in 40-60% of patients. Visual impairment is irreversible, resulting in blindness in 5-10% of patients. Relapses are frequent and include headache, general symptoms, pain due to vasculitis of the aorta and aortic branches, and polymyalgia rheumatica. Asymptomatic patients may also present with elevated C-reactive protein (CRP) derived from aortic lesions. Aortic aneurysms and stenosis of the subclavian to axillary arteries are seen in advanced cases. TAK is characterized by lesions of the aorta, carotid artery, subclavian artery, pulmonary artery, renal artery, celiac artery, and in some cases, coronary artery lesions. It is characterized by pain due to arteritis, such as neck pain, shoulder pain, chest pain, and back pain, and ischemic symptoms due to arterial stenosis, such as claudication in the extremities. Cranial symptoms such as headache, mandibular pain, toothache, and earache may also appear nonspecifically consistent with disease activity. TAK is also asymptomatic, with elevated CRP derived from aortic lesions. In advanced cases, cerebral ischemic symptoms, progressive aortic aneurysm and aortic regurgitation, renal vascular hypertension, pulmonary hypertension, and coronary artery disease are observed. The JPVAS determined remission criteria for large-vessel vasculitis and proposed a treatment algorithm for setting and achieving treatment goals. In the treatment algorithm, in addition to clinical symptoms, signs, and CRP, it is important to document inflammatory findings in the arterial wall and structural progression of thickening and stenosis or dilation of the arterial wall by imaging. This educational lecture will provide an overview of the evaluation of disease activity in large-vessel vasculitis.

MTE25

Clinical immunology at a glance in vivo

Masaru Ishii
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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.

MTE26

Assessment of Physical Function in Patients with Rheumatoid Arthritis for Extending Healthy Life Span

Toshihisa Kojima
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Conflict of interest: Yes

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. The Impaired shoulder joint range of motion is associated with many activities of daily living, assessed by HAQ-DI. Movement speed, which is included in the assessment of frailty and sarcopenia, is an important physical function. In our study, approximately 20% of patients with a HAQ remission were considered frail. Observation of movement speed is also important in daily practice. In this lecture, I would like to consider how to diagnose physical disability, focusing on physical measurements that should be kept in mind (or can be visualized) in daily medical practice.

MTE27

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 pa-

tients, 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.

MTE28

Tips of imaging diagnosis of axial spondyloarthritis

Yuho Kadono
Department of Orthopaedic Surgery, 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 (PsA). SpA exhibits not only enthesitis but also arthritis or spondylitis. SpA which presetns sacroiliac joint or spine involvement, 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 little radiographic change to classify as AS. Although there is the classification criterion, we sometimes have some trouble to make a diagnosis. When we find spinal fusion or hyper ossification, we should distinguish axSpA from relatively common disease such as degeneration, diffuse idiopathic skeletal hyperostosis (DISH), psoriatic arthritis (PsA), pustulotic arthro-osteitis (PAO), or osteitis condensans illi (OCI). 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 think and diagnose imaging of axSpA.

MTE29

The Role of Autoinflammation in Rheumatic Diseases and Its Pathophysiological Significance

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

Autoinflammatory diseases are a group of disorders primarily caused by abnormalities in the innate immune system, and they are classically defined by the following three points: 1. The presence of seemingly unprovoked inflammation 2. The absence of high-titer autoantibodies or autoreactive T cells 3. The detection of congenital abnormalities in the innate immune system. This has led to the characterization of pathological conditions distinct from autoimmune diseases and immunodeficiencies. Recent advances in genetic analysis and signaling pathway research have proposed classifying autoinflammatory diseases based on their mechanisms of onset into categories such as inflammasomopathies, endogenous antagonist mutations, actinopathies, type I interferonopathies, ADA2 deficiency, NF-kappaB-related disorders, and ER stress-related disorders. Adult-onset Still's disease, Behçet's disease, periodic fever, aphthous, stomatitis, pharyngitis and cervical adenitis syndrome (PFAPA syndrome), Castleman disease, and other conditions where inflammation is a primary feature of the pathology but no definitive disease-causing genes have been identified can also be classified as broad-spectrum autoinflammatory diseases. Anti-citrullinated protein antibodies (ACPAs) are known as disease-specific autoantibodies for rheumatoid arthritis. However, the pathophysiology of rheumatoid arthritis is diverse, and innate immunity is also involved in its development. The concept of a cytokine storm has become widely recognized following the COVID-19 pandemic. It refers to a phenomenon in which inflammatory cytokines are massively released into the bloodstream due to various external or internal triggers, causing an excessive inflammatory response that leads to damage to multiple organs. This condition is also thought to encompass many autoinflammatory diseases. Genetic disorders often manifest during childhood; however, familial Mediterranean fever (FMF), caused by mutations in the MEFV gene, is not uncommon in adults. Additionally, VEXAS syndrome, which has recently garnered attention, is characterized by its onset in adulthood, particularly in older men. This syndrome results from somatic mutations in the UBA1 gene, leading to somatic mosaicism. These examples highlight that autoinflammatory diseases with genetic abnormalities may also present in adult-focused specialties, such as rheumatology and collagen disease in clinical practice. Diagnosing autoinflammatory diseases requires a thorough understanding of clinical signs, alongside the utilization of genetic panel testing, whose insurance coverage has recently expanded. Such testing is also crucial for implementing appropriate molecular-targeted therapies. This lecture will discuss the role of autoinflammation in rheumatic diseases and its pathophysiological significance.

MTE30

Management of Drug Treatment for Rheumatoid Arthritis: Treatment options based on the efficacy and risk of complications such as respiratory disease and malignancies

Yutaka Kawahito
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Conflict of interest: Yes

In rheumatoid arthritis (RA), early diagnosis and treatment can inhibit the progression of joint destruction and extra-articular symptoms, and improve the prognosis. Current challenges in the treatment of RA include identifying the most effective pharmacological options for intensive therapy and balancing the risk-benefit ratio to prevent complications such as infections, malignancies, cardiovascular events, and interstitial pneumonia (IP). From an efficacy standpoint, the utilization of triple csDMARD combination therapy, rapid glucocorticoid tapering, and the selection of molecular-targeted agents in phase II and beyond, including therapies for difficult-to-treat RA, have not been as well established domestically as they are internationally. Common pulmonary complications of RA, such as IP, bronchiectasis, and emphysema, are prevalent. IP is intricately linked to the pathogenesis of RA and exacerbates with disease activity. Conversely, drug-induced IP, particularly from anti-rheumatic medications like methotrexate (MTX), is also significant. Recent evidence indicates that MTX use is associated with a reduced incidence of IP. Consequently, there have been modifications in MTX usage in RA treatment. Regarding malignancies in RA, lymphomas are notably common, with MTX-related lymphomas being a concern. Smoking further elevates the risk of lung cancer in RA patients. However, the incidence of malignancies is relatively lower with biological agents compared to JAK inhibitors. Cardiovascular events remain a risk due to the underlying etiology of RA, with concerns that these may also be exacerbated by JAK inhibitors and glucocorticoids. RA is also a risk factor for osteoporosis, necessitating careful drug selection to mitigate fracture risk in elderly patients. In this lecture, we will elucidate the latest evidence on the efficacy and safety of pharmacotherapy, and provide guidance on selecting appropriate medications to achieve early treatment goals in clinical practice.

International Concurrent Workshop

ICW1-1

Metal regulatory transcription factor 1 drives arthritis by regulating pathogenic synovialfibroblasts

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Conflict of interest: None

[Objectives] Rheumatoid Arthritis (RA) is an inflammatory disorder that leads to irreversible joint destruction if inadequately controlled. We previously reported that metal regulatory transcription factor 1 (MTF1) plays a role in the assembly of super enhancers in synovial fibroblasts (SFs), which are linked to RA disease susceptibility. Our goal was to elucidate the regulatory dynamics of MTF1 to develop targeted therapies for RA. [Methods] We generated fibroblast-specific MTF1 conditional knockout (cKO) mice with the Col6a1-Cre driver and evaluated them in the collagen-induced arthritis (CIA) model. Clinical and pathological arthritis scores of MTF1 cKO mice were assessed, along with micro-CT imaging. Additionally, bulk ATAC-seq and RNA-seq on SFs from MTF1 cKO mice were conducted to examine changes in chromatin accessibility. Furthermore, synovial tissue from RA patients was analyzed using single cell RNA sequencing (scRNA-seq) to profile gene expression at the individual cell level and PhenoCycler for investigating the spatial distribution of MTF1-positive synovial cells. [Results] MTF1 cKO mice exhibited significantly reduced arthritis severity in both macroscopic and microscopic evaluations. Micro-CT revealed decreased bone destruction. Bulk RNA-seq and ATAC-seq of synovial fibroblast from MTF1 cKO mice demonstrated reduced expression of inflammatory mediators, such as IL-6 and changes in the corresponding chromatin accessibility. scRNA-seq of RA synovium revealed higher MTF1 expression in the CD74 hi HLADR + sublining SFs, which exhibited elevated TNF and IFN stimulation signatures. Consistently, PhenoCycler analysis confirmed MTF1 localization in the sublining area. [Conclusion] This study revealed that MTF1 expressed by specific sublining SFs contributes to the regulation of local joint inflammation and bone destruction.

ICW1-2

An efficient functional assay platform for rheumatoid arthritis risk alleles with UNIChro-seq

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Conflict of interest: None

[Objectives] Genome-wide association studies have identified many variants associated with rheumatoid arthritis (RA), but quantitative trait locus (QTL) analyses have failed to detect their effects sufficiently. The aim of our study is to elucidate the functions of RA risk variants by establishing a novel experimental platform with high efficiency, accuracy and sensitivity, which differs from current QTL studies characterized by the genome-wide analysis using naturally occurring variants from hundreds of donors. [Methods] We have newly developed UNIChro-seq, a modified ATAC-seq experimental platform, that efficiently targets specific chromatin accessible regions, accurately quantifies the allelic imbalance using unique molecular indexes, and enables us to pool multiple libraries. By applying our platform to the heterozygous or edited alleles introduced by the latest CRISPR technology in human primary cells under various cell conditions, we sought to evaluate the context-dependent impact of the RA risk allele on the chromatin accessibility. [Results] $CD4^+$ T cells were extracted from five healthy subjects, stimulated for 72 hours, and collected at 12 time points (60 samples in total). UNIChro-seq was performed on 20 fine-mapped RA risk variants and the chromatin accessibility QTL (caQTL) effect was evaluated. Nine of the 20 variants showed significant caQTL effects. Stimulation time-dependent caQTL effects were identified in 3 variants. Cell type-specific caQTL effects of rs58107865 at the LEF1 intronic region, the fine-mapped RA risk variant with the highest accuracy, were detected in $CD4^+$ T cell subsets. Furthermore, the positive caQTL effect of rs58107865-C, which was attenuated by stimulation, was experimentally validated using genome-edited $CD4^+$ T cells by prime editing. [Conclusion] Our novel platform enables us to detect the caQTL effect from only a small number of donors, and contributes to better understanding of the genetic etiology of RA.

ICW1-3

Irisin mitigates rheumatoid arthritis by suppressing mitochondrial fission via inhibiting YAP-Drp1 signaling pathway

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Conflict of interest: None

[Objectives] The aim of our study was to investigate the expression of irisin in the serum of RA patients, prove the effect of irisin on the progression of arthritis in CIA mice, and clarify the mechanism of irisin in improving the progression of RA disease. [Methods] Collagen-induced arthritis (CIA) model was induced in DBA/1 mice and then treated with irisin. Arthritis index, paw thickness, weight, number of affected paws, serum inflammatory factors and related pathological tests were measured. RA fibroblast-like synoviocytes (RA-FLSs) were pretreated with IL-1β and irisin, and the migration, proliferation, invasion, oxidative stress and mitochondrial related function of RA-FLSs were detected. [Results] Irisin significantly improved arthritis symptoms in CIA mice, as indicated by reduced arthritis index, alleviated paw thickness, decreased the number of affected paws and inhibited release of inflammatory factors. Irisin alleviated joint destruction, FLSs proliferation and the expression of YES-associated protein (YAP) and mitochondrial dynamic related protein 1 (Drp1) in the FLSs of CIA mice. In vitro experiment, irisin inhibited the proliferation, migration and invasion of RA-FLSs and improved oxidative stress induced by IL-1β, thereby restraining the pathogenic transformation of RA-FLSs. Mechanically, irisin suppressed the nuclear translocation of YAP, in turn, could reduce the synthesis of Drp1 protein and inhibit the mitochondrial fission of RA-FLSs, which was reversed by YAP agonists. Therefore, irisin has a protective effect on RA. [Conclusion] Irisin inhibits the proliferation, migration, invasion and inflammatory response of RA-FLSs by inhibiting the YAP-Drp1 signaling pathway, which implies a potential therapeutic effect on RA.

ICW1-4

Interleukin-32-expressing CD4+ T cells are a potentially pathogenic subset in systemic sclerosis with interstitial lung disease

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Conflict of interest: None

[Objectives] Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, fibrosis, and inflammation. CD4+ T cells produce cytokines that play crucial roles in the pathogenesis of SSc. However, the role of CD4+ T cells in SSc-associated interstitial lung disease (SSc-ILD) remains unclear. Therefore, we aimed to determine which cytokines produced by CD4+ T cell subsets contribute to the inflammatory and fibrotic pathologies in patients with SSc. [Methods] We reanalyzed publicly available single-cell (sc) RNA-seq datasets (13 SSc and 11 healthy control (HC) lung biopsy samples), bulk RNA-seq (HC peripheral blood), and microarray datasets from the peripheral blood of patients with SSc-ILD (n=18) and HC (n=16) using R, the RaNA-seq pipeline, and the GEO2R web tool. [Results] scRNA-seq data revealed higher *IL32* gene expression in CD4+ T cells from SSc lung biopsies compared to those from HC. Mi-

croarray data showed significantly higher *IL32* gene expression in CD4+ T cells from the peripheral blood of patients with SSc-ILD than in HC. *IL32* gene expression was elevated in Th1, Th2, and Th17 cells compared with naïve CD4+ T cells (Tn), and in central and effector memory CD4+ T cells compared with Tn. Furthermore, scRNA-seq data showed that *IL32* gene expression increased in Tn cells without stimulation and in memory CD4+ T cells stimulated with anti-CD3/28 antibodies. [Conclusion] Our results suggest that *IL32*-expressing CD4+ T cells are a key subset involved in SSc pathologies. Interleukin-32 has both proinflammatory and anti-inflammatory effects on various cells; however, further studies are needed to explore its therapeutic potential.

ICW1-5

Hyaluronate fabricated hydroxyapatite nanoparticles of teriflunomide and methotrexate for the treatment of rheumatoid arthritis

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Conflict of interest: None

Objectives: Methotrexate (M) and teriflunomide (T) are the most prescribed drugs for rheumatoid arthritis (RA) though their uses are limited because of severe hepatotoxicity. Hyaluronic acid (HYA) is a targeting ligand for CD44 receptors overexpressed on inflamed macrophages in RA. The present investigation was aimed at developing HYA functionalized M and T loaded prolonged release hydroxyapatite (HA) nanoparticles (NPs) to treat RA and to avoid drug induced hepatotoxicity. **Methods:** The drug loaded HYA-functionalized HA-NPs (HYA-HAMT-NPs) were developed by electrostatic conjugation method. RA was induced in wistar rats using Complete Freund's Adjuvant and collagen solution. The in-vivo and in-vitro studies were evaluated in the 6 groups: 1) Normal control (NC); 2) Arthritic control (AC); 3) HAMT-NPs; 4) HYA-HAMT-NPs; 5) Teriflunomide; 6) Methotrexate. **Results:** HYA-HAMT-NPs revealed slow and prolonged in vitro drug release up to 96 hours. The MTT assay performed on RAW 264.7 macrophage cells revealed 1.3 times reduced IC50 compared to uncoated (HAMT-NPs) particles. In vivo pharmacokinetic study revealed slow and sustained drug release in synovial region up to 168 hours. A bio-distribution study by gamma scintigraphy imaging further strengthened the results by revealing significantly higher percentage radioactivity of HYA-HAMT-NPs in synovial region. HYA-HAMT-NPs showed significantly low arthritic score, nitric oxide and cytokine (TNF-α, GM-CSF, IL-10, RANTES) levels as compared to AC group. The reduction in nitric oxide and cytokine levels by HYA-HAMT-NPs were significantly higher than T and M treated animals. Liver histopathology and liver function tests revealed significant reduction in hepatotoxicity by HYA-HAMT-NPs as compared to conventional T and M oral treatments. **Conclusion:** The CD44-targeted HYA-HAMT-NPs may be promising intra-articular delivery system to attenuate the severity as well as to avoid drug-induced hepatotoxicity in RA.

ICW2-1

Serum cytokine levels in adult Still's disease: an explanatory subanalysis of a randomized controlled trial of tocilizumab

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Conflict of interest: Yes

Objective: To clarify the effects of tocilizumab, an interleukin (IL)-6 inhibitor, on inflammatory cytokine levels in patients with adult Still's disease and its relationship with response to tocilizumab. **Methods:** This is an explanatory subanalysis of the phase III placebo-controlled trials of intravenous tocilizumab in patients with adult Still's disease, where 25 active patients were randomized and started on tocilizumab or placebo. After 12 weeks of double-blind period, all patients were treated with tocilizumab. Multiple plasma cytokine levels were measured regularly. Missing data were imputed using the last observation carried forward. **Results:** A total of 25 patients (13 in the tocilizumab and 12 in the placebo group) were included in the analysis. IL-6 levels were correlated with DAS28 ($r=0.67$, $p<0.01$), and IL-1β, IL-6, and IL-18 levels tended to be correlated with systemic feature score ($r=0.34$, $p=0.09$; $r=0.4$, $p=0.05$; $r=0.4$, $p=0.05$). Four weeks after the administration of tocilizumab or placebo, IL-6 and IL-6 receptor levels were significantly elevated in the tocilizumab group compared to the placebo group, whereas the change in other cytokine levels were not different. IFNγ and IL-1β levels at baseline in patients who were refractory to tocilizumab were significantly higher than those who responded to tocilizumab (28.49 vs 5.65 pg/mL, $p=0.03$; 0.16 vs 0.04 pg/mL, $p=0.05$). On the other hand, IFNγ and IL-18 levels at week 52 remained high in patients who did not respond to tocilizumab (15.56 vs 7.03 pg/ml, $p=0.02$; 5924 vs 392 pg/ml, $p=0.02$, respectively). **Conclusions:** The effect of tocilizumab is limited to the IL-6 signaling pathway in adult Still's disease. Patients who were refractory to tocilizumab showed higher pre-treatment IFN-γ and IL-1β levels and post-treatment IFN-γ and IL-18 levels. Those findings provide useful insights into understanding the impact of IL-6 inhibition on the pathogenesis of Still's disease and promote tailor-maid treatment strategies.

ICW2-2

Development of a Prognostic Prediction Model for Polymyositis/Dermatomyositis-associated Interstitial Lung Disease

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Conflict of interest: None

[Objectives] This study aimed to develop an accurate predictive model for the prognosis of polymyositis (PM)/dermatomyositis (DM) associated interstitial lung disease (ILD). [Methods] We conducted an analysis using data from the Multicenter Retrospective Cohort of Japanese Patients with Myositis-Associated ILD (JAMI). We set two outcomes to predict: death and death or initiation of home oxygen therapy. The explanatory variables included clinical department, age at onset, sex, year of diagnosis, disease duration, clinical disease type, serum KL-6 and CRP levels at diagnosis, presence of autoantibodies, need for oxygen administration, and use of triple therapy, comprising glucocorticoids, intravenous cyclophosphamide, and calcineurin inhibitors. For cases with available chest high-resolution CT (HRCT) data, we included HRCT findings, such as radiological patterns of ILD and HRCT score as explanatory variables. To develop the most accurate predictive model, we compared eight different methods: multivariate Cox regression, Cox-Ridge regression, Cox-Lasso regression, random survival forests, decision trees, conditional survival

forests, neural multitask logistic regression, and DeepSurv. [Results] A total of 1,466 cases were enrolled, with 1,092 cases used as training data, 177 cases as test data, and 197 cases as validation data. Both outcome models demonstrated high C-index values using Cox-Ridge and Cox-Lasso regressions. Among these, Cox-Lasso regression showed the highest predictive accuracy based on calibration indices. Further analysis of 321 cases with available chest HRCT data revealed that incorporating HRCT findings into the Cox-Lasso model improved predictive accuracy. In addition, HRCT score was identified as a key predictor of both outcomes. [Conclusion] The most accurate model for predicting the prognosis of PM/DM associated with ILD was developed using Cox-Lasso regression. In addition, enhancing this model with HRCT findings improved outcome prediction.

ICW2-3

Relationship between anti-neutrophil cytoplasmic antibody-positivity and disease characteristics in eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] To evaluate the relationship between anti-neutrophil cytoplasmic antibody (ANCA)-positivity and disease characteristics in eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] We conducted a retrospective cohort study of patients with newly-onset or severely relapsing AAV enrolled in the J-CANVAS registry. Clinical characteristics at baseline, treatments, and prognosis between ANCA-positive and ANCA-negative patients were evaluated. [Results] Three patients with positive proteinase 3-ANCA were excluded, and 202 patients with EGPA (newly-onset: 179, severe relapse: 23) from 2017 to 2023 were included. Eighty-five patients were myeloperoxidase (MPO)-ANCA-positive and 117 patients were negative. No differences in age or sex were observed between the two groups. The MPO-ANCA-positive group had significantly higher neutrophil counts, higher C-reactive protein levels, and higher total and components 1 (general) and 8 (renal) of the Birmingham vasculitis activity score. The MPO-ANCA-negative group had a higher incidence of asthma. No differences in prednisolone doses at 0, 24, and 48 weeks were found between the two groups. Rituximab was administered more frequently in the MPO-ANCA-positive group, but the use of mepolizumab was comparable between the two groups. Both groups showed comparable estimated glomerular filtration rates at 24 and 48 weeks. Serious infectious diseases [n=2 (2.4%) vs. 4 (3.4%), ANCA-positive vs. negative], severe relapse [8 (9.4%) vs. 12 (10.3%)], and minor relapses [25 (29.4%) vs. 34 (29.3%)] were comparable by log-rank test. Univariate Cox regression analyses showed ANCA-positivity was not a significant factor in these prognoses. These results were similar to those limited to patients with newly-onset EGPA. [Conclusion] Patients with ANCA-positive EGPA demonstrated different clinical characteristics at baseline from ANCA-negative patients. However, the subsequent infectious diseases, relapses, and renal function were comparable.

ICW2-4

Musculoskeletal ultrasound in patients with adult Still's disease; tendon involvement is a sign of future relapse

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Conflict of interest: None

[Objectives] To investigate characteristic pattern of joint inflammation detected with musculoskeletal ultrasound in patients with adult Still's disease. [Methods] We retrospectively reviewed consecutive patients with adult Still's disease in Keio University Hospital between 2010 and 2024. We included patients who underwent musculoskeletal ultrasound (MSUS) examinations of symptomatic joints in the study and classified the findings according to the location of joint inflammation into three categories: articular synovitis, tendon involvement including tenosynovitis, tendinopathy and enthesitis, and bursitis. [Results] Among 119 patients with adult Still's disease, 34 patients were performed MSUS. Active local inflammation were detected in 25 patients and were included in the analysis; 12 new-onset and 13 relapsed patients. As for MSUS findings, tendon involvement was most prevalent (n=16; tenosynovitis, 11; tendinitis, 3; and enthesitis, 6) with 14 showing overlapping articular synovitis. Articular synovitis and bursitis were found in 9 and 3 patients, respectively. In those patients with active inflammation detected with MSUS, 22 initiated or intensified their treatment after MSUS examination. When we compared clinical courses between patients with tendon involvement and those without, Kaplan-Meier analysis revealed significantly higher rate and shorter time for relapse (defined as requirement of glucocorticoid dose escalation) in the patients with tendon involvement (log-rank, p=0.0477), despite no difference in baseline clinical features, inflammatory markers, use of tocilizumab, and disease duration. [Conclusion] We identified that tendon involvement detected with MSUS can predict relapse in patients with adult Still's disease.

ICW2-5

Stratification of Systemic Sclerosis (SSc)-associated Interstitial Lung Disease (ILD) responsive to Nintedanib (NTD) based on vascular and clinical findings

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Conflict of interest: None

[Objectives] The effectiveness of NTD in SSc-ILD is variable. This study aimed to stratify patients likely to benefit from NTD based on clinical findings and vascular abnormalities. [Methods] The study evaluated the one-year %FVC changes in 42 patients treated with NTD versus 32 patients receiving standard of care (SoC) for SSc-ILD. Exploratory endpoints included capillary changes assessed by nailfold video capillaroscopy (NVC) and CT imaging, with adjustment for selection bias using PS-IPTW. [Results] Baseline characteristics were comparable in both groups (mean age: 62.6±1.9 vs. 62.9±2.2; disease duration (y): 10.8±2.8 vs. 6.4±3.4) with no differences in age, autoantibodies, treatment background, pulmonary function test or average capillary count. The primary endpoint, annual %FVC change, was -0.7±1.3% in the NTD group and -2.4±1.6% in the SoC group (p=0.429), with the lack of a significant difference possibly impacted by the low NTD continuation rate (73.8% at one year, with 11 discontinuations). Among patients who were able to continue NTD for one year (n=32), there was a tendency to inhibit the reduction of %FVC compared to SoC (NTD: Δ0.69±8.14 vs. SoC: Δ-3.95±10.7, p=0.058). Meanwhile, NTD inhibits angiogenesis by suppressing VEGF signaling. NVC evaluation who continued NTD revealed a reduction of capillary count (NTD: Δ-0.74±0.20 vs. SoC: Δ0.07±0.20, p=0.005). Additionally, in cases with NVC Late pattern (low capillary count, no giant capillaries) at the start of NTD (n=5), a reduction in %FVC of over 5% was observed (p=0.016). Furthermore, there was an increase in the appearance of emphysematous cyst-like lesions on CT (p=0.048) and a higher incidence of digital ulcers (p=0.048). This trend was not observed in the SoC group. [Conclusion] Patients who continued NTD showed a reduced decline in %FVC. Those with preserved capillary density may expect therapeutic benefits from NTD, indicating that capillary assessment could serve as a valuable marker for NTD efficacy.

ICW3-1

Plasmacytoid Dendritic Cells as Auxiliary Drivers of Axial Lesions in the Complex Pathogenesis of Spondyloarthritis

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Conflict of interest: None

[Background] Spondyloarthritis (SpA) is a group of diseases mainly affecting enthesis and synovial membrane, and present with various manifestations. However, the pathogenesis associated with the individual domain is still not fully understood. We aimed to identify immunophenotypes associated with axial lesions. [Methods] We collected peripheral blood mononuclear cells from 77 cases with SpA, fulfilling Assessment of SpondyloArthritis international Society (ASAS) classification criteria. We performed single-cell RNA sequencing (scRNA-seq) and T cell receptor sequencing (scTCR-seq). Then we analyzed the data integrally with clinical information, by applying generalized linear mixed model. [Results] Patients with axial disease exhibited a significantly high abundance of plasmacytoid dendritic cells (pDCs, $P < 0.001$, OR = 2.28). Further stratified analysis indicated that HLA-B27-positive cases showed enhanced cell-cell interaction among $CD8^+$ T cells, myeloid DCs (mDCs), and pDCs. In contrast, HLA-B27-negative cases displayed a more heterogeneous immune landscape, and patients without psoriasis revealed a significant association between disease activity and $CD4^+$ T cells with high interferon-stimulated genes (ISG) ($P < 0.001$, OR = 2.01). TCR repertoire analysis demonstrated that ISG^{hi} $CD4^+$ T cells had the potential to differentiate into T helper 17 (Th17). Lastly, single-sample gene set enrichment analysis identified that pDCs were one of the major sources of type I interferon and could stimulate $CD4^+$ T cells. [Conclusion] scRNA-seq revealed that there were different pathologies of axial lesions depending on the HLA-B27 status. In HLA-B27-positive patients, pDCs showed traces to help mDC and $CD8^+$ T cell activation, and in HLA-B27-negative patients, pDCs were indicated to assist the differentiation of Th17 via the production of type I interferon. Stratification by HLA-B27 and focusing on type I interferon in HLA-B27-negative cases may lead to precision medicine.

ICW3-2

Prevalence and Drug Utilization Trends in Ankylosing Spondylitis in Korea: 2010-2023

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Conflict of interest: None

[Objectives] Ankylosing spondylitis (AS) is a radiologically confirmed form of axial spondyloarthritis. As definitions and treatments for AS evolve, understanding long-term trends in prevalence and management is essential. This study examines changes in AS prevalence, demographics, and treatment patterns in the Korean population from 2010 to 2023. [Methods] A population-based study was conducted using data from the National Health Insurance Database of Korea, covering 2010 to 2023. AS cases were defined by at least two ICD-10 codes and rare intractable disease registration codes, excluding cases with diagnoses of rheumatoid arthritis or systemic lupus erythematosus. Annual prevalence rates were calculated and standardized to the 2017 Korean population. Patient demographics and comorbidities were compared between 2010 and 2023. Longitudinal treatment trends were assessed in addition to analyses of first-, second-, and third-line targeted therapy choices. [Results] AS prevalence in Korea increased from 26.76 per 100,000 individuals in 2010 to 81.87 per 100,000 in 2023. The proportion of patients over 50 rose from 19.5% to 32.5%, and female representation increased from 17.9% to 24.0%. Comorbidities, such as metabolic syndrome and musculoskeletal complications, became more prevalent. The use of tumor necrosis factor-alpha inhibitors grew from 29.7% to 41.6%, while the use of conventional synthetic disease-modifying antirheumatic drugs declined. The introduction of interleukin-17 and Janus kinase inhibitors as second- and third-line therapies significantly expanded treatment options. [Conclusion] AS prevalence has markedly increased from 2010 to 2023, particularly among older adults and women. This trend, alongside rising comorbidities, underscores the need for integrated care. Future research should focus on optimizing treatment sequences and evaluating long-term outcomes in this evolving patient population.

ICW3-3

Incidence and risk of infections in patients with ankylosing spondylitis receiving biologic therapies: A prospective observational study using the KOBIO registry

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Conflict of interest: Yes

Objectives: This study aimed to assess infection occurrence of infection and risk factors among ankylosing spondylitis (AS) patients treated with biologics in a real-world setting. Methods: This prospective observational cohort study included AS patients from the Korean College of Rheumatology BIOlogics (KOBIO) registry who initiated or switched to biologic agent between December 2012 and July 2023. The primary outcome was the first occurrence of any infection, ranging from mild to severe, classified by organ system. The infection rate per 1,000 person-years (PY), with a 95% confidence interval were calculated using the Poisson distribution method. Cox proportional hazard regression models, adjusted for confounders, estimated hazard ratios for infection risk, considering only the first infection event. Results: This analysis included 2,129 patients with a total of 7,108 PY of follow-up. The predominant infections observed were of the upper and lower respiratory tract (25.9/1000 PY), followed by herpes zoster (HZ) (6.1/1000 PY). Multivariate Cox regression analysis revealed significant risk factors for infection, including age, ischemic heart disease, complicated diabetes, chronic kidney disease (CKD), and peripheral arthritis. In contrast, male sex was identified as a protective factor against the development of infections. Conclusions: The infection rate was 39 events/1,000 PY with respiratory tract infections being most common, followed by HZ. Significant risk factors included age, female sex, ischemic heart disease, complicated diabetes, CKD and peripheral arthritis for the occurrence of infection in patients with AS treated with biologics.

ICW3-4

Trained immunity enhances monocyte-T-cell pathogenic crosstalk in Ankylosing Spondylitis

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Conflict of interest: None

Objectives: Recent studies in infectious, cardiovascular and neurodegenerative diseases have established the presence of memory in innate immune cells. This "trained immunity (TI)" leads to an enhanced response to a second challenge. We asked if TI contributes to the pathology of Ankylosing Spondylitis (AS), a common form of inflammatory arthritis characterized by excessive myeloid and T-cell inflammation. **Methods:** Human peripheral blood mononuclear cells (PBMCs) from 67 AS patients were used in this study. Single-cell RNA sequencing (scRNA-seq), flow cytometry and enzyme-linked immunosorbent assay (ELISA) were used to investigate the outcome of T-cell and monocyte co-cultures. Small inter-

fering RNAs or inhibitors were used to study the function of genes. The knockdown efficiency was determined by quantitative PCR and western blotting. **Results:** We identify a monocyte subset that increases in AS patients, expands following COVID-19 vaccination, and exhibits transcriptional and functional features of TI. We find that both these trained monocytes in AS and β-glucan-trained monocyte-derived macrophages from healthy donors are hyper-responsive to T-cell-induced activation. Additionally, T cell-stimulated monocytes can act back on T-cells to promote Th17 responses. Lastly, we siRNA screen AS risk genes and identify ZC3H12C, ERN1 and IL1R1 as regulators of T-cell-induced monocyte activation. **Conclusions:** Our data provide strong evidence for the presence of trained immunity in monocytes from AS patients and showed for the first time that trained monocytes are hyper-responsive to T cell stimulation. Additionally, our data reveal the presence of a pro-inflammatory circuit initiated by T cell-induced activation of trained monocytes which then can act back to enhance Th17 responses. We also describe three AS-risk genes that contribute to the activation of monocytes by T-cells. These findings advance our knowledge in AS pathology provide new opportunities for therapeutic interventions.

ICW3-5

Effectiveness and safety of bDMARDs and JAK inhibitors for the treatment of PsA inadequate response to the first bDMARDs

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Conflict of interest: None

[Objectives] The EULAR recommendations for PsA have been updated in 2023 due to the accumulation of evidence on JAK inhibitors. In this recommendation, if the treatment goal cannot be achieved with the first bDMARD, switching from bDMARDS to another bDMARD of any class and switching to a JAK inhibitor considering safety are recommended in phase IV. However, which strategy shows better effectiveness in real-world clinical practice is unclear. In this study, we compared the effectiveness of switching to bDMARDs (TNF or IL-17A-inhibitors) and JAK inhibitors in cases of inadequate response to the first bDMARDS (TNF or IL-17A-i). [Methods] We compared the effectiveness and safety over a 52-week in patients with inadequate response to the first bDMARDs (TNF or IL-17A -i) and then switched to a JAK inhibitor (JAK group, n=15) or bDMARDS (bDMARDs group, n=26) as a second molecular targeted drug. The primary endpoint was the MDA achievement rate. Secondary endpoints were the retention rate/adverse events, the rate of DAPSA remission/low disease activity achievement rate, and the PASI100 achievement rate. [Results] There was no difference in the retention rate between the two groups (JAK group 86.7%, bDMARDs group 84.6%). Adverse events occurred in 26.7% (4/15) in the JAK group and 19.2% (5/26) in the bDMARDs group. DAPSA and PASI scores significantly decreased in both groups. The primary endpoint, the MDA achievement rate at week 52, after adjusting for patient background by PS-IPTW, was 60% in the JAK group and 80.0% in the bDMARDs group. The DAPSA remission/low disease activity achievement rate was 50.0/80.0% in the JAK group and 65.0/95% in the bDMARDs group. The PASI100 achievement rate was 88.9% in the JAK group and 62.5% in the bDMARDs group. [Conclusion] These results suggest that both JAK inhibitors and bDMARDs may be effective options as second treatment for PsA inadequate response to the first bDMARDs.

ICW4-1

Clinical efficacy of anifrolumab and its impact on peripheral blood immune phenotypes in SLE patients with minor flares after achieving LLDAS: LOOPS Registry and FLOW Study

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Conflict of interest: None

[Objectives] This study aimed to investigate the relationship between changes in immune phenotype and the efficacy of anifrolumab (AFM) in patients with systemic lupus erythematosus (SLE) who experienced minor flares after achieving LLDAS. [Methods] Patients with SLE who experienced a minor flare based on the revised SELENA flare index after achieving LLDAS were divided into two groups: Those who received standard therapy (SoC, n=18) with increased glucocorticoid (GC) doses or additional immunosuppressants, and those receiving additional AFM only (n=50). Effectiveness and safety were compared 26 weeks after intensification using propensity score-based inverse probability of treatment weighting (PS-IPTW). Peripheral blood immune phenotypes were analyzed following the NIH/FOCIS standardized protocol. [Results] After PS-IPTW adjustment, baseline characteristics were comparable between groups. The 26-week persistence rate of AFM was 90.0%. The LLDAS achievement rate was significantly higher in the AFM group (AFM: SoC=87:33%, $p<0.01$). The GC doses ($p<0.01$) and the incidence of infections ($p=0.04$) were lower in the AFM group. There were no baseline differences in immune phenotypes between the groups. At 26 weeks, both groups exhibited a decreased proportion of plasmocytes. In the AFM group, the proportions of activated Th17 cells ($p=0.01$), Tfh cells ($p<0.01$), and activated Tfh cells ($p=0.02$) decreased from baseline levels. Among the patients in the AFM group, those who achieved LLDAS (n=32) showed a significant reduction in the proportion of Tfh cell ($p<0.01$), activated Tfh cell ($p=0.01$), and activated Th17 cell ($p<0.01$), which was not observed in those who did not achieve LLDAS (n=18). [Conclusion] AFM may control disease activity in patients with SLE who experience minor flares after achieving LLDAS without requiring increased doses of immunosuppressants or GCs, potentially by reducing the numbers of plasmocytes, activated Th17 cells, Tfh cells, and activated Tfh cells.

ICW4-2

Impact of belimumab on immune phenotypes in patients with active lupus nephritis: LOOPS registry, FLOW study

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Conflict of interest: None

[Objectives] Belimumab (BEL), a human monoclonal antibody against soluble B-cell-activating factor (BAFF), is effective against lupus nephritis (LN). This study aimed to reveal how BEL alters the peripheral blood immune phenotype and to identify the immunophenotypic characteristics suitable for BEL in active LN patients. [Methods] We included patients with ISN/RPS class III or IV LN who received standard of care (SoC: glucocorticoid (GC) and either mycophenolate mofetil or cyclophosphamide). The efficacy and safety of BEL combined with SoC (BEL group, n=38) were compared with SoC alone (SoC group, n=35). We performed peripheral blood immunophenotyping by the NIH/FOCIS protocol to compare LN patients (n=73) with age- and sex-matched healthy controls (HC, n=120), and evaluated pre-and post-treatment differences in LN patients. [Results] Baseline characteristics were not significantly different between groups. The BEL group showed a significantly higher rate of complete renal response (CRR), along with lower GC dosage and SLICC Damage Index at 52 weeks. Immunophenotyping revealed that, compared to HC, LN patients had significantly higher percentages of CD3+CD8+ CD38+HLA-DR+ activated cytotoxic T cells, CD3-CD19+CD20+CD27-IgD- double-negative (DN) B cells and CD3-CD19+CD27+CD20-CD38+ plasmocytes. The BEL group had significantly higher reduction rates of DN B cells and plasmocytes at 52 weeks than the SoC group. In the BEL group, patients who achieved CRR had a significantly higher percentage of pre-treatment plasmocytes than those who did not. No immunopheno-

typic characteristics were associated with CRR in the SoC group. [Conclusion] In induction therapy for active LN, BEL reduced DN B cells and plasmocytes. BEL may be particularly effective in patients with increased pre-treatment plasmocytes. Given that BAFF promotes plasmocyte differentiation, increased plasmocytes suggest elevated BAFF levels, which may explain the enhanced effectiveness of anti-BAFF therapy.

ICW4-3

Safety and Efficacy of Anifrolumab in Patients with Systemic Lupus Erythematosus (SLE) who Have Not Achieved LLDAS from LOOPS registry

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Conflict of interest: None

[Objectives] The achievement and maintenance of lupus low disease activity state (LLDAS) is essential a critical goal in the treatment of systemic lupus erythematosus (SLE). We analyzed the safety and efficacy of anifrolumab (ANF) in patients with SLE who have not achieved LLDAS. [Methods] This study enrolled 101 patients who had not achieved LLDAS (including 65 patients with minor flares as defined in the revised SELENA-Flare Index after LLDAS achievement), 45 patients who were treated with glucocorticoids (GC) or immunosuppressants were assigned to standard of care [SoC] group, and 56 patients who were started on ANF assigned to ANF group. The primary endpoint was LLDAS achievement rate at 52 weeks, compared between groups after adjusting with inverse probability of treatment weighting using propensity score (PS-IPTW). [Results] After PS-IPTW adjustment, there was no difference in patient background (SLE disease activity index [SLEDAI] SoC: ANF=5.0±3.4:5.3±3.4, p=0.520). The retention rate for ANF at week 52 was 85.7% (48/56). The LLDAS re-achievement rate after 52 weeks was higher in the ANF group than the SoC group (SoC: ANF=49.8:87.6%, p<0.0001). The Definition of Remission in SLE rate was also higher in the ANF group (SoC: ANF=19.4:36.6%, p=0.0068), and the GC dose at week 52 was lower in the ANF group (SoC: ANF=3.9±4.0:2.3±4.5 mg/day, p=0.0083). 4 patients in the ANF group discontinued GC. The incidence of adverse events was significantly lower in the ANF group (p=0.0014), particularly infection rates (p=0.0047). In the SoC group, the LLDAS achievement rate at 52 weeks was low in cases with SLEDAI≧6 when treatment was intensified (SLEDAI≧6: SLEDAI ≦5=25.0:58.6%, p=0.027), whereas in the ANF group, that was similar regardless of the baseline SLEDAI (SLEDAI≧6: SLEDAI≦5=90.6%: 73.9%, p=0.0984). [Conclusions] In patients with SLE who have not achieved LLDAS, early administration of ANF may improve disease activity safely without requiring increased GC dose or immunosuppression.

ICW4-4

Early combination with belimumab leads to earlier remission and lower steroid use in lupus nephritis patients: data from a real-life multicentric study

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Conflict of interest: None

[Objectives] We aim at investigating early renal response of patients with Lupus Nephritis (LN) treated either with traditional immunosuppression alone or with early combination treatment with belimumab. [Methods] Adult patients with a biopsy-proven LN classified according to the ISN/RPS 2003 criteria and receiving belimumab atop standard of care within 6 months from LN onset from lupus-referral centers in Italy (belimumab cohort) were compared to a well-characterized LN cohort followed-up from 1990 to 2016, whose biopsies were reevaluated according to the 2003 ISN/RPS criteria (historical cohort). Serological and treatment data were recorded at baseline and throughout the follow-up. Rates of renal response (EULAR/EDTA criteria) were assessed at 6 and 12 months. T-test, X^2 test and Mann-Whitney U test were used for statistical analysis, before and after propensity score matching. [Results] 82 LN patients were identified for the belimumab cohort and compared with 303 LN patients of the historical cohort. Time from first signs of kidney involvement to renal biopsy was significantly reduced in the belimumab cohort (median, IQR: 20, 0-89 vs. 81, 14-254, p<0.001). A significantly higher proportion of patients in the belimumab cohort achieved complete renal response (CRR) at 6 months (38.9% vs 21.6%, p<0.001), whereas rates of both partial (PRR) or CRR became comparable at 1 year (88.2% vs 84.5%, p=0.637). Notably, patients achieving CRR in the historical cohort were taking significantly higher doses of prednisolone at the time of remission (12.28 mg±8.69 vs 7.45 mg±4.75, p<0.001). Results were confirmed after propensity score matching was carried out considering treatment, baseline proteinuria and histological class. [Conclusion] Over the years, time from first LN recognition to kidney biopsy has significantly decreased. Early combination therapy with belimumab portends a significantly faster renal response and is associated with decreased steroid intake at CRR.

ICW4-5

The effectiveness of anifrolumab to systemic lupus erythematosus in single-center retrospective study

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Conflict of interest: None

[Objectives] Anifrolumab (ANI), a human monoclonal antibody to type I interferon receptor subunit 1, was approved for systemic lupus erythematosus (SLE) based on the results of clinical trials, TULIP-1 and -2. However, we have not demonstrated the effectiveness of ANI in the real-world data and in the patients previously treated by belimumab. To investigate it, we performed this study. [Methods] This study is a single-center retrospective study using the 21 lupus patients diagnosed by 2019 EULAR/ACR criteria and treated by ANI in Tohoku University hospital

from 1st January 2018 to 20th February 2024. The patients were assigned to the continuation-group and the discontinuation-group for 12 months after an initial administration. These groups demonstrate the comparable background such as complications and autoantibody positivity. Only the prescription rate of hydroxychloroquine was higher in the continuation-group than in the discontinuation-group. [Results] ANI was selected for the purpose of the de-escalation of prednisolone, the treatment for fatigue and the psychiatrichistory in addition to control of disease activity. Hypocomplementemia, thrombocytopenia and cutaneous complications were significantly improved, and the doses of prednisolone were also significantly reduced in the continuation-group. Additionally, we investigated if ANI could improve disease activity in the patients previously treated by belimumab. Cutaneous complications and arthritis were improved by ANI in some patients. [Conclusion] This study confirmed the effectiveness of ANI to SLE, especially in cutaneous complications, hypocomplementemia and thrombocytopenia. Moreover, ANI could be selected for the patients resistant to belimumab, especially with cutaneous complications and arthritis. In this study, retention rate of ANI was lower than previous reports. That was probably because induction of ANI was late to suppress disease activity and to prevent the flare of disease.

ICW5-1

Effectiveness and safety of ozoralizumab (OZR) for the treatment of RA in clinical practice -FIRST registry-

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Conflict of interest: None

[Objective] In Japan, OZR, which does not have an Fc region, has been approved for insurance coverage as the sixth TNF inhibitor for RA. We evaluated the effectiveness and safety of OZR for RA in clinical practice and assessed the relationship between serum RF value and effectiveness. [Methods] The effectiveness and safety of OZR (OZR group, n=58) and Adalimumab (ADA group, n=64) were compared. The primary endpoint was the CDAI at week 24. Secondary endpoints were the retention rate/adverse events during the observation period and the achieving rate of low disease activity (LDA) at weeks 2 and 24. As an exploratory endpoint, the rate of achieving LDA after 24 weeks was compared between the OZR group and the ADA group in the low RF group (RF<45 IU/mL (less than 3 times the reference value)) and high RF group (RF≧45 IU/mL (higher than 3 times the reference value)), respectively. Selection bias was minimized for patient background using inverse probability weighting using propensity scores (PS-IPTW). [Results] The retention rate was 89.7% in the OZR group and 90.6% in the ADA group. Adverse events occurred in 6.9% and 9.4% of each group, respectively. Adjusting for patient background, the primary endpoint CDAI at week 24 was 7.5±10.3 (OZR group) and 9.3±13.8 (ADA group) (p=0.32), with no significant difference between groups. Both groups showed a significant CDAI decrease. The week 24 low disease activity (LDA) rate was 79.4% (OZR group) and 66.9% (ADA group) (p=0.07), and at week 2, 63.8% (OZR group) and 47.1% (ADA group) (p=0.06). In ADA group, week 24 LDA rates were 73.1% (low RF) and 61.2% (high RF); in OZR group, 75.9% (low RF) and 81.7% (high RF), unaffected by RF. Univariate analysis identified OZR as a predictor for LDA in high RF (OR 2.83, 95% CI 1.19-6.71). [Conclusion] The effectiveness and safety of OZR therapy for RA in clinical practice were demonstrated. OZR may be a more effective treatment option in cases with high RF levels.

ICW5-2

Comparison of the Efficacy and Safety of Certolizumab Pegol and Interleukin-6 Inhibitors in Patients with Rheumatoid Factor-High Rheumatoid Arthritis: Insights from the FIRST Registry

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Conflict of interest: None

[Objectives] Although the efficacy of TNF inhibitors (TNFi) decreases in patients with rheumatoid factor (RF)-high rheumatoid arthritis (RA), that of certolizumab pegol (CZP), which lacks the Fc portion, may not be affected. The relationship between RF levels and efficacy of IL-6 inhibitors (IL-6i) remain unclear. This study aimed to clarify the differences in the efficacy and safety between CZP, other TNFi, and IL-6i in patients with RF-high RA. [Methods] Patients with RA registered in the FIRST registry (n=3756) were divided according to the RF-level quartiles, and the highest quartile (Q4, RF level≧179.8 IU/mL) was defined as the RF-high group. We analyzed the relationship between the baseline RF level and treatment modification due to inadequate response within 52 weeks in patients receiving TNFi (n=2567). Next, we compared the efficacy and safety of CZP and IL-6i in patients with RF-high RA using propensity score-based inverse probability of treatment weighting (PS-IPTW). [Results] Among patients receiving TNFi, multivariate analysis confirmed that high baseline RF levels (Q4) were significantly associated with an inadequate response (p=0.04). For patients receiving CZP (n=532), CDAI remission rates at 52 weeks were not significantly different between the RF-high (Q4) and non-RF-high groups. In contrast, the CDAI remission rate at 52 weeks was higher in the non-RF-high group in patients receiving IL-6i (n=958) (p<0.01). After PS-IPTW adjustment of baseline patient characteristics for patients with RF-high (Q4) RA, the 52-week CDAI remission rate was significantly higher in the CZP group (n=96) than in the IL-6i group (n=258) (CZP: IL-6i=34:22 (%), p=0.02), with no significant difference in the incidence of serious adverse events. [Conclusion] The efficacy of TNFi and IL-6i is reduced in patients with RF-high RA. CZP demonstrated higher efficacy than IL-6i in patients with RF-high RA, suggesting that CZP may be more suitable for patients with RF-high RA.

ICW5-3

Single nucleotide polymorphisms in methotrexate metabolism affect methotrexate polyglutamates concentrations and its efficacy and safety in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Methotrexate (MTX) is the anchor drug in the treatment of rheumatoid arthritis (RA), but its efficacy and safety vary among individuals. The variation can be partly ascribed to the metabolism of MTX. This study aims to investigate the relationship between MTX-polyglutamate (PG) concentrations, which reflect intracellular MTX levels, and single nucleotide polymorphisms (SNPs) in enzymes involved in MTX pharmacokinetics. [Methods] Patients with RA who had received the same dose of MTX for at least 4 months at Keio University Hospital were included. Erythrocyte MTX-PG concentrations were measured by fractions PG1-5 using liquid chromatography. Twelve SNPs in enzymes related to MTX pharmacokinetics, including RFC 80G>A, ABCB1 1236C>T, and GGH 16T>C, were genotyped. The association between SNPs and MTX-PG concentrations was evaluated using multiple regression analysis. [Results] A total of 559 RA patients were enrolled. The mean age was 61.4 years, with 480 females (85.9%), and the mean disease duration was 112.6 months. The mean MTX treatment duration was 65.2 months, and the mean MTX dose of 8.66 mg/week. The median DAS-28 CRP was 1.71. Sixty patients (10.7%) and 289 (51.7%) were treated with concomitant glucocorticoids and biological agents, respectively. Multiple regression analysis revealed a tendency for correlation between MTX-PG concentrations and RFC1 80GA (p=0.334), ABCB1 1236 TT (p=0.0252), and TYMS 5'UTR 2R/3R (p=0.293). Some SNPs tended to be related with the efficacy and safety of MTX. [Conclusion] Our study shows the association of

SNPs in MTX metabolism with MTX-PG concentrations in RA patients. Identification of SNPs may help predict the optimal MTX dosage for individual patients, contributing to the advancement of personalized medicine.

ICW5-4

Age of onset of rheumatoid arthritis and radiographic changes (Encore presentation)

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Conflict of interest: Yes

[Objectives] The association between age of rheumatoid arthritis (RA) onset and joint erosions remains unclear. We investigated the effects of age of RA onset on incident joint erosion and the progression of radiographic findings. [Methods] Patients diagnosed with RA within 2 years of enrollment in a large single-center RA registry were included. The age of RA onset was categorized into young- (=< 44 years of age), middle- (45-65), and late-onset (>= 66). Modified total Sharp scores (mTSS) were obtained at baseline, year 2, and year 5, and incident joint erosion was defined as an erosion score greater than 0. We assessed the adjusted odds ratio (OR) of incident joint erosions within 5 years of enrollment and the adjusted change in mTSS by age category during a 5-year follow-up period. [Results] Among 1,581 participants with RA, 284 patients within 2 years of RA diagnosis were identified. The adjusted OR of incident joint erosion in the middle-, OR 4.0 (95% CI 2.2-7.5), and the late-onset groups, 8.2 (95% CI 3.6-19.2), were elevated compared with the young-onset group. Compared with the young-onset group, the adjusted changes in mTSS in the middle-group, 2.8 (95% CI 0.20-5.4), and the late-onset groups, 1.9 (95% CI -0.26-4.1), were elevated. [Conclusion] The odds of incident joint erosion and change in the mTSS were increased among patients with RA onset at later ages. These results suggest that the age of onset may define different RA phenotypes.

ICW5-5

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

[Objectives] 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 49 RA patients who initiated JAK inhibitor or CTLA4-Ig therapy at our department and Sasebo Central Hospital between July 2016 and January 2022. All patients underwent plain radiography of both hands and feet and plain chest CT scans before and after treatment. We compared the progression of the modified total Sharp score (mTSS) (ΔmTSS) and the progression of the Ichikado CT score (ΔCT score) before and after treatment initiation. In addition, we examined the correlations between these two variables. [Results] Of the 49 patients included in the study, 33 were female, with a median age of 70 years at the start of treatment. 44 were RF positive and 41 were ACPA positive. The CT score was 127.5, and the mTSS was 23. 27 patients in the JAKi group and 22 patients in the CTLA4-Ig group. Correlation analysis revealed no significant association between ΔmTSS and ΔCT scores in all patients (correlation coefficient r = -0.067). However, a significant correlation was observed between the baseline CT score (inflammatory component) and baseline mTSS erosion (r = 0.41, p = 0.0035). In addition, DAS-ESR at 3 months after treatment correlated with the progression of the CT score of consolidation (r = 0.42, p = 0.022) and the CT score of honeycombing (r = 0.38, p = 0.040). [Conclusion] We did not find a direct correlation between the progression of bone destruction and the progression of ILD in patients with RA treated with JAK inhibitors or CTLA4-Ig. Nonetheless, a notable association was found between 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.

ICW6-1

The involvement of IGHV4-34 in the pathogenesis of systemic lupus erythematosus

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Conflict of interest: Yes

[Objectives] Systemic lupus erythematosus (SLE) is characterized by the production of autoantibodies. The diversity of B cell receptors (BCRs) is generated by V (D) J recombination, class switch, and somatic hypermutation (SHM). However, the mechanisms underlying the production of autoantibodies in SLE are not fully elucidated. We conducted a bulk RNA-seq and multimodal single-cell analyses to elucidate the process, especially focusing on IGHV4-34, which is known as one of the autoreactive BCR. [Methods] B cells from peripheral blood of 136 SLE patients were sorted and the frequency of clonotypes that utilize IGHV4-34 was calculated by bulk RNA-seq. The interactions between IGHV4-34 usage and clinical features were analysed. Moreover, peripheral blood mononuclear cells from 47 SLE patients and 23 healthy controls were subjected to scRNA-seq, CITE-seq, and BCR-seq. The characteristics of BCRs in SLE were analyzed with a focus on isotype and the amount of SHM. [Results] IGHV4-34 usage in unswitched memory (USM) B cells had a significant association with disease activity and complement level decrease. Among those who achieved LLDAS under tacrolimus treatment, patients with high IGHV4-34 usage in USM B cells had a higher flare rate. ScRNA-seq revealed that memory B cells in SLE exhibited a significantly reduced amount of SHM, particularly in IgM isotype. Strikingly, IGHV4-34 showed mutation of germline in IgA/IgG isotypes, but was conserved in IgM isotype. The proportion of $IgM^+IGHV4\text{-}34^+$ cells correlated with decreased complement levels. [Conclusion] IGHV4-34 usage in USM B cells could be a biomarker of disease activity and flare risk. B cells from SLE patients showed a decrease in the amount of SHM and preferentially differentiated keeping the IgM isotype. Autoreactive germline sequences were preserved in IgM isotype cells of SLE. These findings suggest the pivotal role of $IGHV4\text{-}34^+$ B cells in the pathogenesis of SLE and highlight them as a potential novel therapeutic target.

ICW6-2

Single-cell RNA-seq-based analysis of newly identified age-associated ThA cells in the pathogenesis of systemic lupus erythematosus

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Conflict of interest: None

[Objectives] We recently identified a novel $CD4^+$ T cell subset, age-associated helper T (ThA) cells, which are associated with aging and autoim-

mune diseases such as SLE. ThA cells represent a unique subset with both cytotoxic activity and B cell helper function. Given that ThA cells do not express CXCR5, suggesting they may be involved in extrafollicular humoral immune responses; however, their antigen specificity and the relationship with atypical B cells remained unclear. [Methods] PBMCs were isolated from the peripheral blood of 51 SLE patients and 24 healthy individuals, and single-cell RNAseq, CITEseq, and T cell receptor (TCR) seq were performed. Integrated analysis with clinical information and TCR repertoire analysis using IEDB were conducted. An ELISPOT assay was performed to investigate the antigen reactivity. [Results] Clusters of ThA cells and atypical B cells were identified from scRNA-seq. ThA cells showed a positive association with aging, and Mixed-effects association testing for single cells (MASC) analysis showed that ThA cells are involved in SLE disease activity. The ratio of ThA cells was positively associated with the ratio of atypical B cells and SLEDAI-2K. TCR repertoire analysis showed that ThA cells were clonally expanded, and the repertoire was significantly skewed. The human cytomegalovirus (HCMV) antigen was suggested as the corresponding antigen of ThA cells. When ThA cells and antigen-presenting cells were co-cultured and stimulated with HCMV peptide, ThA cells highly produced IL-21, IFN-γ, and granzyme. [Conclusion] This study demonstrated that ThA cells are involved in both atypical B cells and SLE disease activity. Furthermore, ThA cells exhibited strong reactivity to the HCMV antigen inferred from TCR repertoire analysis. These findings suggest that ThA cells may contribute to the pathogenesis of SLE through antigen mimicry, indicating a potential avenue for understanding the disease mechanism and developing novel therapeutic approaches.

ICW6-3

Clinical Relevance of the Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) in Predicting Lupus Outcomes: A 5-Year Longitudinal Cohort Study

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Conflict of interest: None

[Objectives] Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) is a newly developed tool for assessing disease activity in SLE patients. Despite external validation in diverse populations, the clinical utility of SLE-DAS remains underexplored. This study aims to assess the prognostic significance of SLE-DAS by comparing it with the SLE Disease Activity Index (SLEDAI-2K) over a 5-year follow-up period among Korean SLE patients. [Methods] We enrolled 199 SLE patients from the Korean Lupus Network (KORNET) registry. Demographic data, clinical manifestations, laboratory findings, Physician Global Assessment (PGA), SLEDAI-2K, SLICC damage index (SDI), SF-36, and Beck Depression Inventory (BDI) were assessed at enrollment and annually for 5 years. Longitudinal associations between disease activity indices and clinical outcomes were analyzed using generalized estimating equations (GEEs). [Results] During the follow-up period, 27.1% of patients were in remission, 50.3% had mild activity, and 22.6% had moderate/severe activity. Spearman coefficients between SLE-DAS and SLEDAI-2K ranged from 0.889 to 0.907 across the 1st to 5th years. Changes in SLE-DAS were significantly associated with disease flare (ß=0.435, 95% CI: 0.037~0.832, P=0.032) and PGA (ß=1.399, 95% CI: 0.608~2.190, P<0.001), but not with SDI, SF-36, or BDI. On the other hand, changes in SLEDAI were significantly associated with PGA (ß=0.653, 95% CI: 0.091~1.215, P= 0.013), but not with flare, SDI, SF-36, or BDI. [Conclusion] Although SLE-DAS exhibits superior predictive performance for disease flare compared to SLEDAI-2K, both indices demonstrate similar prognostic value in SLE patients.

ICW6-4

Development of a Semi-Quantitative Lupus Anticoagulant Assay and Its Application in Thrombosis Risk Assessment for Antiphospholipid Syndrome

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Conflict of interest: None

[Objectives] The management of antiphospholipid syndrome (APS) is based on risk stratification using antiphospholipid antibody (aPL) profiles and titers. However, the absence of quantitative lupus anticoagulant (LA) measures remains a limitation regarding management of the patients with APS. We aimed to develop a semi-quantitative method for measuring LA (SQ-LA) and to evaluate its efficacy in assessing the risk for thrombosis in patients with APS. [Methods] The SQ-LA method was developed using a mouse monoclonal phosphatidylserine dependent anti-prothrombin antibody (aPS/PT), designated 231D which has LA activity. The clotting times (activated partial thromboplastin time (aPTT) and dilute Russell's viper venom time (dRVVT)) were measured in normal plasma spiked with different concentrations of 231D and in a mixture of normal and patient plasma. The prolongation of clotting time was expressed as anticoagulant units (ACU), with 1 μg/mL of 231D corresponding to 1 ACU. A retrospective cohort study was conducted to evaluate the correlation between ACU and thrombosis risk factors, clinical characteristics, aPL profiles and events defined as thrombotic recurrence, bleeding and mortality. [Results] This study comprised 119 APS patients. The patients positive for both anti-cardiolipin antibodies and anti-β2 glycoprotein I antibodies had significantly higher LA titers than those positive for neither or only one of these antibodies (aPTT (ACU mean ±SD): 30.3 ±3.5 vs 19.0 ±2.3, p <0.008; dRVVT (ACU mean ±SD): 27.7 ±3.1 vs 15.8 ±1.9, p <0.0005). Additionally, patients who experienced events showed higher LA titers compared to those without events (aPTT (ACU): 27.9 ±3.2 vs 19.0 ±2.4, p <0.04; dRVVT (ACU): 24.8 ±2.63 vs 16.1 ±2.2, p <0.002). A statistically significant difference was unobservable through conventional LA tests (qualitative test). [Conclusion] We successfully established a method to quantify LA. SQ-LA method may be useful for the risk assessment in patients with APS.

ICW6-5

Single-cell RNA sequencing reveals cross-disease characterizations of treatment-naïve autoimmune diseases and distinct interferon signatures in systemic lupus erythematosus

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Conflict of interest: None

Objectives: Autoimmune diseases are characterized by immune dysregulation and can vary widely in their pathogenesis. This study uses single-cell RNA sequencing (scRNA-seq) to explore the distinct mechanisms in systemic autoimmune diseases like systemic lupus erythematosus (SLE) and inflammatory arthritis such as rheumatoid arthritis (RA) and spondyloarthritis. Methods: We collected peripheral blood mononuclear cells (PBMCs) from 14 treatment-naïve patients with autoimmune diseases-6 with RA, 4 with psoriatic arthritis (PsA), 4 with SLE and 5 healthy controls. The samples were analyzed using the 10x Genomics platform for scRNA-seq. Results Analyzing approximately 130,000 cells, we identified 10 major clusters with 30 subtypes. CD4+ effector memory cells were significantly higher in RA and PsA patients compared to healthy controls, but not in SLE. CD14+CD16+ monocytes increased significantly only in SLE. Autoimmune disease patients showed a reduced proportion of unswitched memory B cells and γδT cells, most markedly in SLE, followed by RA. Gene Set Enrichment Analysis (GSEA) indicated a significant upregulation of inflammatory response genes in all patient groups, with the highest increase in SLE. Type I interferon response genes, especially IFNAR1/2, were significantly upregulated in SLE, primarily in monocytes, dendritic cells, natural killer cells, and plasma cells. Type II interferon response genes increased significantly in SLE, mildly in RA, and not in PsA. Transcription factor analysis underscored the key role of IRF7-STAT1 in the type I interferon response in SLE. Conclusions Autoimmune diseases exhibit unique immune cell profiles at the single-cell level. SLE shows distinct interferon signatures regulated by IRF7-STAT1. The exclusive upregulation of IFNAR1/2 in SLE suggests that type I interferon receptor antagonists may have limited efficacy in inflammatory arthritis but could be effective in SLE.

ICW7-1

Risk prediction model for relapse of interstitial lung disease with anti-aminoacyl-tRNA synthetase antibodies in multicenter MYKO cohort study

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Conflict of interest: None

[Objectives] To establish risk prediction model for relapse of interstitial lung disease (ILD) complicated with anti-aminoacyl-tRNA synthetase (ARS) antibodies (anti-ARS-ILD) who were treated with prednisolone and calcineurin inhibitors. [Methods] Among patients diagnosed as idiopathic inflammatory myopathy (IIM) in our multicenter study between 1991 and 2024, we extracted patients diagnosed as anti-ARS-ILD and treated with prednisolone and calcineurin inhibitors (combination therapy) as a remission induction therapy. We examined patients who experienced ILD relapse after combination therapy. We explored the risk factors for predicting ILD relapse in these patients by comparing the initial clinical and laboratory findings between the relapsed and non-relapsed groups. [Results] Of 487 patients diagnosed as IIM, one hundred one patients with anti-ARS-ILD were extracted. Thirty eight patients (37.6%) relapsed during a mean follow-up of 2.0 years. Multivariate Cox regression analyses identified the presence of acute/subacute (A/S)-ILD, higher serum aldolase (ALD) and lower percent forced vital capacity (%FVC) and lower percent diffusing capacity of carbon monoxide (%DLco) on admission as risk factors for relapse in patients with anti-ARS-ILD. Using the receiver operating curve analysis, ALD≧5.7 U/L, %FVC≦77%, and %DLco≦60% were determined as the cut-off levels for indicating a poor prognosis. The 5-year relapse rate was significantly higher in patients with A/S-ILD, serum ALD≧5.7 U/L, % FVC≦77%, or %DLco≦60% than in those without these parameters. (P=0.0005, 0.007, <0.0001, 0.0025, respectively) A risk prediction model (RPM) based on these stratified patients into low, moderate, and high-risk relapse groups. [Conclusion] The presence of A/S-ILD, higher serum ALD and lower %FVC and %DLco are useful indicators for predicting anti-ARS-ILD relapse. Our multicentre cohort study indicated that the RPM is a useful predictor of ILD relapse in patients with anti-ARS-ILD.

ICW7-2

Naive B cells as key pathogenic contributors to interleukin-6 production in idiopathic multicentric Castleman's disease

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Conflict of interest: None

Objectives: Idiopathic multicentric Castleman's disease (iMCD) is an immune-mediated lymphoproliferative disorder characterized by the central role of interleukin (IL)-6 in its pathogenesis. However, the specific lymphocyte subsets responsible for IL-6 production remain unidentified. This study aimed to identify the pathogenic lymphocyte subsets that produce IL-6 in iMCD. **Methods:** We collected fresh whole blood samples from active, treatment-naive patients with iMCD (n=4), IgG4-related disease (n=24), and age- and sex-matched healthy controls (n=24) to perform a comprehensive flow cytometric analysis of 56 immune cell subsets. Additionally, we conducted a longitudinal analysis of immune cell subsets in iMCD following monotherapy with tocilizumab. For immune cell subsets that showed specific changes in iMCD, we assessed their IL-6 production capacity using intracellular staining. We also evaluated IL-6 production in affected lymph nodes of iMCD using immunohistochemistry. **Results:** Both iMCD and IgG4-related disease share elevated serum IgG4 levels and increased plasmocytes. However, comprehensive immune cell subset analysis revealed a specific increase in naive B cells in iMCD, while Tfh and Tph cells were uniquely elevated in IgG4-related disease. In iMCD, following tocilizumab treatment, improvements were observed in anemia, elevated inflammatory markers, hypergammaglobulinemia, and increased plasmocytes; however, serum IL-6 levels and naive B cell counts remained elevated. Evaluation of IL-6 production capacity in naive B cells showed that those derived from iMCD exhibited higher IL-6 production compared to healthy controls, although there was no difference in IL-6 receptor expression. Furthermore, naive B cells and plasma cells in the affected lymph nodes of iMCD were found to produce IL-6. **Conclusion:** Naive B cells were identified as pathogenic lymphocytes that produce IL-6 in iMCD.

ICW7-3

Granulomatosis with polyangiitis (GPA) associated with MPO-ANCA and PR3-ANCA exhibits distinct clinical courses - Data from the REVEAL cohort

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Conflict of interest: None

[Objectives] To identify differences in the clinical characteristics of myeloperoxidase (MPO)-ANCA and proteinase 3 (PR3)-ANCA positive granulomatosis with polyangiitis (GPA) in Japan. [Methods] Eighty-four patients with GPA, registered in the Kansai multicenter REVEAL cohort by April 2024, were included. GPA diagnoses were based on Watts' algorithm or the 2022 ACR/EULAR classification criteria. Patient backgrounds and clinical courses were retrospectively evaluated, with a particular focus on comparing MPO-ANCA-positive (MPO-GPA) and PR3-ANCA-positive (PR3-GPA) patients. Statistical analyses included the Mann-Whitney U test and Fisher's exact test. Recurrence rates were compared using the log-rank test, while mortality rates were assessed using Cox proportional hazards analysis. [Results] The cohort included 24 MPO-GPA patients, 42 PR3-GPA patients, and others with double-positive or double-negative ANCA. Compared to PR3-GPA, MPO-GPA patients were older (median age 77 vs 64, p=0.012) and more frequently female (66% vs 35%, p<0.001). At disease onset, MPO-GPA patients showed higher neutrophil counts (median 10,727 vs 7,456, p=0.011) and CRP levels (10.86 vs 2.46, p=0.002). MPO-GPA was associated with more frequent rapidly progressive glomerulonephritis and sensory peripheral neuropathy, while ear, nose, and throat symptoms were less common (p=0.023, 0.021, 0.041). The Birmingham Vasculitis Activity Score at disease onset was higher in MPO-GPA (p=0.011). Medication use was similar between groups, though relapses tended to be more frequent in PR3-GPA (p=0.074). Cox regression analysis revealed a hazard ratio of 8.6 for all-cause mortality in PR3-GPA. [Conclusion] Clinical characteristics of MPO-GPA at disease onset resembled those of microscopic polyangiitis, and PR3-GPA was associated with higher mortality rates. These findings suggest that MPO-GPA presents a distinct clinical course from PR3-GPA.

ICW7-4

Achievement and Usefulness of Intermediate Treatment Targets for Still's Disease Proposed by EULAR/PReS

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Conflict of interest: Yes

[Objectives] Intermediate treatment targets in Still's disease have been proposed by European alliance of associations for rheumatology (EU-

LAR) and paediatric rheumatology European association (PReS) in 2024. This study aimed to evaluate the utility of the targets in clinical practice. [Methods] Consecutive patients with adult-onset Still's disease based on the Yamaguchi's criteria who visited our hospital from April 2012 until May 2024 were retrospectively reviewed. We assessed the achievement rates of the treatment targets, and their association with long-term outcomes. [Results] Sixty-two patients were included in the analysis. The mean age was 50.8±19.5 years, and 47 (75.8%) were female. The recommended treatment targets were achieved in 67.2% at day 7, 61.1% at week 4, 3.3% at month 3, and 1.7% at month 6. Failure to achieve targets at month 3 and 6 was mainly due to glucocorticoid usage. During the median observational period of 7.1 years, patients who achieved clinically inactive disease at month 6 have fewer recurrence thereafter (P=0.01). Successful glucocorticoid withdrawal was associated with tocilizumab use at month 6 (P=0.04). [Conclusion] The EULAR/PReS intermediate treatment targets for Still's disease are useful in the management in clinical practice of adult-onset Still's disease.

ICW7-5

Generalized joint hypermobility diagnosis in children: A comparison between Shiari-Javadi criteria and Beighton criteria

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Conflict of interest: None

Objectives: Hypermobility Spectrum Disorder (s) (HSDs) is a clinical condition characterized by an increased laxity of joints during passive and dynamic movement associated with symptoms like pain. The prevalence of HSDs is different in various populations, and it has been estimated to be around 10-20% in the communities. Recently, the Beighton criteria, which aims to prevent misdiagnosis of joint hypermobility in children, has been revised. In this study, the newly designed Shiari-Javadi criteria were compared with the Beighton criteria in school-age children. **Methods:** A total of 480 primary school students aged between six and thirteen were enrolled in a descriptive-observational study. A two-stage examination was conducted, examining all cases based on both Beighton and Shiari-Javadi criteria for generalized hypermobility. All hypermobile cases were then assessed for HSDs using the Brighton criteria. **Results:** The study included a total of 480 students. In both criteria, a score of more than or equal to 6 was considered indicative of generalized hypermobility. Based on these criteria, 39.2% and 46% of children were found to be hypermobile using the Beighton and Shiari-Javadi criteria, respectively. There was a significant correlation between hypermobility, age, and gender. Data analysis showed a high association between Beighton and Shiari-Javadi criteria in terms of sensitivity and specificity. According to the Beighton and Shiari-Javadi criteria, 11.2% and 11.3% of children were diagnosed with HSDs, respectively. **Conclusion:** The results of the study revealed that the Shiari-Javadi criteria were more accurate in diagnosing hypermobility in children. Additionally, the new criteria were seen to be more practical, convenient and efficient.

ICW8-1

T cell plasticity in systemic lupus erythematosus revealed by large-scale T cell receptor repertoire and transcriptome studies

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Conflict of interest: Yes

[Objectives] CD4+ T cell plasticity plays a pivotal role in immune homeostasis. However, evidence of T cell plasticity and its pathological role in human systemic lupus erythematosus (SLE) is missing. [Methods] We utilized T cell receptor (TCR) repertoire data as a molecular signatures alongside transcriptomic dataset. Using ImmuNexUT database including 117 SLE cases, we quantified T cell plasticity across 13 fine-sorted T cell subsets. We analyzed 6,392 samples in total and identified two orthogonal signatures of repertoire and transcriptome, the cell-type and disease signatures. We characterized cell-type signatures by comparing the TCR repertoire data or transcriptomes with those of other T cell subsets. Disease signatures of T cell subsets were analyzed, comparing SLE to HC. TCR clonotype overlap and the clinical relevancy of Treg score was evaluated. The identified signatures and correlations were validated using public (single cell) RNA-seq datasets. [Results] Unsupervised canonical correlation analysis revealed a significant correlation between cell-type and disease signatures only in CD4+ T cells. Supervised analysis of cell-type signatures unveiled distinctive TCR features: highly hydrophobic CDR3 amino acids in Fr. II eTreg and acidic amino acids in Th1. Correlation analysis showed the most robust association between the cell-type Fr. II eTreg signature and the disease signature of SLE Th1, suggesting directional plasticity from Treg to Th1 in SLE. TCR clonotype overlap analysis confirmed increased plasticity in SLE, particularly between Fr. II eTreg and effector CD4 T cells, including Th1 (odds ratio = 3.1, $P = 9.1 \times 10^{-6}$ in Th1). Evaluation of Th1 Treg scores in SLE patients revealed a positive correlation with SLEDAI-2K score (Rho = 0.47, $P = 1.7 \times 10^{-7}$). Moreover, Th1 Treg scores were elevated in active SLE patients presenting with fever or nephritis. [Conclusion] Our study provides novel evidence that Treg plasticity is involved in SLE pathology.

ICW8-2

Disease-specific genetic risk variants revealed by case-case GWAS contribute to disease-specific clinical manifestations of SLE and RA

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Conflict of interest: None

[Objectives] While systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are autoimmune diseases with different clinical manifestations, genome-wide association studies (GWASs) have shown that many causal genetic loci are shared in both diseases. To understand the mechanisms behind disease-specific organ manifestations (e.g., renal disorder in SLE or bone destruction in RA), it is essential to clarify the difference in genetic architecture between these two diseases. However, con-

ventional case-control GWAS study design (e.g., SLE vs. healthy) has hindered us from thoroughly investigating the genetic signals specific to each disease. This study aims to identify disease-specific risk variants of each disease and evaluate the contribution of these variants to disease-specific clinical phenotypes. [Methods] To assess disease-specific variants, we applied case-case GWAS (CC-GWAS) to the largest-scale GWAS summary statistics of SLE (10,029 East Asian [EAS] and 6,748 European [EUR] cases) and RA (11,025 EAS and 22,350 EUR cases). We also applied the polygenic risk score (PRS) model based on CC-GWAS to genotype data from Japanese LUNA cohort (494 cases) and European SLE cohort (142 cases) and tested the association between PRS and clinical manifestations. [Results] CC-GWAS prioritized SLE- (e.g., *TNFSF4*, *FCGR3B* locus) and RA-specific risk variants (e.g., *CD40* locus) while canceling the effect of shared causal variants. While PRSs based on conventional case-control GWAS of SLE and RA showed prediction accuracy of the development of each disease, they were not associated with disease-specific clinical manifestations. Intriguingly, PRS based on CC-GWAS better predicted renal disorder involvement ($P=7.2\times10^{-3}$) and anti-dsDNA positivity in SLE cohorts. We are planning to apply this model to RA clinical cohorts. [Conclusion] CC-GWAS can be useful for better understanding disease-specific biology in SLE and RA and for promoting personalized medicine for autoimmune diseases.

ICW8-3

Functional Connectivity Associated with Fatigue in Systemic Lupus Erythematosus: A Resting-State Functional MRI Study

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Conflict of interest: None

[Aim] Fatigue represents a prevalent symptom in patients with systemic lupus erythematosus (SLE). Resting-state functional magnetic resonance imaging (rs-fMRI) has emerged as a powerful technique for mapping extensive neural networks in the human brain through blood-oxygen-level-dependent (BOLD) signal; the temporal synchronization between separate brain regions of interests (ROI) can be termed as functional connectivity (FC). We aim to identify the specific FC linked to fatigue in patients with SLE. [Methods] rs-fMRI data as well as the Chalder fatigue scale (CFS) were acquired from patients with SLE and healthy controls (HC). Demographic and clinical data for SLE patients were collected from medical records. FCs were analyzed and compared among SLE patients and HCs by analysis of covariance (ANCOVA), adjusted for age and sex. Multivariate pattern analysis (MVPA) was conducted to identify specific clusters by integrating information from three-dimensional voxel coordinates. The clusters identified by MVPA were used as seeds for the ROI-to-voxel analysis. The relationship between FC patterns and CFS was evaluated. [Results] A total of 16 SLE patients (94% female; median age: 46 years, IQR: 33-56) and 16 HCs (63% female; median age: 41 years, IQR: 34-46) were enrolled. The median Systemic Lupus Erythematosus Disease Activity Index score was 4 (IQR: 1.5-5.0) and the median prednisolone dose was 6.0 mg/day (IQR: 3.6-11.25). The median CFS scores were 18.5 (IQR:11-24). MVPA identified five distinct patterns differentiating SLE from HC. Seed-to-voxel analysis revealed that connectivity between the MVPA-identifying cluster ROI centering on left superior frontal gyrus and atlas ROI of left inferior lateral occipital cortex correlated with CFS severity ($r=0.86$, $P=0.0009$). [Conclusion] Altered connectivity involving the left inferior lateral occipital cortex was associated with fatigue severity, suggesting a potential neural target for fatigue in patients with SLE.

ICW8-4

MTHFD2 promotes osteoclastogenesis and bone loss in rheumatoid arthritis by enhancing CKMT1-dependent oxidative phosphorylation

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Conflict of interest: None

[Objectives] To elucidate the effect and underlying mechanisms of methylenetetrahydrofolate dehydrogenase 2 (MTHFD2) on osteoclast differentiation and bone loss in rheumatoid arthritis (RA). [Methods] The expression and role of MTHFD2 were examined in CD14+ monocytes and murine bone marrow derived macrophages (BMMs). RNA-sequencing was performed to evaluate the regulatory mechanisms of MTHFD2 on osteoclastogenesis. Extracellular flux assay, JC-1 staining and transmission electron microscopy were used to detect mitochondrial function and energy metabolism changes during osteoclast formation. Collagen-induced arthritis (CIA) mice were used to evaluate the therapeutic effect of MTHFD2 knockdown on bone loss. [Results] Elevated MTHFD2 was observed in RA patients and CIA mice with a positive correlation to bone resorption parameters. During osteoclast formation, MTHFD2 was significantly upregulated in both human CD14+ monocytes and murine BMMs. The application of MTHFD2 inhibitor and MTHFD2 knockdown suppressed osteoclastogenesis, while MTHFD2 overexpression promoted osteoclast differentiation in vitro. RNA-sequencing revealed that MTHFD2 inhibition blocked oxidative phosphorylation (OXPHOS) in osteoclasts, leading to decreased adenosine triphosphate (ATP) production without affecting mitochondrial biogenesis. Mechanistically, inhibition of MTHFD2 downregulated the expression of mitochondrial creatine kinase 1 (CKMT1), which in turn affected phosphocreatine energy shuttle and OXPHOS during osteoclastogenesis. Further, a therapeutic strategy to knock down MTHFD2 in knee joint in vivo ameliorated bone loss in CIA mice. [Conclusion] Our findings demonstrate that MTHFD2 is upregulated in RA with positive relation to joint destruction. MTHFD2 promotes osteoclastogenesis and arthritic bone erosion by enhancing mitochondrial energy metabolism through CKMT1. Thus, targeting MTHFD2 may provide a potential new therapeutic strategy for tackling osteoclastogenesis and bone loss in RA.

ICW8-5

Blockade of Cellular Communication Network Factor 3 suppresses pathological process of rheumatoid arthritis through inhibiting cell senescence and osteoclastogenesis in the joint

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Conflict of interest: None

[Objectives] Aging is an important factor mediating the development of RA, as it is associated with an increase in the number of senescent cells, autoantibodies and proinflammatory cytokines in tissues. CCN3 has been documented to be involved in aging-associated diseases, such as osteoarthritis, coronary artery disease, obesity and cancer. Importantly, CCN3 levels in the serum of patients are associated with the severity of RA. Therefore, we hypothesized that CCN3 might act as factor involving in activation of senescence in the joint, and directed our study on elucidating the role of CCN3 in the progression of RA. [Methods] Human monocytes and fibroblast-like synoviocytes were used for in vitro stimulation assays with recombinant CCN3 and their responses were analyzed by bulk-RNA sequencing. For in vivo administration of CCN3, the recombinant protein was injected into the knee joint and onto the calvarial bone. The effects of CCN3 antibody treatment were examined using Collagen antibody-induced arthritis (CAIA) model. Pathological changes were evaluated by immunohistochemistry. [Results] An analysis of public scRNA-seq data from the RA synovium revealed that CCN3 is expressed by an inflammatory fibroblast subset. CCN3 stimulation resulted in the activation of the senescence pathway in synoviocytes and osteoclast differentiation in monocytes in vitro and in vivo. These findings suggest that CCN3 is pathological factor involved in the activation of cellular senescence and osteoclastogenesis. Consistent with these results, the administration of CCN3 antibody significantly suppressed inflammation score and number of osteoclasts, inflammatory cells and senescent cells in the joints of the RA model mice. [Conclusion] Our data highlight that CCN3 contributes to pathological processes in RA and represents a promising therapeutic target for the treatment of RA.

ICW9-1

Evaluation of the role of anti-IL-17A Treatment for Kidney and Lung Damage in a Pristane-Induced Lupus Model

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Conflict of interest: Yes

Objective: IL17A plays an important role in the pathogenesis of systemic lupus erythematosus (SLE). However, anti-IL17A therapy did not achieve significant results in Phase 3 clinical trials. To explore its mechanism of action, we evaluated the role of an anti-IL17A antibody in a pristane-induced SLE model that develops two different types of lupus-related organ damage under a genetic defect in the ZAP70 gene. Methods: C57 BL/6 (B6)-SKG mice were intraperitoneally injected with 0.5 ml pristane in two divided doses. Anti-IL17A antibody (BZN035), provided by Novartis, was intraperitoneally injected on days 1 and 15 at a dose of 10 mg/kg. Serum anti-DNA antibody titters were determined by ELISA. Kidney and lung tissue were evaluated by PAS and H&E staining. 24 hrs urine were collected to monitor proteinuria. Cellular subsets such as T peripheral helper (Tph) and neutrophils were analyzed by flow cytometry. Results: Exposure to pristane in B6 SKG mice increased anti-DNA antibody levels and caused kidney dysfunction and pulmonary hemorrhage. Anti-IL17A treatment partially reduced anti-DNA antibody levels (367101±59480 mU/ml vs 286978±47256 mU/ml, p=0.159), significantly reduced the 24 hrs urinary albumin (0.34±0.026μg vs 0.164±0.035μg, p=0.0006), and reduced C3 and IgG deposition in kidney glomeruli. Anti-IL17A treatment also reduced pulmonary hemorrhage (43.7% vs 15%). By flow cytometry, the proportion of Tph cells in the kidney (19±1.45% vs 16.9±0.91%) and neutrophils (32.6±2.29% vs 17.4±2.79%) in lung tissue were decreased after the treatment. Conclusions: This study suggests that IL17A inhibitors may have therapeutic benefits in controlling lupus-related organ damage such as kidney and lung by inhibiting inflammatory immune cell infiltration and NET formation in mice. To make anti-IL17A antibodies available for clinical use in human SLE, stratification of lupus patients who respond to anti-IL17A treatment may be necessary.

ICW9-2

Oral delivery of delta-9-tetrahydrocannabinol has pain-modifying effects in mouse models of knee osteoarthritis

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Conflict of interest: None

Objectives: Osteoarthritis (OA) involves pathological joint changes and signaling at the dorsal root ganglia (DRG) that contributes to chronic pain. Some OA patients use cannabis to alleviate symptoms. We found oral administration of delta-9-tetrahydrocannabinol (THC), a prominent phytocannabinoid, had some disease attenuating effects in the destabilization of the medial meniscus (DMM) mouse model of knee (K) OA. In this study, we investigated the effects and signalling mechanisms of THC on pain in KOA mouse models. **Methods:** DMM and monosodium iodoacetate (MIA) mice were administered THC orally. Von Frey tests were used to evaluate pain. Plasma isolated from DMM mice administered THC 10-weeks post-surgery was analyzed by targeted metabolomics. Ipsilateral L3-L5 DRG were collected 3-weeks post-MIA injection and single nucleus RNA sequencing (snRNAseq) was performed to determine THC-induced transcriptomic changes in distinct cell populations. Computational and bioinformatics was used to identify enriched pathways and inferred intercellular communications. **Results:** THC reduced pain in DMM and MIA mice. Metabolomic analyses identified serotonin, carnosine, and 5-oxoproline were reduced upon DMM surgery and rescued with THC administration. snRNAseq analyses identified transient receptor potential melastatin 8 (Trpm8)-expressing neurons, peptidergic nociceptors (Pep), and neurofilament (NF)-expressing neurons as having the highest DEGs in response to THC of all cells identified in the DRG. DEGs of Trpm8 neuronal cells were enriched for neuronal transmission pathways, immune system- and lipid-related pathways. Cell communication analyses determined a putative decrease in ligand-receptor signaling between Trpm8 neurons and Pep/NF neurons after THC administration. **Conclusions:** In mouse models of KOA, THC reduced pain, systemic metabolic changes and gene expression/pathway/communication changes in DRG Trpm8 neuronal cells, implicating mechanisms for KOA pain modulation by THC.

ICW9-3

Pathogenetic role of IFNg producing CD4+ T cells in IMQ-induced lupus model mice

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Conflict of interest: Yes

[Objective] To evaluate the pathogenic role of IFNγ-producing CD4+ T cells in IMQ induced lupus model mice using IFNγ-deficient (KO) mice, because our previous study revealed splenic CD4+ T cells were highly produced IFNγ after the administration of IMQ in C57BL/6 WT mice. [Methods] After administration of IMQ in WT and KO mice, 1) Lupus phenotype was evaluated by measuring serum anti-dsDNA antibody titer, urinary protein, and deposition of C3 and IgG in kidney. We also evaluated 2) CD4+ T cell subsets, 3) Cytokine production from CD4+ T cells, and 4) B cell subsets in spleen by FCM. 5) Splenic CD4+ T cells of WT-Control or WT-IMQ treated mice were co-cultured with CD19+ 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. 7) CD4+ T cells of WT or KO-IMQ treated mice were co-cultured in the same way described in 5-6), B cell differentiation and IgG levels were evaluated. [Results] The results of KO mice compared with WT mice in 1-4) were as follows: 1) Antibody titer and urinary protein were significantly decreased, and deposition of C3 and IgG tended to be attenuated. 2) There was no significant difference in Tfh and Tph cells. 3) IL-17 producing cells were significantly increased and IL-10 producing cells were significantly decreased. 4) Plasmablasts were significantly increased and plasma cells tended to be decreased. Co-culture experiment revealed 5) Plasmablasts were significantly increased, and 6) IgG levels also tended to be increased co-cultured with CD4+ T cells of IMQ-treated mice. 7) ABC and Plasmablasts tended to be decreased and IgG levels were significantly decreased co-cultured with CD4+ T cells of KO 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.

ICW9-4

Interleukin-26 as a potential therapeutic target in an antigen-induced arthritis model

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Conflict of interest: None

[Objectives] Although advances in treatment for RA led to substantial improvement in prognosis, unmet needs such as resistance to current therapies are still remaining. In-depth understanding of the pathology of human RA is required to further improve clinical outcomes. Interleukin-26 (IL-26) is an inflammatory cytokine primarily produced by Th17 cells. Recent studies have shown that IL-26 levels are markedly increased in the synovial fluid of RA patients, suggesting the potential role of IL-26 in the pathogenesis of RA. However, due to the absence of IL-26 gene in rodents, the role of IL-26 in arthritis has not yet been understood. Our objective is to elucidate the role of IL-26 in an arthritis model utilizing human IL-26 transgenic (hIL-26Tg) mice and to investigate the efficacy of humanized anti-IL-26 mAb developed in our laboratory. [Methods] The role of IL-26 in an antigen-induced arthritis (AIA) model in hIL-26Tg mice was examined. Fibroblast-like synoviocytes were collected from the synovium of mice and their characteristics were examined by qRT-PCR and ELISA. Pathological and flow cytometry analyses of joints were conducted. [Results] Expression levels of inflammatory cytokines (IL-17A, TNF, etc.) and chemokines (CXC chemokine, CCL20) in the synovial tissue of hIL-26Tg mice were significantly higher than those of control mice. Neutrophils, T, and B cells were more abundant in the joint of hIL-26Tg mice, and marked cartilage erosion and synovial hyperplasia were observed in hIL-26Tg mice compared to control mice. Following treatment with anti-IL-26 mAb, arthritis symptoms in hIL-26Tg mice were significantly improved, with reduced inflammation and joint damage. [Conclusion] Our data strongly suggest that IL-26 plays a role in exacerbating arthritis and that IL-26 may be a novel promising target for the treatment of RA patients. We are investigating the more detailed cellular and molecular mechanism of IL-26-mediated cartilage destruction and hyperplasia of synovium.

ICW9-5

Upregulated Neddylation in Arthritic SKG mice: A Potential Therapeutic Target for Arthritis

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Conflict of interest: None

[Objectives] Neddylation, NEDD8 conjugating process, is a post-translational modification that plays a crucial role in regulating ubiquitination by targeting cullin (CUL)-ring E3 ubiquitin ligases. Our previous research indicated that neddylation is dysregulated in RA FLS, and that its inhibition can reduce arthritis severity in the K/BxN serum transfer model. However, the dysregulation of neddylation in SKG mice remains largely unexplored. This study aims to investigate whether neddylation is dysregulated in arthritic SKG mice and to evaluate its potential as a therapeutic target for arthritis. [Methods] Arthritis was induced in SKG mice through intraperitoneal injection of zymosan. The neddylation status of CUL1 in joint tissue was compared between arthritic and naïve SKG mice using Western blotting. In vitro, we assessed the effects of the selective neddylation inhibitor TAS4464 on the induction and maturation of bone marrow-derived dendritic cells (BMDCs), on T cell proliferation, as well as on co-culture T cells with TAS4464-treated BMDCs. [Results] We first investigated the neddylation status in arthritic SKG mice and discovered that the neddylation of CUL1 is markedly upregulated in the joints of arthritic SKG mice. Subsequently, we assessed the effects of neddylation inhibition on DC differentiation, maturation, and T cell proliferation. The neddylation inhibitor promoted the differentiation of PD-L1-positive DCs, reduced the maturation of MHC II-positive DCs without altering PD-L1 expression, and suppressed T cell proliferation. Co-culturing DCs with T cells revealed that neddylation inhibitor-treated DCs tended to diminish T cell proliferative capacity. In vivo, the neddylation inhibitor demonstrated a tendency to alleviate arthritis severity in SKG mice. [Conclusion] Our findings reveal an upregulation of neddylation in the inflamed joints of SKG mice, suggesting that neddylation inhibition could serve as a novel therapeutic approach for arthritic diseases.

ICW9-6

The anti-inflammatory effect of theaflavins in a murine model of collagen-induced arthritis

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Conflict of interest: Yes

[Objectives] The theaflavins are found in black tea, exhibits several bioactive properties, including the ability to lower systemic inflammation. Our study was to investigate the effect of theaflavins on dendritic cell (DC) maturation. The potential of therapeutic agent was evaluated in a murine model of collagen-induced arthritis (CIA). [Methods] The cytotoxicity of theaflavins on of mouse bone marrow-derived DCs was evaluated. We investigated whether theaflavins affected the some cytokines secretion (TNF-α, IL-6, IL-12) and NO production in LPS-stimulated DCs. In the murine model of CIA, mice were dosed daily with theaflavins differnt dosage among two groups. [Results] Theaflavins may effectively inhibit lipopolysaccharide-induced DC maturation as shown by reductions in the production of proinflammatory cytokines/chemokines, the expression of costimulatory molecules and the antigen-specific T cell priming ability of DCs when given at noncytotoxic doses. In addition, the decrease of LPS-induced MAPK and NF-κB signaling activation may contribute to the inhibitory activity of theaflavins. In mice with CIA, the oral administration of theaflavins ameliorated the severity of arthritis, reduced the levels of anticollagen Type II (CII) IgG and limited the proliferation of T cells. [Conclusion] This study showed that theaflavins can manipulate the immunostimulatory properties of DCs and thus represents a potential therapeutic for the treatment of rheumatoid arthritis.

ICW10-1

Prognostic Value of AI-Based Quantitative CT in Anti-MDA5 Antibody-Associated ILD: A Longitudinal Study of CT Pattern Changes

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Conflict of interest: None

Background: Interstitial lung disease (ILD) associated with anti-MDA5 antibodies is often rapidly progressive and intractable. Decision for intensifying immunosuppressive therapy is usually made based on deterioration of respiratory status or subjective chest CT pattern evaluations. Recently, an artificial intelligence-based quantitative CT image analysis software (AIQCT) was developed to automatically categorize and quantify CT patterns. This study aimed to objectively assess longitudinal changes in CT patterns using AIQCT and assess their predictive value for prognosis. **Methods:** We included 22 patients with anti-MDA5 antibody-positive ILD treated with the same induction regimen. Patients were divided into two groups: favorable (16 patients) and intractable groups (4 died and 2 deteriorated to require oxygen therapy). AIQCT was performed at each time point (weeks 0, 2, 4, 8, and 12) to measure four radiological parameters: ground-glass opacity (GGO), reticulation, consolidation, and honeycombing. Linear mixed-effects models assessed the effects of time, prognosis, and their interaction. Additionally, we compared the rate of GGO scores change between week 0 and week 2 to predict intractable disease course in the early phase of the disease. **Results:** GGO significantly decreased overall ($p < 0.001$), but more slowly in intractable group ($p < 0.001$). Honeycombing increased over time ($p < 0.001$), without group differences ($p = 0.20$). Reticulation showed no overall change ($p = 0.87$), but increased faster in unfavorable group ($p < 0.001$). Consolidation showed no time effect ($p = 0.22$), but worsened more rapidly in the intractable group ($p < 0.001$). GGO scores change from week 0 to 2 was greater in the intractable group (0.97 vs 0.40, $p < 0.01$). **Conclusions:** Patients with poor prognosis showed minimal improvement in GGO, particularly those with stable GGO at week 2, indicating a poor outcome. Early moni-

toring of GGO using AIQCT may help optimize treatment strategies for ILD management.

ICW10-2

Increased Risk of Medication-Related Osteonecrosis of the Jaw in Rheumatologic Patients Treated with Denosumab Following Intravenous Bisphosphonate Therapy

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Conflict of interest: None

[Objectives] Given the lifelong nature of rheumatic diseases, investigating the long-term safety and efficacy of osteoporosis treatments, including treatment sequences, is crucial. Denosumab offers advantages in reducing drug burden and simplifying administration, but MRONJ risk factors, especially in those switching from bisphosphonates, remain unclear. This study examines MRONJ prevalence and risk factors in rheumatic patients treated with denosumab, focusing on prior osteoporosis treatments. [Methods] We retrospectively reviewed 310 patients with rheumatic diseases who received denosumab therapy from 2005 to 2022 at Kyung Hee University Hospital. The cohort included rheumatoid arthritis (RA), osteoarthritis (OA), and other connective tissue diseases. Patients were categorized based on prior osteoporosis treatment. T-score changes and MRONJ incidence were assessed, and regression analysis was conducted to identify MRONJ risk factors. [Results] Of the patients, 64.2% were aged 65 or older, and 89.4% were female. 43.5% had no prior osteoporosis treatment, while 29.3% had used oral bisphosphonates (BP), 22.9% intravenous BP, and 4.2% selective estrogen receptor modulators (SERM). The oral BP to denosumab sequence group showed significant T-score improvement ($p< 0.0001$). MRONJ occurred in 9 patients (2.9%), all aged 65 or older. Six MRONJ cases were in the IV BP to denosumab group, and two in the oral BP group. Cox regression identified glucocorticoid use (OR=18.15), RA (OR=9.54), IV BP (OR=24.88), dental disease (OR=4.64), and alveolar bone surgery (OR=18.27) as significant risk factors for MRONJ. [Conclusion] This study underscores the need for clear guidelines on transitioning from bisphosphonates to denosumab, as increased MRONJ risk was observed in rheumatic patients following IV BP. Those with risk factors like advanced age, IV BP use, long-term glucocorticoid therapy, RA, dental conditions, or prior surgeries need careful management.

ICW10-3

Associations between Cardiovascular Risk and Seropositive Rheumatoid Arthritis

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Conflict of interest: Yes

[Objectives] Despite the increasing burden of cardiovascular disease (CVD) among patients with rheumatoid arthritis (RA), large-scale studies examining the association between RA characteristics and CVD risk, especially those adjusting for various confounding factors, remain limited. In this nationwide cohort study, we aimed to investigate the association between CVD risk and seropositive RA, as well as identify factors that may contribute to an elevated CVD risk, using data provided by the Korean National Health Insurance Service (NHIS). [Methods] We enrolled 15,385 patients with seropositive RA who underwent national health examinations within two years of their diagnosis between 2010 and 2017, along with age- and sex-matched non-RA controls (n=76,727). The primary outcomes were the incidence of myocardial infarction (MI) and stroke. MI was defined as first hospitalization with ICD-10-CM codes I21 or I22, while stroke was defined as first hospitalization with ICD-10-CM codes I63 or I64. We utilized Cox proportional hazard models for the statistical analyses. [Results] In total, there were 3,455 new cases of myocardial infarction (760 in the seropositive RA cohort and 2,695 in the control cohort), and 3,982 new cases of stroke (729 in the seropositive RA cohort and 3,253 in the control cohort). Multivariable analysis indicated that seropositive RA was significantly associated with an increased risk of myocardial infarction (hazard ratio [HR]: 1.41, 95% confidence interval [CI]: 1.29-1.52, $P<0.001$), stroke (HR: 1.11, 95% CI: 1.02-1.20, $P=0.108$), and all-cause mortality (HR: 1.84, 95% CI: 1.73-1.96, $P<0.001$). [Conclusion] Seropositive RA is associated with a significantly higher risk of incident cardiovascular disease. As such, regular cardiovascular screening should be a key component of the management strategy for patients with seropositive RA.

ICW10-4

Trajectory of lipid profiles in rheumatoid arthritis patients receiving tofacitinib: evidence from the prospective CENTRA cohort

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Conflict of interest: None

[Objectives] The cardiovascular risk of tofacitinib has been highly concerned. In this study, we investigated the trajectory of lipid profiles in patients with rheumatoid arthritis (RA) after receiving tofacitinib. [Methods] Patients were recruited from the prospective CENTRA cohort of RA patients. The data of RA disease activity, triglyceride (TG), total cholesterol (TCHO), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL) and ratios of TCHO/HDL and HDL/LDL were collected at baseline, week 4, 12, 24, and 52. Lipid and lipoprotein concentrations were compared between tofacitinib exposure group and non-exposure group by propensity score matching (PSM). [Results] Totally 374 patients were enrolled, with 137 received tofacitinib and 237 not. After 4 weeks of tofacitinib treatment, the levels of TG, TCHO, HDL and LDL were increased. TCHO and LDL concentrations returned to baseline levels by weeks 24 and 52, respectively, while TG and HDL levels remained elevated throughout 52 weeks. After 1:1 PSM, 133 patients in tofacitinib exposure group and 133 in non-exposure group were identified. Compared to non-exposure group, tofacitinib-exposure group showed significantly more increased TCHO levels at week 4 and continuously higher TCHO till week 24; HDL and LDL levels were also elevated from week 12 to week 24. [Conclusion] Four-week exposure of tofacitinib induced elevation of TG, TCHO, HDL and LDL in serum. LDL and TCHO returned to baseline levels at week 24 and week 52 respectively, nevertheless, TG and HDL displayed continued elevated levels. Tofacitinib exposure was generally associated with more remarkable elevation of lipid profiles.

ICW10-5

Clinical profile and Outcomes of Patients with Immune-related Adverse Events to Immune Checkpoint Inhibitors

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Conflict of interest: Yes

Background and Objectives: Immunotherapy represents an increasing trend in cancer treatment, significantly enhancing patient outcomes. Among the various modalities of cancer immunotherapy, immune checkpoint inhibitors (ICI) are the most widely utilized. However, despite its benefits serious immune-related adverse event (irAE) can develop. While these events have been described in case series and observational studies, data remains limited. This paper aims to describe the profile, clinical course and outcomes of irAEs evaluated and managed by the Rheumatology at St. Luke's Medical Center, Philippines. **Methods:** This is a case series of cancer patients who had irAEs following ICI treatment. **Results:** We described 8 cancer patients who developed irAE after receiving ICI

(pembrolizumab-7, Durvalumab-1). Five of the eight patients developed rheumatic irAE, which included myositis (1), pneumonitis (2), and arthritis (2). The most common presentations were arthritis and pneumonitis. Arthritis cases presented as inflammatory symmetric oligoarthritis. Pneumonitis cases presented as progressive cough, exertional dyspnea, and desaturation. Both cases required intubation, but one refused and was transferred to another hospital. Two of the three patients who had severe adverse events tested positive for ANA but were not known to have any autoimmune disease and has no typical clinical features prior to treatment. Most patients were treated with steroids, while those with severe reactions also received intravenous immunoglobulin. In general, 5 of the cases were mild and improved, 3 were severe with 2 case fatality and 1 unknown outcome. **Conclusion:** Increasing utilization of ICI among cancer patients led to increase incidence of immune related adverse events with different presentation and treatment response. Thus, there is a need to continue to collect case studies and consolidate information for a more generalizable description of the clinical course of irAE in future research.

ICW11-1

Real-world comparative effects of IL-6 inhibitors on HbA1c in patients with rheumatoid arthritis: The ANSWER Cohort Study

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Conflict of interest: None

[Objectives] To examine the real-world effect of biologics and Janus kinase inhibitors (JAKi) on HbA1c reduction in patients with rheumatoid arthritis (RA) in a multicenter cohort study. [Methods] Patients with RA treated with biologics or JAKi and with available HbA1c data were included. The primary outcome was HbA1c change at 3, 6, 12, and 18 months. Multiple imputation by chained equations was performed for missing values, followed by propensity score matching for the IL-6 inhibitor (aIL-6R) use group based on baseline data (sex, age, disease duration, and CDAI). [Results] Of 7816 treatment courses (TCs), 432 TCs with longitudinal HbA1c data were analyzed (TNF inhibitors=121, aIL-6R=112, CTLA4-Ig=105, and JAKi=94). In the Kruskal-Wallis and ad hoc multiple comparison tests, HbA1c was significantly more reduced in the aIL-6R group than in the JAKi group at 3, 6, and 12 months ($p<0.001$, $p<0.001$, $p=0.015$, respectively). In a subgroup analysis, HbA1c reduction was compared among tocilizumab (TCZ), sarilumab (SAR), and others (TCZ=79, SAR=33, Others=320). Compared to the Others group, HbA1c reduction was significant in the TCZ group at 3 and 6 months ($p=0.0043$, $p=0.0071$), as well as in the SAR group at 3, 6, 12, and 18 months ($p=0.035$, $p=0.0020$, $p=0.036$, $p=0.042$). The SAR group also showed significant CDAI improvement at 3 and 6 months ($p=0.012$, $p=0.0394$) compared to the Others group. Multivariate analysis on HbA1c reduction was performed with covariates including aIL-6R use, sex, age, CDAI, glucocorticoid dose, and antidiabetic drug use. The following were identified as significant factors: aIL-6R use (estimate=-0.24, SE=0.12, t=-2.0, $p=0.047$) and female sex (estimate=-0.012, SE=0.005, t=-2.3, $p=0.023$). In a subanalysis separating aIL-6R into TCZ and SAR, SAR use (estimate=-0.54, SE=0.19, t=-2.9, $p=0.005$) was identified as a significant factor. [Conclusion] This real-world study demonstrates that IL-6 inhibitors significantly reduce HbA1c levels in patients with RA.

ICW11-2

Impact of seropositivity on drug retention of biologics and JAK inhibitors: the ANSWER cohort study

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Conflict of interest: Yes

[Objectives] While the influence of RF and ACPA on the efficacy of bDMARDs and Janus kinase inhibitors (JAKi) has been previously studied, there have been no reports directly comparing the retention rates of bDMARDs and JAKi stratified by RF or ACPA levels. We aimed to identify the optimal bDMARDs and JAKi in patients with rheumatoid arthritis stratified for RF or ACPA. [Methods] This multicenter retrospective study included 5312 treatment courses of bDMARDs or JAKi (TNFi = 2704, aIL-6R = 1218, CTLA4-Ig = 903, JAKi = 487; RF positivity 78.3%; ACPA positivity 82.8%). Patients were stratified for RF or ACPA titer into three groups; negative, low-positive, and high-positive. To calculate hazard ratios for each treatment discontinuation reason (categorized into ineffectiveness, toxic adverse events, non-toxic reasons, or remission), we used multivariate Cox proportional hazards modeling, adjusted for potential confounders. The clinical disease activity index (CDAI) was used to monitor change of disease activity for 12 months. [Results] aIL-6R showed the lowest discontinuation rates due to ineffectiveness regardless of RF titer. In the RF-positive group, TNFi showed lower retention rates, whereas CTLA4-Ig and JAKi followed aIL-6R in the retention rates. When stratified based on ACPA, aIL-6R also exhibited the highest retention rates across all ACPA groups. TNFi showed lower retention rates compared with other agents in the ACPA-positive group, whereas CTLA4-Ig showed lower retention rates in the ACPA-negative group compared with other agents. In terms of disease activity, JAKi showed poor improvement in CDAI compared with TNFi in seronegative cases. [Conclusion] Novel finding of this study is that aIL-6R showed the highest retention rates regardless of seropositivity considering effectiveness. Although CTLA4-Ig and JAKi followed aIL-6R in RF or ACPA-positive cases, CTLA4-Ig showed the lowest retention rates in ACPA-negative cases.

ICW11-3

Treatment Strategies for Pregnancy in Women of Childbearing Age (WoCBA) Rheumatoid Arthritis (RA) Patients with High Disease Activity: Insights from the FIRST registry

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Conflict of interest: None

[Objectives] This study aimed to analyze the efficacy and impact on pregnancy outcomes of biologic/targeted synthetic (b/ts) disease-modifying antirheumatic drugs (DMARDs) in WoCBA with RA with high disease activity. [Methods] The study enrolled 82 WoCBA with RA who expressed a desire to become pregnant and were monitored for up to 5 years within the FIRST registry, which includes 5250 patients with RA. The primary endpoint was the pregnancy rate during the observation period; the secondary endpoint was a comparison of patient background and clinical disease activity index (CDAI) between pregnant and non-pregnant patients. Factors associated with pregnancy were analyzed by multiple logistic regression analysis. [Results] The participants had a mean age of 30.9±6.5 years old, a mean disease duration of 39.2±55.2 months, and a mean CDAI of 21.3±11.9 at the initiation of b/tsDMARDs treatment. The pregnancy rate was 35.3% (29/82), with an average maternal age of 32.1 years. CDAI at the time of pregnancy was 3.0±4.7, and 22 patients (76%) were in remission. The pregnant group was younger than the non-pregnant group at b/tsDMARDs start (27.7±6.7 vs 32.7±5.7, respectively, $p<0.01$), and had a lower CDAI 3 months after initiation of b/tsDMARDs (3.9±4.3 vs 7.4±6.5, respectively, $p<0.01$). The CDAI cutoff value associated with pregnancy was 1.8. Multiple logistic regression analysis indicated that both the age at b/tsDMARDs initiation ($p<0.01$) and a low CDAI score three months after b/tsDMARDs iniitiation ($p<0.01$) were associated with pregnancy. 24 patients (82.7%) resulted in live births, while 5 (17.3%) miscarried. 7 patients (24.1%) underwent arthritis flare, especially those discontinued bDMARDs during pregnancy were more likely to flare. ($p=0.04$). [Conclusion] In WoCBA with RA with high disease activity who are considering pregnancy, early initiation of b/tsDMARDs to control disease activity and maintain deeper remission may improve the likelihood of pregnancy.

ICW11-4

Heterogeneous treatment effects of biological DMARD versus JAK inhibitor on disease activity in patients with rheumatoid arthritis: the ANSWER cohort study

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Conflict of interest: Yes

[Objectives] Traditional subgroup analyses in treatment effect studies often oversimplify complex characteristics, limiting identification of patients with varied treatment responses. We aimed to investigate whether biological DMARDs (bDMARDs) or JAK inhibitors (JAKi) achieved higher remission in specific rheumatoid arthritis (RA) subpopulations, and to identify characteristics of patients predicted to benefit highly. [Methods] RA patients initiating bDMARD or JAKi were included. After variable-ratio propensity score matching, the conditional average treatment effects of biological DMARD versus JAK inhibitor on remission, defined by the Clinical Disease Activity Index (CDAI) at 3 months were examined using a causal forest algorithm. We compared the characteristics of patients with positive predicted benefits for bDMARD versus JAKi. [Results] Among 730 RA patients (bDMARD: 480, JAKi: 250) in our propensity score-matched analysis, remission proportions at 3 months were similar (bDMARD: 20.0% vs. JAKi: 14.8%, $p=0.10$). However, the causal forest model showed significant treatment heterogeneities. Older patients, for instance, had higher predicted benefits from JAKi. Patients with high CRP or platelet levels derived more benefit from IL-6 receptor inhibitors compared to JAKi, while those with low CRP, high ALT levels, or concomitant methotrexate use favored TNF inhibitors. Female patients with low CRP or minimal glucocorticoid use benefited more from CTLA-4 immunoglobulin. On the contrary, poor prognostic factors (e.g., positive ACPA or $\geqq$2 prior bDMARD/JAKi failures) were not associated with high benefits. [Conclusion] While average remission proportions were similar for bDMARDs and JAKi, substantial heterogeneity in response was noted. Drugs more effective for patients with poor prognostic factors do not necessarily yield greater benefits compared to other drugs. Differentiating high-benefit profiles from poor prognostic factors can aid in tailored RA treatment selection.

ICW11-5

Differences in responsiveness of composite measures and their components reflecting disease activity over initial therapy in early rheumatoid arthritis: a post-hoc analysis of a multicenter cohort study

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Conflict of interest: None

[Objectives] This study aimed to identify which composite measure or disease parameter was most sensitive to change in early rheumatoid arthritis (RA) treated according to a treat-to-target (T2T) strategy. [Methods] This is a post-hoc study using the data from a multicenter cohort study conducted in Hiroshima from June 2018 to March 2022: Three Arrow Study (Registered in CIN No. 644). Newly diagnosed RA patients naïve to disease modifying anti-rheumatic drugs (DMARDs) were enrolled and subsequently started treatment with DMARDs for 52 weeks following the T2T strategy. We explored the sensitivity to change in RA composite measures (DAS-ESR, DAS-CRP, CDAI, SDAI) as well as their components over 24- or 52-week treatment by using the standardized response mean (SRM). [Results] We included 204 patients with early RA. Median age was 67 with a female ratio of 64.7%. Positivity of anti-CCP antibodies and rheumatoid factor were observed in 68.0% and 73.0%, respectively. The median of CDAI and SDAI at baseline were 17.0 and 18.85, respectively. According to the SRMs of composite measures, DAS28-ESR and DAS28-CRP were comparable and more sensitive to change than CDAI or SDAI (the SRM of DAS28-ESR was -1.50/-1.67 over 24-/52-week treatment, DAS28-CRP was -1.51/-1.67, CDAI was -1.38/-1.52, and SDAI was -1.37/-1.47). Among subjective components, investigator's global assessment (GA) was more sensitive to change than patient's GA (-1.36 vs. -0.93/-1.50 vs. -0.97). On the other hand, among the objective components, swollen joint count (JC) was more sensitive than tender JC (-0.97 vs. -0.73/-1.07 vs. -0.81) and ESR was more sensitive than CRP (-0.88 vs. -0.64/-0.94 vs. -0.62). [Conclusion] For assessing response to treatment with DMARDs in early RA, DAS28 was more sensitive to change than CDAI or SDAI. Among these components, investigator's GA, swollen JC and ESR showed higher sensitivity to change.

ICW12-1

Lung-Joint Associations: AI-Based CT Analysis Reveals Distinct Lung Patterns Predicting Rheumatoid Arthritis Outcomes

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Conflict of interest: None

[Objectives] The relationship between lung and joint involvement in rheumatoid arthritis (RA) remains unclear. This study aimed to quantify lung lesions in RA patients using novel AI-based CT image analysis and assess their association with functional disability and joint destruction. [Methods] AI-based quantitative CT analysis software (AIQCT) was applied to CT scans of RA patients at Kyoto University Hospital in 2018. AIQCT quantified 10 parenchymal patterns (e.g. ground-glass opacities [GGO], bronchi, honeycombs) reporting their volumes as percentages of total lung volume. In the primary analysis, patients were grouped into clusters via Ward's hierarchical method using these parameters, guided by dendrograms and clinical relevance. Longitudinal functional disease activity was compared across clusters. In the secondary analysis, lung parameters associated with radiographic progression were evaluated. [Results] A total of 408 RA patients were included. Patients were grouped into following 5 clusters: Cluster I (68.6%), nearly normal lungs; Cluster II (23.5%), mild lesions with honeycombs or GGOs; Cluster III (5.6%), predominance of GGOs; Cluster IV (1.0%), hyperlucent areas; and Cluster V (1.2%), extensive lung abnormalities. HAQ scores at 5 years (mean [SD]) were: Cluster I, 0.5 (0.7); Cluster II, 1.0 (0.9); Cluster III, 1.1 (1.0); Cluster IV, 0.4 (0.4); Cluster V, 1.0 (0.8) ($p < 0.001$). In the secondary analysis, only bronchial volume (%) correlated with ΔmTSS/year ($\rho = 0.17$, $p < 0.05$). Multivariable analysis suggested that bronchial volume (%) independently predicted radiographic progression (ΔmTSS/year ≧ 0.5) (OR 2.3, 95% CI 1.1-4.9), irrespective of baseline autoantibodies, disease activity, or treatment. [Conclusion] Using novel AI-technology, lung lesions in RA patients are comprehensively evaluated. The AIQCT-derived clustering of lung lesions was associated with RA clinical outcomes. Notably levels of bronchiectasis were associated with radiographic progression.

ICW12-2

Polygenic score analysis of refractory rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] The prognosis of rheumatoid arthritis (RA) has improved with expanding therapeutic options, including biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs). However, a subset of patients exhibits resistance to various medications, referred to as refractory RA or "Difficult-to-Treat RA" (D2T RA). Currently, no definitive measures have been established to predict refractoriness. The polygenic score (PGS) is an emerging tool for assessing genetic risk. In this study, we explored the behavior of PGSs in refractory RA. [Methods] Data were collected from 1097 patients with RA in the Department of Rheumatology, Institute of Science Tokyo Hospital (formerly Tokyo Medical and Dental University Hospital). Genotypes were determined for 181 patients. Three previously published PGSs for disease susceptibility and radiographic progression were calculated. Using PRSice2 and PRS-CSx, new PGSs for disease predisposition and the use of b/tsDMARDs were developed, utilizing participants from the UK Biobank as the training cohort, and applied to the study cohort. [Results] Among 1097 patients, 188 experienced failures of two or more b/tsDMARDs with different mechanisms of action, and 84 were classified as D2T RA. Patients with multiple treatment failures were characterized by a younger age of onset (mean ± SD: 48.3 ± 14.6 years vs. 51.9 ± 15.5 years, $p = 0.009$) and a higher frequency of positivity for rheumatoid factor (83.4% vs. 74.3%, $p = 0.008$) or anti-citrullinated protein antibody (73.8% vs. 64.1%, $p = 0.023$). Among patients without treatment restrictions due to socioeconomic factors or refusal, those with multiple failures had a higher PGS for radiographic progression (z-score median [IQR]: 0.17 [-0.18, 0.79] vs. -0.06 [-0.75, 0.65], $p = 0.071$). [Conclusion] Refractory patients exhibited higher PGSs. The potential of genetic risk models to stratify RA patients who require more intensive treatment has been suggested.

ICW12-3

The effect of biologic/targeted synthetic DMARDs on bone mineral density of patients with rheumatoid arthritis: a five-year observation from FIRST registry

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Conflict of interest: None

[Objectives] Osteoporosis (OP) is a common comorbidity of rheumatoid arthritis (RA), leading to increased fractures and impaired physical function. While b/tsDMARDs have been expected to improve OP in RA, our one-year study showed significant bone loss in RA patients treated with b/tsDMARDs. The current study evaluated the five-year change in bone mineral density (BMD) in real-world practice. [Methods] Patients from FIRST registry who initiated their first b/tsDMARDs were followed for five years. The primary endpoint was to evaluate the change in BMD. Secondary endpoints included the change in T-scores, factors associated with the BMD change, and the proportion of patients meeting the OP criteria. [Results] 797 patients (median follow-up 3.1 years, 0.4-5.5 years, 2,489 person-years) underwent 4,056 BMD measurements. Patients were 61±14 years old and 77% female, with receiving 74% concomitant methotrexate and 22% glucocorticoids. At baseline, 40% of patients met the OP criteria, of whom 75% received anti-OP drugs (bisphosphonates 18%, anti-RANKL 6%, others 6%). b/tsDMARDs improved CDAI from 25.7 to 6.6. Meanwhile, BMD decreased significantly in both the femur (0.628 to 0.618 g/cm^3) and radius (0.603 to 0.588). 16% of patients without baseline OP developed OP during the study period. Subgroup analysis showed that both sexes and all age groups experienced BMD loss, whereas patients on concomitant anti-OP drugs had preserved BMD. Multivariate analysis showed that older age, female sex, and higher baseline BMD correlated with BMD loss, while concomitant anti-OP drugs associated with BMD improvement. A Gaussian mixture model identified that 42% of patients improved BMD during the study, who had lower BMD, fracture history, and were receiving anti-OP drugs at baseline. [Conclusion] This long-term study showed that b/tsDMARDs without anti-OP drugs do not prevent BMD loss, and a considerable proportion of patients developed OP. Regular OP evaluation and intervention are essential.

ICW12-4

Psychological Changes in Rheumatoid Arthritis Patients After Achieving Treatment Goals with b/tsDMARDs: A Longitudinal KURAMA Cohort Study

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Conflict of interest: Yes

[Objectives] To elucidate the psychological changes in rheumatoid arthritis (RA) patients after achieving treatment target with biologics and targeted synthetic DMARDs treatment (b/tsDMARDs). [Methods] We conducted annual measurements of the Hospital Anxiety and Depression Scale (HADS) in RA patients from 2014 to 2023. The study included patients who were treated with b/tsDMARDs and had achieved low disease activity at baseline. We analyzed the changes in HADS anxiety (HADS-A) and depression (HADS-D) scores in patients who remained on the same b/tsDMARDs throughout the study period. The drugs were categorized into tumor necrosis factor inhibitors (TNFi) and non-TNFi (including JAK inhibitors). The primary outcome was the proportion of patients showing a clinically significant improvement, defined as a change greater than the minimal clinically important difference (MCID) in HADS-A and HADS-D at the final observation. Statistical analysis was performed using a weighted generalized linear model adjusted for background factors such as sex, age, disease activity, and psychiatric history. [Results] A total of 415 treatment courses (TNFi: 201, Non-TNFi: 214) from RA patients who remained on the same drug for more than one year and had multiple HADS assessments were analyzed. The MCID was 1.77 for HADS-A and 1.82 for HADS-D. A higher rate of significant improvement in HADS-A was observed in the Non-TNFi group compared to the TNFi group (TNFi: 24.4%, Non-TNFi: 34.1%, relative risk 1.39, 95%CI: 1.06-1.83). However, there was no significant difference in the rate of significant improvement in HADS-D between the two groups (TNFi: 26.9%, Non-TNFi: 36.0%, relative risk 1.22, 95%CI: 0.95-1.58). [Conclusion] Non-TNFi, compared to TNFi, significantly improves psychological well-being, particularly anxiety, in RA patients even after achieving treatment goals.

ICW12-5

Current practice, trends and attitudes of rheumatologists towards glucocorticoids use for rheumatoid arthritis (GURANTEE): a national cross-sectional survey across China

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Conflict of interest: None

Objective: There were mixed practices and attitude towards glucocorticoids (GC) use as a bridging therapy combined with csDMARDs and lots of controversies exist over the current guidelines as well. We aimed to investigate current practices, changes, and perceptions of rheumatologists regarding GC use in RA patients. Methods: A cross-sectional survey was conducted using a structured questionnaire between April and August 2023. Rheumatologists from 31 province-level regions of Mainland China were invited to participate. Results: 1,717 rheumatologists from 598 hospitals completed the survey with a response rate of 92%. Up to 60% of participants expressed currently infrequent initiation of GC co-therapy with csDMARDs (hardly ever 7.0%; occasionally 24.6%; sometimes 29.1 %), accompanied by a decline of frequency over time reported in 64.2% (Figure 1). Regarding attitudes towards bridging therapy with GC, 604 (35.2%) participants supported this approach, 468 (27.3%) opposed it, and 645 (37.6%) remained inconclusive. Time to GC discontinuation in context of csDMARDs was commonly reported within 6 months in current practice which has been narrowed over time. Reasons for chronic GC use were mostly reported due to suboptimal disease control, followed by the need of RA complications, and pre-existing comorbidities. After failure of GC cessation, majority of respondents (84.4%) would escalate RA therapy (commonly by addition of JAK inhibitors, TNF inhibitors), which usually or often facilitated the GC cessation. Regarding long-term low-dose GC use for RA, the percentage of respondents who supported, opposed, or depended on the situation were 15.9%, 17.2%, and 66.9%, respectively. Conclusions: The current data demonstrate that GC initiation for RA treatment is not as frequent as before and the awareness of GC discontinuation is growing in current practice. Attitudes towards GC co-therapy with csDMARDs vary considerably and long-term low-dose GC use remain situation dependent.

ICW13-1

Single-cell analyses with host genetics reveal the cell state-dependent genetic regulation of transcriptional profiles and T and B cell receptors repertoire in immune cells from 234 Japanese

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Conflict of interest: None

[Background] Expression quantitative trait locus (eQTL) analyses have answered functional annotation of the variants and elucidate biological mechanisms of human diseases. However, current eQTL catalogues are mostly at bulk resolution and centered on European ancestry. [Methods] We constructed a multi-omics single-cell atlas of > 1.5 million peripheral blood mononuclear cells with whole-genome sequencing data from 234 Japanese, including COVID-19 patients and healthy subjects. [Results] We mapped the genetic effects on gene expression within 7 major cell types and 28 fine cell types, and identified ~34,000 cis-eQTLs. We further elucidated dynamic genetic regulation of gene expression across cell states by testing an interaction between genotype and cell state, and identified that such eQTLs (i.e., dynamic eQTLs) were more enriched in enhancer regions than cis-eQTLs. We revealed cell type and context-specific HLA and genome-wide associations with T/B cell receptor (TCR/BCR) repertoires (e.g., COVID-19 and HLA class I interactions in $CD8^+$ T cells). We assessed genome-wide association studies (GWAS) signal colocalizations of 13 autoimmune diseases and blood cell traits in East Asian population and our cis-eQTLs, providing evidence that cell types which exhibited colocalization were specific to the traits. In addition, by using dynamic-eQTLs, we showed a value of dynamic genetic regulation of gene expression across continuous cell states to interpret GWAS signals (e.g., the *PLD4* locus in systemic lupus erythematosus). Differential gene expression analysis with COVID-19 polygenic risk scores revealed that the polygenic risks affected transcriptional profiles in a cell type and context-specific manner. [Conclusions] We demonstrated the cell state-dependent genetic regulation of transcriptional profiles and TCR/BCR repertoire in immune cells, highlighting the value of multi-omics analyses anchored by single-cell data to understand human complex traits at fine resolution.

ICW13-2

Machine Learning-Driven Integrative Analysis of Long Non-Coding RNAs Driving Mitochondrial Dysfunction in Rheumatoid Arthritis Using Single-Cell Metabolomics and Epigenetic Profiling

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Conflict of interest: None

Objectives: Mitochondrial dysfunction drives inflammation and joint damage in rheumatoid arthritis (RA). While long non-coding RNAs (lncRNAs) regulate mitochondrial processes, their role in RA-related metabolic changes remains unclear. This study aims to identify lncRNAs linked to mitochondrial dysfunction in RA and assess their potential as therapeutic targets. Methods: Single-cell metabolomics and DNA methylation data from the Human Cell Atlas and Metabolomics Workbench were analyzed for 600 RA patients and 250 controls. Data from 120,000 cells were integrated to assess epigenetic changes linked to lncRNA expression. A machine learning framework using random forest-based feature selection and convolutional neural networks identified lncRNAs associated with mitochondrial dysfunction. Model performance was validated on 20% of the

data using AUC-ROC, MCC, and balanced accuracy metrics. Results: The analysis identified several lncRNAs, including MALAT1 and HOTAIR, significantly associated with mitochondrial dysfunction. MALAT1 expression was upregulated by 5.6-fold in active RA (95% CI: 5.0-6.3, p<0.0001), correlating with hypermethylation of mitochondrial DNA regions, leading to a 6.3-fold decrease (95% CI: 5.8-6.9) in respiratory chain complex I activity. HOTAIR showed a 4.2-fold increase (95% CI: 3.7-4.8) and was linked to elevated reactive oxygen species (ROS) production, increasing ROS levels by 4.3-fold (95% CI: 3.9-4.8). The model achieved an AUC-ROC of 0.89 (95% CI: 0.86-0.92), MCC of 0.81, and balanced accuracy of 87%. Pathway analysis revealed that these lncRNAs were involved in disrupted glutamine metabolism, fatty acid oxidation, and TCA cycle activity. Conclusion: This study identifies key lncRNAs, such as MALAT1 and HOTAIR, as drivers of mitochondrial dysfunction in RA, offering novel therapeutic targets to restore mitochondrial function and reduce inflammation.

ICW13-3

Target Specific Suppression mediated by Treg cells

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Conflict of interest: None

[Objectives] Target of Foxp3+ Treg suppressive function is effector T cells (Teff). Treg has been known to work in antigen specific manner in that Treg requires specific antigen stimulation by APC. However, which Teff cells are targeted in such physiological polyclonal Treg cell is not well understood. [Methods] (1) To address target Teff of Treg cells, polyclonal Tregs were generated in vitro from Foxp3 GFP KI C57BL/6 naive CD4+ T cells with allo dendritic cells (DC), TGFβ and IL-2. GFP+ cells were cell sorted. For the Teff side, C57BL/6 naive CD4+ T cells and antigen specific T cells were mixed and stimulated with allo-antigen and antigen peptide in the presence of the above Treg cells in vitro or in vivo. In vivo condition, mixed lymphocytes were transferred into retro-orbital vein of C57 BL/6 recipients and splenocytes were analyzed at day4. Suppression effect (Cell trace violet dilution) in the mixed two Teff was compared in the presence of allo-specific Treg or of peptide specific Treg. (2) Target specificity was similarly studied as above, with DC presenting both allo-antigen and peptide antigen together on the same cell surface. [Results] (1) Only the selected Teff was suppressed by polyclonal Treg, suggesting that target of Treg is antigen specific when two antigens were given on separate DC both in vitro and in vivo. (2) When two antigens were presented on the same APC, the suppression was still target specific in vivo but not specific in vitro. [Conclusions] Non-targeted Teff was also suppressed in vitro, suggesting some difference of suppression pathways between in vitro and in vivo. The target specific suppression by Treg may enable us to develop immune suppressive therapy without the risk of infections or cancer susceptibility.

ICW13-4

AEBP1+ fibroblast-like synoviocytes Promote Synovial Pannus Formation in Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] This study aims to investigate the role of AEBP1+ fibroblast-like synoviocytes (FLS) in promoting rheumatoid arthritis (RA) progression and underlying mechanisms. [Methods] We analyzed single-cell sequencing data from osteoarthritis (OA) and RA patients to identify FLS subpopulations and marker genes potentially involved in disease progression, selecting AEBP1 as a candidate gene. RT-PCR and Western blot were initially used to detect the expression of two AEBP1 isoforms in OA and RA FLS. Immunohistochemistry (IHC) was then performed to analyze AEBP1 expression in OA and RA synovium. AEBP1 knockdown in RA FLS was conducted to assess its effects on proliferation, migration, and invasion. Additionally, we co-cultured AEBP1-knockdown RA FLS with HUVECs in vitro to evaluate the impact of AEBP1 on HUVEC proliferation and tube formation. [Results] Single-cell sequencing analysis showed a significant increase in AEBP1+ FLS in RA synovium. AEBP1 knockdown significantly inhibited RA FLS proliferation, migration, and invasion, while the addition of recombinant AEBP1 protein (rAEBP1) to AEBP1-knockdown RA FLS reversed these inhibitory effects. Integrating JASPAR predictions and single-cell sequencing, we identified transcription factors potentially regulating AEBP1 expression. Furthermore, co-culture experiments demonstrated that AEBP1 knockdown in RA FLS notably reduced their ability to promote HUVEC proliferation and tube formation, which was restored by adding rAEBP1 to the co-culture system. [Conclusion] This study reveals that the increase of AEBP1+ FLS subpopulations in RA plays a crucial role in RA progression by inducing pannus formation in the synovium. Our findings suggest that AEBP1 may be a promising therapeutic target for RA.

~~ICW13-5~~

~~Circadian Clock Gene Dysregulation as a Predictor of Fibromyalgia Syndrome in Young Women: Interplay with Circadian Hormones and Gut Microbiota~~

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~~Conflict of interest: Yes~~

~~[Objectives] Fibromyalgia syndrome (FMS) is a complex chronic condition characterized by widespread pain, fatigue, and disrupted sleep, with a high prevalence among young women. Evidence suggests circadian clock gene dysregulation may play a role in FMS pathogenesis, interacting with circadian hormones and gut microbiota. This study investigates whether dysregulation of circadian clock genes could serve as a predictor for FMS in young women, focusing on its relationships with hormonal rhythms and microbial diversity. [Methods] This cross-sectional study included 100 young women aged 18-30, with 50 diagnosed with FMS and 50 healthy controls. Expression levels of circadian clock genes (BMAL1, CLOCK, PER1, CRY1) were analyzed via RT-PCR from blood samples. Serum levels of melatonin, cortisol, and serotonin were measured using ELISA. Gut microbiota diversity was profiled through 16S rRNA sequencing to assess taxa related to inflammation and circadian regulation. [Results] FMS patients showed significant downregulation of BMAL1 and CLOCK genes ($p < 0.01$) and altered PER1 and CRY1 patterns. These genetic changes correlated with evening cortisol elevation and reduced nocturnal melatonin levels ($p < 0.05$). Lower serotonin levels were also observed in the FMS group. Microbial analysis showed decreased Bacteroides and Lactobacillus, with an increased Firmicutes/Bacteroidetes ratio in FMS patients, correlating with BMAL1 and CLOCK dysregulation. [Conclusion] Dysregulated circadian clock genes, combined with altered circadian hormones and gut microbiota composition, may predict FMS in young women. These findings highlight circadian disruption and microbial imbalance as potential therapeutic targets, offering insights for early intervention and management in FMS.~~

ICW14-1

Unravelling the gene regulatory networks driving the polygenic risk of human complex diseases

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Conflict of interest: None

[Objectives] Leveraging causal variants of human complex diseases as an analytical tool has accelerated our understanding of disease mechanisms. These causal variants contribute to pathology by disrupting transcription factor (TF) activity and subsequent transcriptome dysregulation, given their enrichment at TF binding sites. To exploit the potential of extensive open-resource transcriptome databases, robust pipelines are needed to extract transcriptome components unbiasedly and integrate them with GWAS results. Therefore, we aimed to construct an unsupervised analytical pipeline to identify TF-mediated gene expression regulatory networks (TF-GRN) underlying transcriptome datasets and to assess disease pathology. [Methods] Our method comprises three steps: (1) constructing TF-GRN units based on TF chromatin immunoprecipitation sequencing (ChIP-seq) results, (2) performing unsupervised integration of transcriptomes with TF-GRN units using canonical correlation analysis (CCA), (3) integrating these with GWAS results, including heritability enrichment inference within the TF-GRN annotations using stratified linkage disequilibrium score regression (S-LDSC) and fine-mapped GWAS variant enrichment. [Results] As a proof-of-concept analysis, we demonstrated that our method correctly captured the TF-GRN program using RNA-sequencing data from a T cell line with modified RELA (NF-κB subunit) expression. Moreover, our method successfully identified heritability enrichment in critical tissues or cell types for autoimmune diseases and neurological disorder. It also highlighted heritability enrichment of autoimmune diseases in TF-GRN programs where RELA was enriched. Notably, enriched components did not necessarily have the largest variance in each dataset, indicating that conventional supervised approaches may be inefficient in capturing such components. [Conclusion] Our study provides insights into the disease pathology, which will be a solid foundation for future studies.

ICW14-2

Hybrid reclassification of ANA-RMD using deep learning techniques is replicable in continental European and UK based cohorts and predicts key long-term outcomes better than existing diagnoses

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Conflict of interest: None

[Objectives] ANA-associated RMDs like SLE, Sjogren's, Scleroderma, Myositis, and mixed/undifferentiated CTD have variable access to therapeutics despite overlapping clinical/immunological features. We developed a data-driven reclassification using clinical and biomarker data to define more homogeneous cohorts for therapies and trials. [Methods] A variational autoencoder was trained on the European PRECISESADS cohort (876 ANA-RMD patients) using R, keras, and tensorflow. ANA-RMD specialists and patient focus groups prioritized 25 covariates. Data was compressed to an 8-neuron latent space for clustering. Kmeans centroids from PRECISESADS were validated in the UK DEFINITION cohort (219 patients), with cluster durability assessed via M3C in R. Gene expression was analysed through heatmaps and summary statistics. Clinical impact was evaluated cross-sectionally and longitudinally via descriptive statistics, PROs (e.g., SF36), physician assessments (e.g., BILAG-2004, PGA), gene expression, and 5-year follow-up outcomes (e.g., hospitalization). [Results] Five ANA-RMD classes (ARC classes) were identified, all including patients from various diagnoses: (i) Sicca-mostly pSS, SLE, or UCTD with low disease activity, high IFN-I expression; (ii) Quiescent-low gene expression/activity, high pain; (iii) Active MSK-high MSK activity/inflammatory gene expression; (iv) Polyinflammatory-frequent therapeutic changes, high myeloid/IFN/inflammatory gene expression, many undifferentiated patients; (v) Myeloinflammatory-high healthcare use and physician-assessed disease activity. Significant differences in hospital admission ($p<0.01$) and emergency visits ($p<0.01$) were seen across ARC classes, but not legacy diagnoses. [Conclusion] ARC classes subclassify the ANA-RMD spectrum into more homogeneous groups, suggesting suitability for shared therapies and better prediction of long-term outcomes. Trials in ARC classes may enhance effect sizes, apply to more patients, and reduce healthcare inequality.

ICW14-3

Semaphorin 7A promotes Neutrophil extracellular trap formation and contributes to the pathogenesis of ANCA-associated vasculitis

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Conflict of interest: None

[Objective] Semaphorins were identified as axon guidance molecules, and they also play roles in immune responses and inflammation. Semaphorin 7A (SEMA7A) is known as a promoter of neutrophil migration, but the effect of this molecule on other neutrophil functions remains largely unknown. The purpose of this study is to investigate the role of SEMA7A in neutrophil activation and its impact on the pathogenesis of ANCA-associated vasculitis (AAV). [Method] Recombinant SEMA7A proteins were coated on a 96-well plate and isolated human neutrophils were added. Reactive oxygen species (ROS) and neutrophil extracellular trap (NET) formation were assessed using Fluorimetric hydrogen peroxide assay kit (Sigma-Aldrich) and immunofluorescence staining with SYTOX green dye, respectively. Expression of SEMA7A and its receptors, integrinβ1 and Plexin-C1, on neutrophils and vascular endothelial cells was detected by flow cytometry. 44 serum samples and 7 kidney biopsy samples were obtained from AAV patients. Serum SEMA7A levels were determined by ELISA. SEMA7A expression in kidney tissue was also assessed by immunostaining. [Result] At baseline, unprimed neutrophils and endothelial cells do not express SEMA7A. TNF-α priming induced SEMA7A expression on endothelial cells. A soluble form of SEMA7A was also detected in the culture supernatants. Direct contact between neutrophils and SEMA7A proteins significantly increased neutrophil ROS production and NET formation. SEMA7A-induced NET formation was reduced by using anti-Plexin-C1 antibody. Serum SEMA7A levels were significantly higher in AAV patients than in healthy controls and correlated with serum creatinine levels. SEMA7A expression in the vascular endothelium of renal tissue was increased in AAV patients. [Conclusion] Increased SEMA7A expression on inflamed endothelial cells promotes neutrophil activation and may be involved in the pathogenesis of AAV.

ICW14-4

Thrombogenicity of neutrophil extracellular traps induced by anti-phosphatidylserine/prothrombin complex antibodies

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Conflict of interest: None

[Objectives] Anti-phosphatidylserine/prothrombin complex antibodies (aPS/PT), which are antiphospholipid antibodies often detected in antiphospholipid syndrome (APS), can bind to neutrophils and induce neutrophil extracellular traps (NETs). Although it has been reported that aPS/PT are strongly linked with thrombosis, the mechanism of thrombosis in APS is not revealed completely. We hypothesized that NETs induced by aPS/PT would activate platelets and contribute to the thrombogenicity in APS. This study aimed to compare the morphology and platelet activation potential of NETs induced by aPS/PT and anti-neutrophil cytoplasmic antibodies (ANCA). [Methods] Neutrophils isolated from human peripheral blood were stimulated by aPS/PT or ANCA to induce NETs in 4-well chamber slides. After immunofluorescent staining for DNA, citrullinated histone H3, and autoantibodies that bound to neutrophils, the area and cir-

cularity of NETs were analyzed using ImageJ. Washed platelets were added during NET induction and then the quantity of platelets trapped in each type of NETs was assessed by CD61 staining. Platelet activation was also assessed by CD62P staining. Platelets trapped in NETs were quantified as CD61-positive area/NET DNA area, and platelet activation as CD62P-positive area/CD61-positive area. [Results] NETs induced by aPS/PT had a larger area ($p<0.01$) and smaller circularity ($p<0.01$) than those induced by ANCA. There was no difference in the rate of platelets trapped between aPS/PT-induced and ANCA-induced NETs, but the platelets trapped in aPS/PT-induced NETs were more activated than those trapped in ANCA-induced NETs ($p<0.01$). [Conclusion] aPS/PT-induced NETs had a larger and more explosive morphology and a higher potential to active platelets than ANCA-induced NETs. The aPS/PT-induced NET-mediated activation of platelets could be involved in the thrombogenicity in APS.

ICW14-5

The Therapeutic Role of TREM-1 Signaling Pathway in Atherosclerosis through Regulation of Mitochondrial Fission

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Conflict of interest: None

[Objectives] Atherosclerosis (AS) is a chronic inflammatory disease marked by excessive mitochondrial fragmentation in vascular cells. Triggering receptor on myeloid cells 1 (TREM-1), an inflammation amplifier, has gained attention for its role in AS. The TREM-1 inhibitor LR12 is in phase III trials. This project investigates how the TREM-1 pathway regulates mitochondrial fission in AS, supporting anti-inflammatory therapies and identifying optimal drugs to slow disease progression. [Methods] In vivo experiments: An AS mouse model was treated with LR12, and efficacy was evaluated via HE, Masson, Oil Red O staining, and lipid profiling. Immunofluorescence and immunohistochemistry examined MID49/51 expression, while flow cytometry analyzed T cell subset changes in spleen and bone marrow. In vitro experiments: An inflammatory environment was simulated using IL-8 and PDGF-BB, followed by siRNA treatment. Immunofluorescence assessed mitochondrial morphology in smooth muscle and endothelial cells, and Western blot analyzed MID49/51 and adhesion protein changes. [Results] TREM-1 was highly expressed in aortic endothelial and smooth muscle cells of AS mice; LR12 treatment reduced plaque formation in AS mice; LR12 treatment reduced Th1/Th2 and Th17/Treg ratios, as well as DN B cell levels, in the spleen and peripheral blood; MID49/51 expression in AS mice aorta decreased with LR12 treatment; TREM-1 knockdown in vitro inhibited IL-8 and PDGF-BB-induced mitochondrial fission in HUVECs; TREM-1 knockdown reduced MID49/51 expression in IL-8 and PDGF-BB-induced HUVECs. [Conclusion] The TREM-1 inhibitor LR12 slows AS progression by reducing mitochondrial fragmentation in vascular cells and modulating T cell subsets. As mitochondrial fission-related proteins, MID49/51 recruit p-DRP1, which accelerates mitochondrial fission, promoting vascular cell proliferation and adhesion and ultimately advancing AS. LR12 inhibits this process, indicating that TREM-1 may serve as a therapeutic target for AS.

ICW15-1

Phosphodiesterase 1B mediates neuropsychiatric manifestations in lupus-prone mice via microglial activation

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Conflict of interest: None

[Objectives] Recent studies have shown that abnormal activation of microglia plays an essential role in the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE). This study aimed to identify potential novel therapeutic targets for NPSLE by focusing on microglia. [Methods] RNA sequencing (RNA-Seq) of microglia isolated from MRL/*lpr* mice and MRL/MpJ mice was performed to explore genes involved in microglial activation. We focused on a candidate gene as a potential therapeutic target for NPSLE, and its function in microglia was assessed by evaluating the effects of an inhibitor of the gene on MRL/*lpr* and the conditional knockout (cKO) mice using *Cx3cr1*$^{CreERT2/+}$ mice. The expression assay of proinflammatory cytokines by real-time PCR and phagocytosis assay was performed in primary microglia. RNA-Seq and pathway analysis of cKO and control mice microglia were also performed to clarify the mechanism of altered expression of the candidate gene. Behavioral tests were performed on MRL/*lpr* mice receiving intracerebroventricular (ICV) administration of inhibitor or vehicle. An imiquimod-induced lupus model was used to assess behavioral abnormalities in cKO and control mice. [Results] Among the upregulated genes in RNA-Seq, we focused on phosphodiesterase 1b (*Pde1b*), one of the top-fold changed genes. Gene expression of proinflammatory cytokines and phagocytosis were significantly suppressed in PDE1B inhibitor-treated MRL/*lpr* and *Pde1b* cKO microglia. Gene Ontology analysis showed that pathways related to positive regulation of cytokine production and inflammatory response were downregulated in *Pde1b* cKO mice. ICV administration of the PDE1B inhibitor ameliorated behavioral abnormalities in MRL/*lpr* mice. Furthermore, *Pde1b* cKO mice showed reduced behavioral abnormalities in the imiquimod-induced model. [Conclusion] Our data suggest that PDE1B is involved in the pathogenesis of NPSLE via microglial activation. PDE1B could be a novel therapeutic target for NPSLE.

ICW15-2

Generation and Pathophysiological Analysis of M694I Variant Knock-in Mice of Human MEFV Gene: Insights from Single-Cell RNA Sequencing

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Conflict of interest: None

[Objectives] The primary objective of this study was to generate knock-in mice with the M694I variant of the human MEFV gene, a critical variant in the pathogenesis of FMF, and analyze the resultant pathophysiological changes. Additionally, we aimed to explore the molecular mechanisms of splenocytes through single-cell RNA sequencing (scRNA-seq) and gene set enrichment analysis. [Methods] M694I knock-in mice were generated using the CRISPR/Cas9 gene editing system. The insertion of oligo DNA was confirmed using Sanger sequencing. The study involved monitoring the survival rate and growth curves of mice, collecting peritoneal macrophages, and stimulating them with lipopolysaccharide (LPS) and ATP to analyze inflammatory responses. Flow cytometry was used to evaluate the cellular composition of the spleen, and cytokine levels were measured in serum samples. Furthermore, scRNA-seq was performed on splenocytes, followed by GSEA to identify the activated pathways in different cell populations. [Results] The M694I group exhibited a significantly lower survival rate and failure to gain weight than the wild-type (WT) group, suggesting an inflammatory pathology. M694I mice showed enlarged spleens and increased splenocyte counts, indicating an abnormal immune response. The M694I mutation leads to a higher percentage of IL-17 producing cells, suggesting a role in Th17 cell differentiation. scRNA-seq and GSEA of splenocytes revealed that T cells in M694I knock-in mice exhibited increased activity of HALLMARK_INTERFERON_ALPHA_RESPONSE and HALLMARK_INTERFERON_GAMMA_RESPONSE, whereas monocytes showed elevated activity of HALLMARK_TNFA_SIGNALING_VIA_NFKB. Serum analysis revealed elevated G-CSF, IFN-g, IL-6, TNF-a, and IL-5 levels in the M694I group. Notably, a significant increase in IL-17 producing cells. [Conclusion] scRNA-seq analysis provided further insights into the molecular mechanisms, highlighting the involvement of interferon responses in T cells and TNFa signaling in monocytes.

ICW15-3

Spatial Transcriptomics of Joint Space-Interfacing Tissues Using a Pre-Clinical Mouse Model of Osteoarthritis

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Conflict of interest: None

Objectives: Osteoarthritis (OA) is a joint degenerative disease that affects multiple tissues, including synovium, meniscus and articular cartilage. Changes in gene expression, while retaining spatial information, have not been investigated in pre-clinical OA models. We aimed to use spatial transcriptomics in surgically-induced OA mice to localize changes in gene expression in joint space interfacing tissues. **Methods:** Joints from 12-week-old mice subjected to destabilization of the medial meniscus (DMM) surgery or surgically naïve mice (n=3/group) were collected 5 weeks post-op or at 17 weeks of age, respectively. Joints were processed and sectioned at 5 um with tissues meeting RNA quality of DV200 greater than 50%. Spatial sequencing was performed using the Visium platform. Libraries were sequenced at a depth of 25000 read pairs/spot. Synovium, meniscus and articular cartilage were manually traced on tissue images to select voxels for analysis. Spatial transcriptomics analysis was completed using Seurat and Goseq R packages. **Results:** In total, 201 differentially expressed genes (DEGs) were identified (181 upregulated, 20 downregulated). GO enrichment analysis of the upregulated DEGs, found extracellular matrix (ECM) terms were enriched, and for downregulated DEGs, GO terms related to chromatin structure were enriched. Spatial visualization of select upregulated DEGs, *Nfasc* and *Acan*, showed spatial changes primarily in the synovium and across all tissues, respectively, while downregulated histone genes DEGs *Hist1h3d* and *Hist1h1a* primarily showed spatial changes across all tissues and in the meniscus, respectively. **Conclusion:** Spatial transcriptomics identified localized gene expression on tissues of mouse joints. Gene expression changes occurring with DMM were found to be across joint-interfacing tissues or in specific tissues, with upregulated genes mostly associated with ECM, while majority of the downregulated DEGs were primarily associated with chromatin structure.

ICW15-4

Dynamics of neutrophil activation in the TLR9-induced mouse model of macrophage activation syndrome

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Conflict of interest: None

[Objectives] To define the kinetics and function of neutrophils in the repeated TLR9-induced model of MAS. [Methods] Wild type C57BL/6 mice were treated with CpG ODN1826 five times in 10 days. Mice were sacrificed one day after the last injection (acute MAS) or after 21 days (resolution). For single-cell RNA sequencing (scRNA-seq), neutrophils were processed with 10X Genomics platform and the libraries were processed via Cell Ranger followed by integrated analysis in Seurat 3. Differential expression and gene regulatory prediction analysis were performed using the software cellHarmony. Cytokine levels were determined from culture supernatant with or without LPS stimulation. Neutrophil depletion were induced by in vivo antibody treatments with combination of anti-Ly6G antibody and anti-rat Kappa immunoglobulin. [Results] To define the diversity of neutrophils, scRNA-seq was performed. We identified six distinct neutrophil populations in blood neutrophils, representing both immature and mature neutrophils. The mature cells included aged populations and populations enriched with interferon-stimulated genes (ISG). In acute MAS, we observed increased proportions of immature neutrophils and ISG high neutrophils. Compared to control neutrophils, genes associated with interferon alpha and/or beta signaling were significantly upregulated in most populations. Notably, *CD274* (*PD-L1*) was upregulated in MAS, suggesting neutrophil exhaustion and a potential suppressive effect on T cell activation. Functionally, both IL-6 and KC release were significantly suppressed in neutrophils from both acute MAS and resolution compared to control upon LPS stimulation. Lastly, clinical, laboratory, and immunologic features of MAS were exaggerated by antibody mediated neutrophil depletion, suggesting potential reguatory role of neutrophils in experimental MAS. [Conclusion] Neutrophils in TLR9-induced MAS model show dual roles with both pro-inflammatory and suppressive functions during MAS.

ICW15-5

Effect of periodontitis on arthritis using the ligature-induced periodontitis model mouse

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Conflict of interest: None

[Objectives] It is well known that patients with rheumatoid arthritis (RA) and periodontitis have worse disease activity than those with RA. In animal model, collagen induced arthritis (CIA) was exacerbated in a periodontitis mouse model infected with *Porphyromonas gingivalis* (*Pg*), a human periodontitis-causing organism. However, *Pg*-infected mouse is a species-mismatched model because the bacterium does not originally host mice. Here, we used a more physiological mouse model of periodontitis, in which periodontitis is induced by commensal bacteria, to induce arthritis in an environment with no bias toward specific bacteria, with the aim of identifying important bacteria previously unknown, evaluating the exacerbation of arthritis and elucidating its mechanisms. [Methods] We used a combined mouse model of ligature-induced periodontitis (LIP) as a model of periodontitis and CIA as a model of arthritis in the same individual. Clinical score and ankle thickness were used to evaluate severity of arthritis. We also analyzed the bacteria expanded in periodontal lesion site. To examine whether the bacterium contributes to the exacerbation of arthritis, we intravenously injected the bacterium into CIA mice. [Results] Mice with LIP showed exacerbation of CIA compared to mice without LIP. We also found that *Enterococcus spp*. significantly expanded in the periodontitis sites. Induction of CIA with intravenously injection of *Enterococcus spp*. exacerbated arthritis more than the CIA alone group. [Conclusion] Periodontitis contributed to the exacerbation of arthritis even in the absence of *Pg*, suggesting the involvement of *Enterococcus spp*. in this mouse model. In a previous report, *Enterococcus* DNA was detected in synovial fluid of RA patients, and a more detailed elucidation of the mechanisms in this mouse model may have clinical applications.

ICW15-6

Rebamipide attenuates renal injury via antioxidative effects on podocytes in an animal model for systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Rebamipide is a widely used gastroprotective agent. Beyond its muco-protective effects, this agent presented immune-modulatory effects for various rheumatologic diseases such as rheumatoid arthritis, osteoarthritis, Sjogren's syndrome, and Behcet's disease in multiple pre-clinical and clinical studies. However, its efficacies on lupus have not been evaluated yet. Here, we determined the therapeutic potential of rebamipide in lupus animal models and suggested a plausible mode of action. [Methods] We administered rebamipide (5 mg/kg) or vehicles in 8-week-old MRL/*lpr* mice by daily oral feeding for 8 weeks and determined therapeutic efficacies on lupus-like phenotypes and immune cell profiles using their sera and tissues. Through *in vitro* experiments using immune cells and podocytes acquired from mice, and podocyte cell lines, potential therapeutic mechanisms were evaluated. [Results] Oral rebamip-

ide administration in lupus-prone mice significantly reduced proteinuria and pathologic scores in renal tissues with increased expression of podocyte-related proteins such as nephrin, synaptopodin, and podocin. Sizes of spleen tissues were significantly more decreased in mice treated with rebamipide than those treated with vehicles. Rebamipide increased the proportion of circulating regulatory T cells in lupus-like mice. In contrast, other immune cell populations such as double negative T cells, CD4+ T cells, CD8+ T cells, and plasma cells were not changed by *in vivo* treatment of rebamipide. *In vitro* treatment of rebamipide in primary-cultured murine podocytes resulted in increased expression of structural proteins of podocytes including synaptopodin and podocin, as well as antioxidative factors. These results were replicated in experiments using human and murine podocyte cell lines. [Conclusion] Rebamipide could be considered as one of the adjunctive treatment options in managing renal manifestations in lupus according to the present results from lupus-prone mice.

ICW16-1

Autoantibody Titers to MDA5 Epitopes as Biomarkers for Predicting Resistance in Interstitial Lung Disease Associated with Anti-MDA5 Dermatomyositis

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Conflict of interest: None

Background: Anti-melanoma differentiation-associated gene 5 (MDA5)-positive dermatomyositis (DM) is frequently associated with rapidly progressive interstitial lung disease (ILD), which often results in a poor prognosis. Although initial triple combination therapy has improved outcomes, some patients remain resistant. This study aimed to identify MDA5 epitopes and their clinical significance in predicting resistance. **Methods:** Candidate epitopes were identified using T7 phage display with sera from 16 anti-MDA5-positive DM-ILD patients. Anti-MDA5 positivity was confirmed by immunoprecipitation. The MDA5 protein was divided into overlapping 100-amino-acid segments, expressed in *E. Coli*, and tested using ELISA. Further epitope mapping was conducted using 10-mer linear peptides, shifting by one amino acid. Next, we classified 30 patients who received initial combinational therapy into resistant or non-resistant groups, defined by disease exacerbation within 6 months, which resulted in death or required additional therapies including plasmapheresis. Antibody titers to candidate epitopes were compared between the two groups using the Wilcoxon signed-rank test. **Results:** The study identified two main inter-domain regions: X (amino acids 201-300) and Y (601-700), which correlated between phage display and ELISA (r=0.57, p=0.023; r=0.60, p=0.016; respectively, Spearman's correlation), suggesting them as principal epitopes of MDA5. Epitope mapping of region X and Y showed no specific reactivity to linear peptides, suggesting the importance of conformational structure. Autoantibody titers for these regions were significantly higher in the resistant group (n=16) than in the non-resistant group (n=14) (0.623 vs. 0.0995, p=0.0021 for X; 0.409 vs. 0.0488, p=0.0011 for Y). **Conclusion:** Two main epitopes in MDA5 were identified. Autoantibody titers against these regions were significantly elevated in resistant cases, indicating they could serve as biomarkers for predicting resistance.

ICW16-2

Association Between Anti-SS-A Antibody Positivity and Mental Distress in a General Population: Results from the Nagasaki Islands Study

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Conflict of interest: None

[Objectives] Anti-SS-A antibodies are autoantibodies commonly found in the serum of patients with Sjögren's syndrome (SS). Patients with SS often experience increased anxiety and depression, as well as tendencies toward nervousness and low sociability. However, the impact of anti-SS-A antibody positivity on mental health in the general population remains unclear. [Methods] We analyzed data from 1,599 participants who consented to the Nagasaki Islands Study (NaIS) survey conducted in Goto City, Nagasaki Prefecture. Serum samples were collected between April and September 2014, and participants completed the Kessler K6 non-specific distress scale (K6; 0-24 points). Differences in K6 scores between anti-SS-A antibody-positive and antibody-negative groups were assessed using the Wilcoxon rank-sum test. [Results] In the anti-SS-A antibody-positive group (68/1599, 4.25%), K6 scores were significantly higher than in the antibody-negative group (positive group: mean 2.07, standard deviation [SD] = 2.79; negative group: mean 1.71, SD = 2.96; p = 0.025). Item-specific analysis showed that the items "feeling nervous" and "feeling depressed" were rated higher in the antibody-positive group. Spearman correlation analysis indicated a positive correlation between K6 scores and anti-SS-A antibody levels ($\rho = 0.07$, p = 0.004). When analyzed by gender, there was no significant difference in K6 scores between antibody-positive and -negative groups among women; however, in men, K6 scores were significantly higher in the antibody-positive group (positive group: mean 2.78, SD = 1.99; negative group: mean 1.48, SD = 2.85; p = 0.003). The correlation between K6 scores and anti-SS-A antibody levels was significant in men only ($\rho = 0.158$, p = 0.0002). [Conclusion] In a general population, the presence of anti-SS-A antibodies in men may contribute to mental distress, suggesting a potential role in identifying individuals at risk for mental health concerns.

ICW16-3

Urinary neutrophil gelatinase-associated lipocalin (NGAL) as a mediator of the association between particulate matter exposure and disease activity in systemic lupus erythematosus

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Conflict of interest: Yes

[Objectives] Neutrophil gelatinase-associated lipocalin (NGAL) is an acute-phase glycoprotein increased by inflammatory stimuli, oxidative stress, and tissue injury. Although NGAL is associated with global and renal disease activity in systemic lupus erythematosus (SLE), it is not known whether particulate matter (PM) affects NGAL levels and lupus activity in these patients. Thus, we investigated the mediating role of NGAL in the association between PM_{10} and $PM_{2.5}$ exposure and lupus activity in a prospective, longitudinal cohort. [Methods] The study enrolled 386 patients from three metropolitan regions in Korea. The daily average PM_{10} and $PM_{2.5}$ concentrations were measured using portable air quality monitors and based on data from the National Ambient Air Monitoring System. Urinary NGAL (uNGAL) was measured at the time of enrollment and at 12 months, and disease activity was evaluated using the SLE Disease Activity Index 2000 (SLEDAI-2K) every 3 months for 1 year. Mixed Cox proportional hazard regression was performed to evaluate the associations of PM_{10} and $PM_{2.5}$ with uNGAL and SLE disease activity. [Results] Changes in PM_{10} and $PM_{2.5}$ were associated with changes in uNGAL (β = 1.038, 95% confidence interval [CI]: 1.017-1.059, $p < 0.001$; β = 1.030, 95% CI: 1.001-1.045, $p = 0.013$, respectively), and with changes of SLEDAI-2K scores of > 8 over 1 year in SLE patients (β = 0.097, 95% CI: 0.048-0.146, $p < 0.001$; β = 0.100, 95% CI: 0.054-0.146, $p < 0.001$, respectively). In addition, changes in uNGAL were significantly associated with changes in SLEDAI-2K scores of > 8 (β = 1.000, 95% CI: 1.000-1.002, p = 0.043). [Conclusion] The association between PM exposure and SLE disease activity may be partially explained by uNGAL levels.

ICW16-4

Clustering of patients with anti-synthetase antibodies based on serum protein profiling

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Conflict of interest: None

[Objectives] To explore heterogeneity in the pathophysiology of patients with anti-synthetase antibodies by serum protein expression analysis. [Methods] We selected 77 patients from a prospective, single-center cohort of patients with anti-synthetase antibodies detected by RNA immunoprecipitation assay based on the availability of serum samples obtained before treatment initiation. Sera from eight healthy individuals were used as controls (HCs). Using Olink Explore 384 Inflammation platform, we evaluated serum levels of pre-determined 368 proteins. Hierarchical clustering on protein expression profiles classified the patients and HCs into subgroups. We identified differentially expressed proteins in each cluster. Inter-cluster differences in clinical phenotype including interstitial lung disease (ILD) progression were also assessed. [Results] Cluster analysis identified three subgroups with graded differences in overall protein expression profiles: high (cluster #1, n = 15), low (cluster #2, n = 27), and intermediate (cluster #3, n = 35). Interestingly, all HCs were classified into cluster #3. The most up-regulated proteins in cluster #1 included DFFA, HEXIM1, and MGMT, related to apoptosis, innate immune activation, and DNA repair, while most down-regulated proteins in cluster #2 included SH2D1A, EGLN1, and PRDX5, related to lymphocyte activation or oxidative stress. In terms of clinical features, cluster #1 presented the highest prevalence of myositis (60%), fever (33%), and acute ILD (77%) with a high progression rate, resulting in rapidly progressive ILD (40%). Contrarily, cluster #2 was characterized by the lowest prevalence of myositis (15%) and more chronic ILD (54%) with a low progression rate. Cluster #3 also included ILD-predominant cases with an intermediate progression rate. [Conclusion] Patients with anti-synthetase antibodies were stratified into three subgroups based on continuous serum protein expression profiles that correlated with clinical phenotype.

ICW16-5

Skin Sodium Accumulation as a Potential Disease Biomarker in Psoriatic Arthritis

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Conflict of interest: None

[Objectives] A high sodium environment can lead to expansion of pathogenic Th17 cells, and it has been shown that sodium accumulation in the skin of patients with psoriasis reflects disease activity. This study aimed to assess the potential of sodium magnetic resonance imaging (^{23}Na MRI) as a biomarker for psoriatic arthritis (PsA) by comparing ^{23}Na MRI findings between PsA patients and healthy controls. [Methods] Skin sodium content in the lower leg was measured using ^{23}Na MRI in 5 PsA patients and 6 healthy controls. Ultrasound assessments of the both wrists and fingers, Psoriasis Area and Severity Index (PASI), Disease Activity Score of 28 joints (DAS28), and serum inflammation markers were collected. Skin sodium content was subsequently compared between PsA patients and controls. [Results] The five PsA patients had a mean age of 62.4 ± 6.8 years; one was male, and four were female. One patient was treated with a JAK inhibitor, another with a PDE-4 inhibitor, and all patients received NSAIDs. Mean PASI was 4.2 ± 3.8, and mean DAS28-ESR was 2.6 ± 1.1. Ultrasound examination revealed enthesitis in three cases, synovitis in one case, and confirmed tenosynovitis in another case. Mean serum levels of MMP-3 and C-reactive protein were 68.7 ± 48.8 ng/mL and 0.3 ± 0.4 mg/dL, respectively. PsA patients showed higher tendency in skin sodium content (15.2 ± 3.0 mmol/L) compared to controls (12.7 ± 1.3 mmol/L), though the difference did not reach statistical significance (p = 0.0866). [Conclusion] PsA patients, including those with low serum inflammatory markers and subclinical arthritis, showed a trend toward elevated skin sodium levels compared to healthy controls. These findings suggest that sodium accumulation in skin may be a potential biomarker for early detection of PsA.

ICW17-1

Pathogenic Mechanisms of Idiopathic Inflammatory Myopathies revealed by Single-Cell RNA-sequencing of Peripheral Blood

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Conflict of interest: None

[Objectives] Idiopathic inflammatory myopathies (IIMs) are heterogeneous diseases characterized by diverse organ involvement and variations in underlying pathological mechanisms. This study aimed to elucidate the difference in disease phenotypes and activity patterns in IIM patients through single-cell resolution analysis. [Methods] Peripheral blood mononuclear cells (PBMCs) were collected from IIM patients and healthy controls (HC). Single-cell RNA sequencing (scRNA-seq) was performed on PBMCs, alongside data collection on disease activity, organ manifestations, and the presence of myositis-specific antibodies. Co-varying neighborhood analysis (CNA), mixed-effects association testing for single cells (MASC), and differentially expressed gene (DEG) analyses were applied to examine immune cell profiles and their associations with clinical features. [Results] scRNA-seq was conducted on 337,217 cells from 78 IIM patients and 25 age- and sex-matched HCs. Through CNA and MASC, we identified that *CXCL8*^{high} classical monocytes (CL Mono) were associated with overall disease activity, while RNASE2^{high} CL Mono were associated with cutaneous manifestations. Furthermore, type I interferon signature genes were upregulated in active patients compared to inactive patients, especially within the monocyte subsets of those with anti-melanoma differentiation-associated gene 5 antibodies, but not in patients with antisynthetase syndrome. Additionally, cell-cell interaction analysis revealed that the CXCL signaling pathway network was enriched between RNASE2^{high} and *CXCL8*^{high} CL Mono, and plasmacytoid dendritic cells and natural killer cells, compared to HC. [Conclusion] We identified distinct cells and signatures linked to disease activity and specific phenotypes, highlighting monocyte roles in disease exacerbation. These findings advance IIM pathogenesis understanding and support targeted therapy development.

ICW17-2

Cancer Screening Strategies for Patients with Idiopathic Inflammatory Myopathies: The 2023 IMACS Guideline vs. Real-World Practice in a Japanese Myositis Referral Center

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Conflict of interest: None

Objectives: The International Myositis Assessment and Clinical Studies Group (IMACS) recently published the first cancer screening guideline for patients with idiopathic inflammatory myopathies (IIMs). We aimed to evaluate the performance of our real-world cancer screening practice compared to the IMACS guideline. **Methods:** We retrospectively assessed 183 consecutive adult IIM patients who were diagnosed in the Scleroderma and Myositis Center of Excellence (SMCE), Nippon Medical School Hospital, from August 2014 to May 2024. IIM patients were stratified into high, moderate, or standard-risk of cancer according to the IMACS guideline. Our real-world screening practice was compared to the IMACS screening strategy in terms of cancer detection rates, direct costs, and radiation exposure. **Results:** Median age at IIM onset was 61 [IQR 48-70] years and 66.7% were female. The IMACS guideline risk stratification model classified 75 (41%), 100 (54.6%), and 8 (4.4%) patients into high, moderate, and standard-risk, respectively. In our practice, only 7 (9.3%) and 21 (28.0%) in the high-risk group, and 1 (1.0%) and 16 (16%) in the moderate-risk group completed the IMACS enhanced and basic screening panels, respectively. None in the standard-risk group completed the IMACS basic screening. Within three years following IIM diagnosis, cancer diagnosis was made in 23 (12.6%) patients. Our screening practice identified 22/23 (95.7%) of the cancer, while IMACS screening strategy detected 18/23 (78.3%). Compared to our practice, median direct costs in IMACS screening strategy were higher (20130 [IQR 4800-34865] *vs*. 36460 [IQR 36460-148025] JPY), and median radiation exposure was slightly lower for IMACS guideline (13.90 [IQR 6.2-14.11] *vs.* 12.31 [IQR 12.31-35.01] mSv). **Conclusion:** We identified substantial inconsistencies between our real-world cancer screening practice and the IMACS guideline, highlighting the need for refinement of the guideline according to the local clinical practice.

ICW17-3

CX3CR1+cytotoxic T cells drive the pathogenesis in late-onset rheumatoid arthritis: Insights into inflammation and treatment resistance

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Conflict of interest: Yes

[Objectives] Emerging evidence highlights the role of clonally expanded cytotoxic T cells in several autoimmune diseases. Late-onset rheumatoid arthritis (LORA) presents distinct clinical characteristics compared to younger-onset RA, implying unique immunological mechanisms. In this study, we examined the involvement of cytotoxic T cells in LORA. [Methods] Peripheral blood samples were obtained from 78 treatment-naïve active RA patients, 12 with difficult-to-treat RA, 19 with non- difficult-to-treat RA and 16 healthy controls. Flow cytometry was used to quantify CX3CR1+ cytotoxic CD4 and CD8 T cells. Immunohistochemical staining of lymph node and synovial biopsies from RA patients was also performed. [Results] CX3CR1+ cytotoxic CD4 T cells were significantly elevated in untreated active LORA patients, showing markers of senescence and intermediate CXCR3 expression, characteristic of age-associated ThA cells. Their proportions positively correlated with CDAI and DAS28 in LORA. These cells originated from enlarged lymph nodes, entered peripheral blood, and infiltrated synovial tissues of LORA patients, where they contributed to inflammation and angiogenesis through FGFBP2. Treatment with methotrexate, TNF inhibitors, and IL-6 inhibitors reduced their numbers, whereas T-cell activation modulators had no effect. Additionally, a distinct population of PD-1+CD38+CX3CR1+ CD4 T cells, more abundant in difficult-to-treat RA than in non-difficult-to-treat RA, was identified as a potential treatment-resistant subset. [Conclusion] Our findings suggest that the immunopathogenesis of RA varies with age of onset, with CX3CR1+ cytotoxic T cells driving synovial inflammation in LORA. Furthermore, the presence of a unique CX3CR1+ T-cell subset may contribute to treatment resistance.

ICW17-4

Examination of risk factors for predicting severe infections after remission induction therapy in patients with idiopathic inflammatory myopathy: multi center MYKO cohort study

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Conflict of interest: None

[Objectives] To identify predictors of severe infection in patients with idiopathic inflammatory myopathy (IIM) after remission induction therapy. [Methods] Of the 487 patients diagnosed with IIM in a multicenter study, 376 patients were extracted, who received immunosuppressive therapy between February 2001, and April 2024, and for whom pre-treatment data were available. We identified cases that developed severe infections following immunosuppressive therapy and compared the pre-treatment characteristics between the severe infection group and non-infection group to explore the predictors of severe infections. [Results] Among 376 patients, 55 patients developed severe infections after immunosuppressive therapy, with a median time to onset of 1.5 years. Of the severe infection cases, 50.9% were respiratory infections. Pre-treatment age (p=0.046), serum LDH (p=0.028), and CRP (p=0.006) were significantly higher, while serum albumin (Alb) was significantly lower (p=0.009) in the severe infection group than in the non-infection group. In addition, a higher proportion of patients in the infection group received initial treatment with methylprednisolone (mPSL) pulse therapy or plasma exchange. ROC curve analysis showed that patients with age ≧ 47 years, LDH ≧ 361 U/L, Alb ≦ 3.1 g/dL, and CRP ≧ 0.8 mg/dL were useful clinical factors for predicting severe infections. The 5-year severe infections rate was significantly higher in patients with age ≧ 47 years, LDH ≧ 361 U/L, Alb ≦ 3.1 g/dL, and CRP ≧ 0.8 mg/dL than in those without these parameters. (p=0.004, 0.006, 0.0002, <0.0001) [Conclusion] Our study suggests that older age, elevated LDH, elevated CRP, and low Alb levels are predictive factors for severe infections following immunosuppressive therapy in patients with IIM.

ICW17-5

Clinical and Laboratory Characteristics of Idiopathic Inflammatory Myopathies in Cipto Mangunkusumo Hospital, Jakarta: a Single Centre Study

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Conflict of interest: None

[Objectives] Idiopathic inflammatory myositis (IIM) in Jakarta patients has been rarely studied due to the lack of available data. Myositis specific antibodies testing was just commercially available in Indonesia since 2023. This study aimed to identify the clinical and laboratory features of patients in a single tertiary care centre. [Methods] This retrospec-

tive study reviewed the medical records of Cipto Mangunkusumo Hospital, Jakarta, Indonesia to collect clinical and laboratory data between November 2023 and Maret 2024 as follows: age at disease onset, gender, follow-up duration and disease duration; clinical symptoms; laboratory result; presence and type of myositis-specific autoantibody or myositis-associated autoantibody; presence of malignancy, disease course, and outcome. [Results] There were 68 patients with a mean age of 36.6, and 87.6% were women. The most prevalent form of IIM was dermatomyositis (n=43, 66.15%), and the most affected organ was the skin. Muscle weakness was observed in 63 patients (92.6%), and Gottron's Papules was the most common sign (n=30, 44.1%). From 68 patients, 2 (2.94%) were positive for anti-Jo-1, 1 (1,47%) was positive for anti-Mi-2 alpha, 2 (2,94%) were positive for anti-Mi-2 Beta, 2 (2,94%) were positive for anti-MDA5, 1 (1,47%) was positive for anti-Ku, 1 (1,47%) was positive for anti-OJ, and 3 (4,41%) were positive for anti-R0-52. None of the patients developed a malignancy or died. We did not perform muscle biopsy due to the unavailability of stainings needed for histopathological examination in our pathology anatomy laboratorium. [Conclusion] In our patients, dermatomyositis was the most common form of myositis, and skin and muscle manifestations were the most prevalent clinical characteristics. The number of patients that have been checked for autoantibody were still limited due to availability of the test.

ICW18-1

Distinct clinical outcomes based on multiple serum cytokine and chemokine profiles rather than autoantibody profiles and ultrasound findings in rheumatoid arthritis

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Conflict of interest: None

Objectives: To evaluate the potential of clinical factors, ultrasound findings, serum autoantibodies, and serum cytokine and chemokine profiles as predictors of clinical outcomes in rheumatoid arthritis (RA). Methods: We included 200 patients with RA treated with biologic and targeted synthetic disease-modifying antirheumatic drugs in a prospective multicenter ultrasound cohort study. Their serum levels of multiple cytokines and chemokines, rheumatoid factors, and serum autoantibodies (anti-cyclic citrullinated peptide-2 [anti-CCP2] and anti-carbamylated protein antibodies) were measured at baseline, 3 months, and 12 months. Results: Dimensionality reduction using 38 cytokines and chemokines demonstrated four distinct clusters that differed significantly regarding the frequencies of remission defined by clinical composite measures and ultrasound evaluations. Prominent differences in IL-1β, IL-5, IL-7, IL-10, IFNγ, GRO, IP-10, MCP-1, and MIP-1β characterized the between-cluster differences. Two distinct groups made of four clusters showed a significant difference in IgM-anti-CCP2 positivity. The least absolute shrinkage and selection operator regression of 38 cytokines and chemokines for Clinical Disease Activity Index (CDAI) remission at 12 months resulted in the selection of MIP-1β. Logistic regression using baseline levels of anti-citrullinated protein antibody measured with a commercial immunoassay kit, IgM-anti-CCP2 positivity, the CDAI, the total power Doppler score, the cluster by cytokines and chemokines, MIP-1β, methotrexate dose, and mechanisms of action revealed that cluster by cytokines and chemokines was the sole significant factor for CDAI remission at 12 months. Conclusion: Specific patterns of cytokines and chemokines, not other clinical factors and autoantibody profiles, were important to distinguish RA patients achieving remission at 12 months.

ICW18-2

Oral Microbiota as Prognostic Factors for Difficult-to-Treat Rheumatoid Arthritis: A Prospective Study using KURAMA cohort database

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Conflict of interest: Yes

[Objectives] Rheumatoid arthritis (RA) and oral bacteria are closely related; however, long-term effects leading to difficult-to-treat RA (D2T RA) have not yet been reported. [Methods] We collected saliva samples from RA patients registered in the KURAMA cohort in 2016 and performed 16S rRNA analysis. Patients were stratified into D2T and non-D2T RA groups after five years (D2T-5y and non-D2T-5y), comparing baseline clinical characteristics using wilcoxon or chi-squared test ($p < 0.05$). To identify predictors of D2T RA, we compared oral bacteria between D2T and non-D2T-5y using MaAsLin2 ($q < 0.25$). D2T RA was defined as 1) CDAI > 10, 2) DAS28-ESR > 3.2, or 3) difficulty in reducing prednisolone (PSL) dosage to below 7.5 mg, despite switching biologic agents (Bio) or targeted synthetic DMARDs twice or more times. [Results] Of 403 patients, 278 continued attending the hospital after five years. Excluding 20 patients who were classified as D2T RA in 2016, 258 were included in the analyses. 15 were classified as D2T-5y. D2T-5y showed no association with baseline age, disease duration, DAS28-ESR or methotrexate use, but did show higher BMI (24 vs 22 kg/m^2), CDAI (5.2 vs 2.0), oral PSL dosage (0.0 vs 0.0 mg/day), and Bio use (87 vs 47) (median or %; D2T vs non-D2T-5y). Regarding oral bacteria, we identified 126 genera in total, and D2T-5y had higher levels of *Allobaculum* ($q = 0.03$) and lower levels of *Granulicatella*, *Porphyromonas*, *Haemophilus*, *Neisseria*, and *Filifactor* ($q = 0.01$, 0.06, 0.06, 0.10 and 0.20, respectively). In addition, D2T-5y had lower levels of *Granulicatella,* conducting covariate analyses with BMI, CDAI, PSL dosage and Bio use ($q = 0.16$). *Granulicatella* is a commensal bacteria in the oral cavity and nutritionally variant streptococcus. The requirement for L-cysteine and vitamin B6 for growth suggests a deficiency in these nutrients in D2T RA. [Conclusion] The proportion of *Granulicatella* may be associated with future D2T RA.

ICW18-3

Daily wearable device data predict disease activity in rheumatoid arthritis using machine learning: AMED RA IoT multicenter prospective observational study for digital biomarkers

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Conflict of interest: Yes

[Objectives] The condition of patients with rheumatoid arthritis (RA) is known to be related to their daily physical activity level [1], sleep and mental state. To predict disease activity in RA patients only from daily sensing data obtained by a wearable device. [Methods] A smartphone (iPhone 12) and a wristband-type smartwatch (Google Fitbit Sense 2) were lent to each patient from 3 hospitals for free. An original mobile app was developed and installed into the smartphones to collect daily patient reported outcomes such as patient-pain-visual analogue scale (VAS), patient-general-VAS, patients' self-reported swollen/tender joints, etc. Also, the Fitbit data including steps, metabolic estimates, heart rate and sleep and physicians' clinical assessment including laboratory data were prospectively collected from the same subject. The patients visited the outpatient clinic every 4 weeks and were observed for a total of 12 weeks. Machine learning (ML) models (Lasso, Ridge regression, Random Forest, XGBoost) were used to estimate RA disease activities (detailed numerical score and remission of CDAI and SDAI) based solely on daily Fitbit data. [Results] A total of 129 patients (108 women; 21 men) of RA were includ-

ed. The mean age was 55±13 years; mean disease duration was 8.48±10.3 years. Mean CDAI and SDAI were 13.5±10.7 and 13.8±11.0, respectively. ML models were developed to predict CDAI remission (AUC-ROC 0.90) and CDAI score (MAE 5.04), and SDAI remission (AUC-ROC 0.82) and SDAI score (MAE 5.12). [Conclusion] Disease activity of RA was predicted from daily wearable device data alone. Digital biomarkers obtained from wearable devices could be used to help make clinical decisions in conventional practice and future telemedicine.

ICW18-4

Hyaluronate functionalized teriflunomide and thymoquinone loaded nanoliposomes for the management of rheumatoid arthritis

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Conflict of interest: None

Objectives: Teriflunomide (TF) is a specific drug for rheumatoid arthritis (RA), but its use is limited due to severe hepatotoxicity on long term use. Hyaluronic acid (HYA) is a targeting ligand for CD44 receptors overexpressed on inflamed macrophages in RA. Thymoquinone (TQ), is known to have anti-inflammatory and anti-arthritic activity. The present study was aimed to reduce the dose of TF and to avoid dug induced liver toxicity by developing HYA functionalized TF and TQ loaded nanoliposomes. **Methods:** In the first step, conventional TF and TQ loaded nanoliposomes (TF-TQ-LIPO) were prepared by thin-film hydration method. In second step, HYA coating was performed on TF-TQ-LIPO formulation by ionic interaction mechanism to develop HYA-TF-TQ-LIPO. RA was induced in Wistar rats using Complete Freund's Adjuvant and collagen solution. After the visibility of arthritis sign on the 13th day, treatment was started on day 14 by intravenous route and continued up to the next 21 days. The developed nanoliposomes were characterized and evaluated by in-vitro and in vivo studies. **Results:** Cell cytotoxicity, cell viability and intracellular uptake study on RAW 264.7 macrophage demonstrated the active targeting of HYA-TF-TQ-LIPO towards CD44 receptors. The arthritic rats treated with HYA-TF-TQ-LIPO showed significant reduction in paw inflammation, pro-inflammatory cytokines (TNF-α, IL-6) and low radiographic score as compared to TF-TQ-LIPO, TF and TQ groups. Under hepatotoxicity evaluation, liver histopathology, AST and ALT assay revealed significant reduction in hepatotoxicity by HYA-TF-TQ-LIPO as compared to TF alone. **Conclusion:** The results showed higher efficacy of CD44-targeted HYA-TF-TQ-LIPO in preventing disease progression and promoting articular regeneration. Therefore, the developed nanoliposomes would be promising delivery for an effective treatment of RA.

ICW18-5

Sex differences in treatment response to targeted therapy in rheumatoid arthritis

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Conflict of interest: None

Objectives: To investigate whether male and female patients with rheumatoid arthritis (RA) exhibit different treatment responses to their first targeted therapies. **Methods:** This post hoc analysis utilized data from a quasi-experimental, multicenter, prospective study involving patients with RA who initiated targeted therapy (either biologic disease-modifying antirheumatic drugs or Janus kinase inhibitors) for the first time. The primary outcome was remission, assessed using the DAS28-ESR at week 24. The proportions of patients achieving remission were compared between male and female participants. Logistic regression models were employed to analyze the independent effect of sex on treatment response. **Results:** Among the 506 patients, 78 (15.4%) were male, and 428 (84.6%) were female. In the per-protocol analysis using complete cases, the DAS28-ESR remission rate at week 24 was higher in male patients (44.1%) than in female patients (29.9%) (p=0.03). Univariable logistic regression analysis showed that male sex was associated with greater likelihood of achieving DAS28-ESR remission at week 24 (odds ratio 1.85, 95% confidence interval 1.09-3.14). However, after adjusting for covariates, the association with sex was not statistically significant (adjusted OR 1.42, 95% CI 0.79-2.54). A longer RA duration (aOR 0.96, 95% CI 0.93-0.99) and a higher baseline DAS28-ESR score (aOR 0.43, 95% CI 0.32-0.57) were associated with lower likelihood of achieving remission. In the subgroup of patients with early RA (disease duration<2 years), male patients had a significantly greater likelihood of achieving DAS28-ESR remission at week 24 (aOR 3.12, 95% CI 1.18-8.74) compared to female patients. **Conclusion:** This study demonstrates that male patients with RA exhibit a higher rate of remission at 24 weeks compared to female patients when initiating targeted therapies, particularly in those with early RA. Our findings underscore the potential need for sex-specific strategies in managing RA.

ICW19-1

Decoding the Epigenetic Regulation of Fibroblast Activation in Systemic Sclerosis: A Multi-Omics Machine Learning Approach Integrating DNA Methylation, Histone Modifications, and Single-Cell Transcriptomics

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Conflict of interest: None

Objectives: Systemic sclerosis (SSc) involves excessive fibrosis and vascular issues, leading to severe morbidity. Fibroblast activation is key in SSc, but the underlying epigenetic mechanisms remain unclear. This study aims to improve fibrosis risk prediction in SSc using a multi-omics machine learning model, identifying epigenetic biomarkers and therapeutic targets to advance precision therapy. **Methods:** Data were sourced from the European Scleroderma Trials and Research biobank and the Gene Expression Omnibus, including 1,200 SSc patients and 800 controls. Skin biopsies underwent fibroblast isolation, with DNA methylation assessed using whole-genome bisulfite sequencing (WGBS) and histone marks (H3K27ac, H3K4me3, H3K9me3) profiled via ChIP-seq. Single-cell RNA sequencing (scRNA-seq) covered over 50,000 cells. A multi-omics model integrated a deep neural network for scRNA-seq with gradient boosting decision trees for epigenetic data. Severe fibrosis was defined as a modified Rodnan skin score > 20. Data processing included normalization, batch correction, t-SNE, and Bayesian hyperparameter optimization. **Results:** The model achieved an AUC-ROC of 0.82 (95% CI: 0.79-0.85), with 87.3% sensitivity (95% CI: 84.0%-89.9%) and 85.2% specificity (95% CI: 82.1%-88.0%), outperforming single-omics models (AUC-ROC: 0.73 for DNA methylation, 0.71 for histone modifications, 0.69 for scRNA-seq). Forty-two differentially methylated regions (DMRs), such as hypermethylation at the SMAD3 promoter linked to a 3.6-fold higher fibrosis risk (95% CI: 2.9-4.4), were identified. H3K27ac enrichment was noted at COL1A1 and TGFBR1 enhancers (p<0.0005), while scRNA-seq identified myofibroblasts expressing ACTA2, FN1, and TGFB1. **Conclusion:** This multi-omics approach improves fibrosis prediction in SSc, identifying novel biomarkers and therapeutic targets. Integrating DNA methylation, histone modifications, and scRNA-seq provides a robust strategy for precision treatment.

ICW19-2

Clinical Characteristics and Prognosis of Pulmonary Hypertension in patients with Autoimmune Diseases

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Conflict of interest: None

[Objective] This study focuses on evaluating the prognosis of pulmonary hypertension (PH) associated with systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), and systemic sclerosis (SSc), which is acknowledged as a poor prognostic factor in these diseases. [Methods] We conducted a retrospective analysis of a total 123 patients including 19 SLE, 23 MCTD, and 81 SSC diagnosed with PH based on right heart catheterization between June 2005 and September 2024. PH was defined by a mean pulmonary artery pressure > 20 mmHg and pulmonary vascular resistance > 2 Wood units. The primary endpoint was the 10-year survival rate. [Results] The mean age was highest in SSc (SLE: MCTD: SSc=52.2 vs 55.7 vs 70.5 years). The prevalence of interstitial lung disease (ILD) was lower in SLE compared to MCTD and SSc (33.3% vs 66.7% vs 62.5%). Survival rates were higher for SLE and MCTD at 72.9% and 74.5%, compared to only 38.7% for SSc (p=0.0092). All patients with SLE and MCTD were treated with immunosuppressive therapy (IS), including glucocorticoids, intravenous cyclophosphamide (IVCY), rituximab (RTX), and tacrolimus. Cox regression analysis highlighted the positive impact of IVCY on survival for both SLE (p=0.0064) and MCTD (p=0.0008). Conversely, 46.9% of SSc patients received IS, especially those with ILD (84.2% vs 53.5% with and without IS, p=0.0025). Among those treated, positive anti-SS-A antibodies (p=0.0001), use of IVCY (p=0.0006), nitric oxide pathway drugs (p=0.0022), endothelin receptor antagonists (ERA) (p=0.0027), and RTX (p=0.0078) were associated with improved survival. Specifically, anti-SS-A positive patients had a 10-year survival rate of 90.9% (p=0.0095). In SSc patients not receiving IS, ERA use was correlated with improved survival (p=0.0362). [Conclusion] PH associated with SLE and MCTD showed good survival, benefiting from IVCY treatment. In contrast, SSc-PH had poorer outcomes, although IS notably helped those with anti-SS-A antibodies.

ICW19-3

The efficacy and infectious risk of tofacitinib in anti-melanoma differentiation-associated gene 5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objectives] This study aimed to evaluate the efficacy and infectious risk of tofacitinib (TOF) in patients with anti-melanoma differentiation-associated gene 5 antibody-positive dermatomyositis (MDA5+DM). [Methods] A retrospective observational study included patients diagnosed with MDA5+DM at our department from 2016 to 2024. The effects of TOF on the mortality and infections except for cytomegalovirus were analyzed. Patients were divided by a serum ferritin levels of 500 ng/mL as a poor prognostic factor, and statistical analyses were performed. Continuous variables were presented as median (interquartile range). [Results] A total of 35 patients were included, with a median follow-up of 740 (132-1727) days. The clinical characteristics were as follows; age, 53 (44-67) years; CRP, 0.24 (0.1-1.6) mg/dL; ferritin, 525 (129-1070) ng/mL; KL-6, 828 (440-1072) U/mL; rapidly progressive interstitial lung disease (RP-ILD), 24 (69%). Tacrolimus and cyclophosphamide were used in 34 patients (97%). Besides, TOF and plasma exchange (PE) were added in 21 (60%) and 12 (34%) patients, respectively. Mortality occurred in 8 patients (23%) and infections in 14 patients (40%), with a tendency for reinfection in affected patients. The ferritin level >500 ng/mL was observed in 18 patients (53%); age, 61 (50-68) years; ferritin, 1054 (642-3174) ng/mL; KL-6 882 (537-1072) U/mL; RP-ILD, 14 (78%). Death was observed only in this group (44%), with TOF usage reducing mortality (HR 0.21, 95% CI 0.05-0.85), while the effect of PE was not significant (HR 0.90, 95% CI 0.21-3.79). TOF increased the risk of infection (HR 5.22, 95% CI 1.42-33.68), with fungal infections being common (43%); however, no infection-related deaths due to TOF were observed. [Conclusion] TOF was more effective than PE in severe cases with ferritin >500 ng/mL, although it was associated with an increased risk of infection, especially fungal infections, warranting caution.

ICW19-4

CCR4+Tfh2 cell is a key interleukin-4 producer driving IgG4-related disease pathogenesis

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Conflict of interest: Yes

[Objectives] T follicular helper (Tfh) cells are key regulators of B-cell differentiation and antibody production, consisting of three main subsets: Tfh1, Tfh2, and Tfh17. Tfh2 cells are uniquely characterized by the absence of CXCR3 and CCR6, indicating a heterogeneous population. This study aimed to determine whether CCR4 serves as a specific marker for IL-4-producing Tfh2 cells and to explore its mechanistic role in IgG4-related disease (IgG4-RD). [Methods] We conducted RNA-seq and single-cell analysis of Tfh subsets from peripheral blood to identify IL-4-producing cells. Blood samples were collected from 23 treatment-naïve patients with active IgG4-RD and 21 healthy controls. Flow cytometry and immunohistochemical staining were used to assess CCR4+ Tfh2 cells in both peripheral blood and affected tissues. [Results] CCR4+ Tfh2 cells were identified as IL-4-producing Tfh subset, expressing higher levels of the transcription factor GATA-3 and the co-stimulatory molecule ICOS compared to their CCR4- counterparts. However, levels of BCL-6, the canonical Tfh regulator, and FOXP3, associated with regulatory T cells, remained unchanged, highlighting a distinct phenotype. Patients with IgG4-RD had a significantly higher proportion of CCR4+ Tfh2 cells in their blood compared to healthy controls. These cells were even more abundant in affected lacrimal gland tissues, with immunohistochemistry revealing their presence in tertiary lymphoid structures and storiform fibrosis. The frequency of CCR4+ Tfh2 cells strongly correlated with serum IgG4 levels. Notably, glucocorticoid therapy did not reduce the prevalence of CCR4+ Tfh2 cells. [Conclusion] CCR4 was identified as a reliable marker for IL-4-producing Tfh2 cells, a subset that plays a crucial role in IgG4-RD pathogenesis by promoting B-cell activation and tissue remodeling. The persistence of CCR4+ Tfh2 cells despite glucocorticoid therapy underscores the need for targeted therapies to modulate this population.

ICW19-5

Prognostic factors in connective tissue disease-associated thrombotic microangiopathy

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Conflict of interest: None

[Objectives] Thrombotic microangiopathy (TMA) is associated with poor survival or renal outcomes in connective tissue diseases (CTD). However, the prognostic factors in CTD-associated TMA (CTD-TMA) remain unknown. This study aimed to identify which factors may influence prognosis in CTD-TMA. [Methods] This single-center retrospective observational study comprised 32 patients with CTD-TMA who visited our hospital from 2006 to 2024. 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. The primary endpoint was defined as death or permanent hemodialysis. Prognostic factors at the time of TMA onset and within 14 days after treatment initiation were evaluated using univariate and multivariate Cox regression analyses. Receiver operating characteristic (ROC) analysis was applied to determine the cutoff values. [Results] Of the 32 patients, 26 were female, with a mean age of 49 years. Six patients were diagnosed with TTP. Eighteen patients had underlying systemic lupus erythematosus and 11 had systemic sclerosis. During the observation period, 16 patients died and 2 required hemodialysis. The one-year event-free rate was 56.3%. Multivariate Cox regression analysis showed that LDH levels at the TMA onset (hazard ratio=1.12, p=0.04) was identified as an independent prognostic factor. The increase rate of platelets from baseline to day 10 (hazard ratio=0.71, p=0.04) was also identified as an independent prognostic factor after treatment initiation. ROC curve analysis indicated that a LDH>560 U/L at baseline was the optimal cutoff point for predicting poor prognostic outcome. [Conclusions] Elevated LDH at the TMA onset and platelet

non-recovery within 10 days of treatment were identified as independent poor prognostic factors in CTD-TMA, suggesting that rapid intensive treatment would be recommended in these patients.

ICW20-1

Mass cytometry analysis revealed a similarity in the synovial fluid immune cell composition between elderly-onset seronegative rheumatoid arthritis and polymyalgia rheumatica

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Conflict of interest: Yes

[Objectives] The diagnosis of elderly-onset rheumatoid arthritis (EORA) can be challenging due to its clinical similarity to polymyalgia rheumatica (PMR), particularly in seronegative patients. This study aimed to perform a detailed analysis of synovial fluid cells to characterize EORA and PMR, providing a foundation for accurate diagnosis in elderly patients with arthritis and understanding the immune dysregulation in these conditions. [Methods] Patients aged 60 or older with shoulder effusion, diagnosed with RA or PMR according to established or proposed classification criteria, were enrolled. The synovial fluid samples were analyzed using a CyTOF XT. Mass cytometry data were processed using FlowJo software, followed by downstream analyses with scDataviz. [Results] Fourteen patients were recruited in this study. The average age was 73.5 years, and 7 participants were female. The cohort included 5 anti-citrullinated protein antibody (ACPA)-positive RA, 5 ACPA-negative RA, and 4 PMR cases. ACPA-positive RA included 2 recurrent cases, while the others were newly diagnosed at the time of study recruitment. There was a trend toward a higher number of synovial fluid cells in ACPA-positive RA compared to PMR, although the difference was not statistically significant ($p = 0.095$). In mass cytometry analyses, neutrophils were higher in ACPA-positive RA ($p = 0.005$). CD4+ T cells were less common in ACPA-positive RA; however, a notable proportion of CD4+ T cells was observed in ACPA-negative RA and PMR ($p = 0.015$). Among CD4+ T cells, no distinct cluster was identified that could discriminate between ACPA-negative RA and PMR. [Conclusion] ACPA-negative EORA and PMR exhibited similar synovial fluid cell compositions, with an increased T cell population, suggesting that these conditions may share common immune dysregulation. Despite the use of high-parameter synovial fluid cell analysis, distinguishing between ACPA-negative EORA and PMR remains challenging.

ICW20-2

Comparative Analysis of Clinical Presentations and Intravenous Immunoglobulin Response in Typical and Incomplete Kawasaki Disease: A Cohort Study of 717 Patients

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Conflict of interest: None

[Objectives] The research aimed to investigate Kawasaki Disease (KD), a pediatric coronary vascular inflammatory condition. Incomplete KD was the focus, which lacks one or more principal clinical features but still involves coronary artery inflammation. The study sought to understand its clinical manifestations, laboratory findings, coronary arterial lesions (CAL) or aneurysm (CAA), and intravenous immunoglobulin (IVIG) treatment responses. [Methods] Our analysis is based on a comprehensive dataset from patients with KD treated at Chang Gung Memorial Hospital (CGMH) from 2000 to 2023. The cohort consisted of 717 patients, 577 of whom were diagnosed with typical KD and 140 with incomplete KD. [Results] The study suggests incomplete KD is more commonly observed in infants younger than one year ($p=0.024$). It also reported that these cases typically show higher platelet counts and lower hemoglobin levels, GOT, GPT, and C-reactive protein (CRP) (all $p<0.001$). There were also notable differences in CRP levels between typical and incomplete KD, particularly a higher prevalence of lower CRP levels in patients over one year old with incomplete KD. Moreover, incomplete KD exhibited a significantly higher incidence of CAL ($p<0.001$) before IVIG administration and lower resistance to IVIG treatment ($p=0.008$). Fortunately, after six months of treatment for KD, no significant differences were observed in the incidence of CAL or CAA ($p=0.091$ and 0.307, respectively). [Conclusion] The study underscores critical differences between typical and incomplete KD, with incomplete KD showing more severe coronary complications and distinct laboratory profiles. Incomplete KD, prevalent in infants under one year, is associated with elevated risks of CAL and CAA before treatment. However, following the timing of the IVIG administration, no significant occurrences of CAL or CAA were observed in either typical or incomplete KD cases.

ICW20-3

Association of induction therapy with intravenous cyclophosphamide and pulmonary outcome in patients with interstitial lung disease associated with anti-synthetase syndrome

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Conflict of interest: None

[Objective] To investigate whether induction regimens including intravenous cyclophosphamide (IVCY) yield better pulmonary outcomes in patients with interstitial lung disease associated with anti-synthetase syndrome (ASS-ILD). [Methods] We retrospectively reviewed patients with ASS-ILD who received induction therapy at Keio University Hospital from 2005 to 2024. ASS-ILD is defined as ILD determined with HRCT with a positivity of anti-ARS antibodies confirmed with immunoprecipitation assay or enzyme-linked immunosorbent assay. All patients received high dose glucocorticoid (GC) at first and the regimens were stratified into two groups: IVCY followed by other immunosuppressants (IST) such as tacrolimus, cyclosporine and/or azathioprine (IVCY-IST group) or IST without IVCY (IST group). [Results] 42 cases were included. The mean age was 59.4 years and 73.8% were female. The IVCY-IST group had lower %FVC and %DLCO (68.5% vs 84.2%, $p=0.001$; 40.7% vs 53.6%, $p<0.001$, respectively), higher extent of disease on HRCT, and higher Hugh-Jones score (2.5 vs 1.8, $p=0.005$) at baseline. During the mean observation period of 7.6 years, relapse occurred in 29 patients (54.8%) with the mean duration of 1,397 days. Patients in the IVCY-IST group were administered higher initial GC dosage (51.8 vs 42.8 mg, $p=0.026$). After induction treatment, HRCT findings at 6 months improved more frequently in the IVCY-IST group than the IST group (35.0% vs 14.3%, $p=0.024$). In contrast, no difference was observed in relapse rate and progression to end stage lung disease (odds ratio [OR], 0.82; 95% confidence interval [CI], 0.52-1.29; OR, 0.90; 95% CI, 0.61-1.35, respectively). [Conclusion] IVCY-IST therapy improved ASS-ILD at 6 months on HRCT despite worse ILD findings at baseline compared with IST therapy. Rate of relapse and progression to end stage were comparable between the two groups, suggesting optimal treatment during maintenance phase should be established after induction therapy with IVCY.

ICW20-4

Disability prevalence and influencing factors in patients with systemic vasculitides: Insights from a regional study

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Conflict of interest: None

[Objectives] Patients with systemic vasculitides (SV) are an intricate category requiring thorough, comprehensive assessment to precisely determine the disease's activity, seriousness, impact, and future outlook, as well as its effects on physical capabilities and quality of life. The research focused on evaluating how common disabilities are among patients with SV and determining the factors that affect disability outcomes. [Methods] The study involved patients over 18 diagnosed with SV by rheumatologists of Shymkent Regional Clinical Hospital and Almaty City Rheumatology Center between 2019 and 2021. Out of the 162 patients diagnosed

with SV, 44 (27.1%) had varying groups of disability. [Results] Of the 44 patients with SV, 79.5% are females; the average age of patients is 41 (SD=12). 61.4% of patients are residents of rural areas. More than half of the patients (54.5%) are classified as group II disabled (n=24), 36.4% (n=16) are group III disabled, and the remaining 9.1% (n=4) are classified as group I disabled; 90.9% of patients are unemployed. Comorbid conditions were detected in 32 (72.7%) patients, while 19 (43.2%) patients had complications of the underlying disease. Among patients with Takayasu's arteritis (TAK), the disability rate is the highest (52.3%). This can be explained by the delayed diagnosis in a given group of patients; the average time from debut to diagnosis of TAK is seven times longer (4.61 months) than that of IgA-vasculitis (0.66 months). Almost 69% of patients are on steroid therapy. The average BMI of the patients was 24.2; only two patients had grade II obesity. [Conclusion] This study highlights the significant prevalence of disability among patients with SV, which indicates a close relationship between the type of disease and a specific category of disability. The results highlight the need to develop awareness-raising approaches, as well as early diagnosis, to reduce disability in patients with SV and improve treatment outcomes.

ICW20-5

Pulmonary Manifestations and Prognosis in 10 Cases of Idiopathic Multicentric Castleman Disease with Lung Involvements

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Conflict of interest: None

[Objectives] Idiopathic multicentric Castleman disease (iMCD) is a lymphoproliferative disorder with various systemic symptoms including diverse pulmonary complications. This study aimed to evaluate the characteristics and treatment outcomes of pulmonary involvements in iMCD patients. [Methods] We performed a retrospective study on 19 iMCD patients (excluding TAFRO syndrome) who visited our institution from January 2010 to June 2024, of which 10 (52.6%) developed pulmonary lesions. Clinical progression, imaging, and treatment were evaluated to classify lung lesions and assess the efficacy of treatment. [Results] Of the 10 cases, ground-glass opacities were seen in 8 cases (80.0%), nodular lesions in 5 (50.0%), cystic lesions in 3 (30.0%), reticular patterns in 1 (10.0%), and chest wall masses in 1 (10.0%), with some cases exhibiting more than one type of pulmonary lesion. Tocilizumab was administered to all 10 cases, with 6 (60.0%) also receiving prednisolone. Additionally, mycophenolate mofetil was used in 3 cases (30.0%), Janus kinase inhibitors in 2 (20.0%), rituximab in 1 (10.0%), tacrolimus in 1 (10.0%), and methotrexate in 1 (10.0%). In the 3 cases with cystic lesions, all 3 cases worsened. One patient experienced an acute exacerbation of interstitial pneumonia requiring respiratory support during the course. Of the 7 cases without cystic lesions, improvements in computed tomography (CT) scan images were seen in 3 cases with ground-glass opacities, nodular lesions, or both. Exacerbation of CT scan images was seen in only 1 patient, who had both ground-glass opacities and nodular lesions. The other 3 cases remained stable. [Conclusion] Various types of pulmonary lesions were observed in iMCD patients, especially ground-glass opacities, nodular lesions, and cystic lesions. Patients with cystic lesions faced higher risks of disease progression, while most cases without cystic lesions remained relatively stable or improved with immunosuppressive treatment.

ICW21-1

Efficacy and safety of canakinumab in patients with Adult-Onset Still's Disease: Interim results from an open-label study in Japan

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Conflict of interest: Yes

[Objectives] There is an unmet need for effective treatment options for Adult-Onset Stills Disease (AOSD) in Japan. The current study was designed to evaluate the efficacy and safety of canakinumab 4 mg/kg every 4 weeks administered subcutaneously in Japanese AOSD patients. [Methods] In this interim analysis, we present efficacy data on the first 11 patients who reached Week 28 (5 of which had prior biologic use) and safety data on all 14 patients (7 of which had prior biologic use) up to the Week 28 interim cut-off (48-week results will be included in the presentation). The primary endpoint assessed ACR30 response, with a pre-defined 95% CI lower limit requirement of 40% at Week 8. Secondary endpoints included: the ability of canakinumab to taper glucocorticoids starting from Week 8 to 28; ACR30/50/70/90/100 responses over time; systemic feature score (SFS) over time. [Results] The primary endpoint was not met (6/11 [54.5%]; 95% CI: 20.6, 88.5; one-sided p-value = 0.249). From Week 8 to 28, 6/11 patients (54.5%) successfully tapered oral glucocorticoids. At Week 28, of the 11 patients assessed, 70% achieved ACR30 and ACR50, 60% achieved ACR70 and ACR90 and 40% achieved ACR100. At Week 28, the mean (SD) change from baseline in SFS was -4.3 (2.06). All 14 patients had at least one treatment emergent adverse event. Adverse events of special interest included infections in 9 patients (64.3%), abnormal hepatic function in 3 patients (21.4%) and hepatic steatosis in 1 patient (7.1%). [Conclusion] Although the primary endpoint was not met, the Week 28 analysis showed that the treatment of Japanese AOSD patients with canakinumab led to an improvement in various efficacy outcome measures. The Week 28 interim analysis safety findings are consistent with the established safety profile of canakinumab with no unexpected safety signals observed.

ICW21-2

Clinical characteristics and outcome of Posterior Reversible Encephalopathy Syndrome in patients with Autoimmune Rheumatic Diseases: A Retrospective Observational Study

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Conflict of interest: None

Objectives: To delineate the clinical presentation, imaging features and outcomes of Posterior Reversible Encephalopathy Syndrome (PRES) in Autoimmune Rheumatic Diseases (AIRD), with a specific focus on Systemic Lupus Erythematosus (SLE). Methods: We reviewed the Electronic Medical Records (EMR) of inpatients with AIRD diagnosed as PRES between January 2005 and July 2024 and noted their clinical variables, disease activity, serological profile, investigation and changes in magnetic resonance imaging (MRI). Results: We identified 33 patients (31 females; mean age±SD 25±10 years) with PRES (SLE - 28, Takayasu arteritis - 2, Rheumatoid arthritis, polyarteritis nodosa and ANCA vasculitis - 1 each). Pre-existing hypertension was identified in 9 (27%) patients; 24 (72%) presented with new-onset hypertension, while 5 (15%) were normotensive at presentation. One patient developed PRES in the postpartum period. Seizures in 26 (92%) and headaches in 28 (100%) were the most common symptoms. Others included focal neurological deficits in 3 (10.7%), visual impairment in 12 (42%), and altered sensorium in 10 (35%). Significant proteinuria and active urinary sediments were noted in 25 (89%) each. Concurrent infections were observed in 17 (60.7%). PRES was diagnosed as a presenting feature in 3 (10.7%) patients with SLE. Anti-phospholipid were noted in 15 (53%) patients. Two patients (3%) with SLE experienced a PRES relapse within six months. Four patients (12%) died of PRES (3 SLE, 1 PAN). Most common MRI finding was T2 hyperintensity in the occipital (97%), parietal (90%), frontal (78%), temporal (57.6%) lobes, with atypical involvement of the brainstem (48%), cerebellum (30%), and basal ganglia (13%) Conclusion: Patients with AIRD and PRES had fa-

vourable outcomes over nearly three years of follow-up. Atypical MRI findings were common. PRES may present with normal blood pressure and can be a presenting feature in SLE. Thus, it could be included as a neuropsychiatric manifestation of SLE.

ICW21-3

Identification of five clinical subtypes in patients with anti-synthetase syndrome -associated interstitial lung disease using cluster analysis: multicenter MYKO cohort study

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Conflict of interest: None

Objective: This study aimed to identify new clinical phenotypes of anti-synthetase syndrome (ASS)-associated interstitial lung disease (ILD) using a principal components analysis (PCA)-based cluster analysis. Methods: Of the 487 IIM patients, 172 were positive for ARS antibodies. A total of 118 patients with ASS with interstitial lung disease (ILD) between January 2016 and March 2024 were enrolled from a multicenter cohort in Japan (MYKO cohort). Categorical PCA and cluster analysis were performed based on clinical characteristics with ASS-ILD. Clinical characteristics and outcomes, including relapse rate were compared between each cluster. Results: Thirteen clinical variables were transformed into five components using categorical PCA and synthetic variables were created. Additionally, a cluster analysis was performed using these variables to classify 118 patients with ASS-ILD into subgroups. Five distinct clinical subgroups were identified: Cluster 1 was comprised of severe muscle involvements (N=27). Cluster 2 was youngest, skin-dominant, and severe ILD (N=20). Cluster 3 was comprised of skin and microvascular abnormality. (N=17). Cluster 4 is associated with malignancy and severe ILD. (N=32). Cluster 5 is eldest, male-dominant, have highest inflammation, and develops the most severe ILD. (N=22). There were significant differences in prognosis between five clusters. Especially, cluster 5 showed the highest ILD relapse rates among five clusters. Conclusions: Our study identified five unique subgroups with different outcomes in ASS-ILD. Individualized treatments for each subgroup may be needed to improve the prognosis of ASS-ILD.

ICW21-4

Diffusion-Weighted Imaging: An Alternative to CT for Detecting Renal Parenchymal Lesions in IgG4-Related Kidney Disease

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Conflict of interest: None

[Objectives] To compare the efficacy of magnetic resonance imaging (MRI) with that of plain or contrast-enhanced computed tomography (CT) in the detection of renal parenchymal lesions of immunoglobulin G4-related kidney disease (IgG4-RKD). [Methods] Patients who performed plain, contrast-enhanced CT and MRI around the kidney region in our hospital were enrolled. The consensus diagnosis of IgG4-RKD was made by combining available histopathology, imaging findings, laboratory tests, and response to glucocorticoid therapy. Five blinded observers independently assessed image datasets by confidence scores to assess diagnostic accuracy, sensitivity, specificity, areas under the receiver operating characteristic curve (AUROC), and Cronbach's alpha coefficient. [Results] A total of 31 patients were included in the study. 24 out of 31 patients were diagnosed as IgG4-RD. Among the patients with IgG4-RD, nine patients (37.5%) had renal parenchymal lesions of IgG4-RKD. The AUROC and sensitivity were higher in diffusion-weighted imaging (DWI)-b800 than in plain CT ($p<0.05$). Cronbach's alpha coefficient was 0.44 for plain CT and over 0.80 for contrast-enhanced CT and DWI-b800. The causes of false positives for each modality were summarized. There was a high false positive rate for contrast-enhanced CT on images of renal infarction and a high false positive rate for DWI-b800 on images of hydronephrosis. [Conclusion] Plain MRI, especially in DWI-b800, can effectively detect renal parenchymal lesions in IgG4-RKD. In difficult cases to use a contrast agent of CT, DWI-b800 can be an alternative for the screening of IgG4-RKD.

ICW21-5

Oral pulse steroid therapy for polymyalgia rheumatica

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Conflict of interest: None

[Objectives] A novel regimen of oral steroid pulse therapy (oral-P), involving intermittent steroid dosing via the oral route, was introduced for treating polymyalgia rheumatica (PMR). This study retrospectively evaluated its efficacy and safety. [Methods] Medical records of PMR patients diagnosed using ACR/EULAR criteria, treated with oral-P between April 2015 and July 2020, and followed until July 2024, were reviewed. The oral-P regimen involved 0.4 mg/kg/day prednisolone (PSL) for three days followed by 0.1 mg/kg/day for 11 days (0.4P), or 0.8 mg/kg/day followed by 0.2 mg/kg/day (0.8P). After three or five courses, the dose was tapered. The treatment plan was chosen by the physician. Serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were monitored. Disease duration prior to oral-P, follow-up after withdrawal, and adverse events were assessed. [Results] The study included 34 patients (22 women, 12 men; aged 66-86 years; 0.4P/0.8P: 15/19; three/five courses: 11/4 in 0.4P, 13/6 in 0.8P). Before oral-P, CRP and ESR were significantly higher in the 0.8P group than in the 0.4P group [CRP: 8.93 (4.83-12.0) vs. 4.96 (4.15-6.31) mg/dL; ESR: 113.5 (92.75-129) vs. 84 (66-95.5) mm/h]. Disease duration till oral-P introduction was longer in the 0.8P group but not significantly. After the first course, CRP and ESR significantly decreased in both groups, with no significant difference between them. A total of 21 patients successfully discontinued steroids without relapse during a median follow-up of 27 (14-49) months. The remaining 13 patients were tapering [4.75 (4.75-4.75) mg/day] at their last visit. No severe adverse events were reported. [Conclusion] Oral-P is an effective and safe treatment for PMR, offering rapid relief and supporting steroid withdrawal.

ICW22-1

Rapid glucocorticoid reduction does not affect renal outcome in proliferative lupus nephritis -A multicenter retrospective survey in Japan

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Conflict of interest: None

Objectives: Recent guidelines and recommendations for lupus nephritis (LN) recommend rapid glucocorticoid (GC) reduction; however, there is little strong evidence to support this. We aimed to assess the effect on renal outcome of rapid GC reduction in the treatment of proliferative LN. **Methods:** A multicenter retrospective chart review was conducted involving GC-naïve, recent-onset proliferative LN patients who had data on the urinary protein-to-creatinine ratio (UPCR) both before and 52 weeks after GC treatment. Patients who reduced their prednisolone equivalent dose to ≦ 7.5 mg/day by 6 months (rapid GC reducers) were compared with those who did not (conventional GC reducers) in achieving partial renal response (PRR) at 12 months. Modified Poisson regression analysis was performed to adjust for multiple confounding factors. **Results:** A total of 344 patients from 17 institutes were enrolled, consisting of 50 rapid GC reducers and 294 conventional GC reducers). Achievement of PRR at 12 months was 43/50 (86%) and 248/294 (84.4%), respectively. After adjusting for possible background factors, including age, initial UPCR, initial eGFR, initial GC dose, use of methylprednisolone pulse therapy, use of strong immunosuppressants (mycophenolate mofetil, cyclophosphamide, or rituximab), and use of hydroxychloroquine, we found no significant difference in achieving PRR at 12 months (incident rate ratio 0.92, p=0.760). Follow-up found that the incidences of recurrence and serious adverse events were similar between the groups during the first two years. **Conclusion:** Our findings suggest that rapid GC reduction does not affect renal outcomes.

ICW22-2

Urinary biomarkers associated with pathogenic pathways reflecting histological findings in lupus nephritis

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Conflict of interest: None

[Objectives] There is a pressing need to understand the pathogenesis of histological findings and identify the biomarkers for predicting the histological severity in lupus nephritis (LN). This study aimed to identify the pathogenic signal pathway and elucidate urinary biomarkers for predicting the presence or severity of histological findings in LN. [Methods] Urine samples from patients with biopsy-proven active LN were screened for 1305 proteins using an aptamer-based proteomic assay. The diversity and expansion of individual renal histological features in LN were quantified to identify the urinary proteins associated with the histological findings found in each score. Candidate urinary proteins were validated in a validation cohort. Immunohistochemical staining of the renal tissues was performed to clarify the localisation of the candidate proteins. [Results] Cluster analysis extracted five histological subgroups according to their correlations with each histological finding in LN. Protein groups which correlated with each histological subgroup revealed a distinct pathogenesis in LN using pathway analyses. Enzyme-linked immunosorbent assay validation revealed that urinary calgranulin B (S100A9), MCP-1, and IGFBP-5 levels could specifically predict the presence and severity of active glomerular lesions, interstitial inflammation, and interstitial fibrosis, respectively. Immunohistochemical staining revealed the localisation of these proteins in each lesion. [Conclusion] Renal histological findings may reflect the different pathogeneses involved in each lesion, and estimating the urinary calgranulin B, MCP-1, and IGFBP-5 levels may be useful in predicting the presence and severity of histological findings in LN.

ICW22-3

Effectiveness and safety of rituximab (RTX) in patients with lupus nephritis (LN) -LOOPS registry-

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Conflict of interest: None

[Objective] Rituximab (RTX) was approved for lupus nephritis in August 2023 in Japan. However, the effectiveness and safety in real-world clinical practice have not been validated. This study aimed to assess the efficacy and safety of RTX for LN in real-world clinical practice. [Methods] The patients with LN treated with high/middle-dose GC or GC pulse and HCQ+RTX (RTX group, n=32), +MMF (MMF group, n=76), or +CYC group (CYC group, n=24) in remission induction therapy after May 2016, when MMF was approved in Japan, were included. The effectiveness and safety were compared among groups. The primary endpoint was the achievement rate of Complete Renal Response (CRR) and uPCR <1.0 at week 52. The secondary endpoints were retention rate, adverse events, and GC-sparing effect. In addition, peripheral blood immunophenotyping was performed on age- and gender-matched HCs and RTX groups before and after RTX treatment. [Results] There were no differences in patient background among groups. Treatment retention was 90.6% in the RTX group, 90.8% in the MMF group, and 70.8% in the CYC group. The most common adverse events were infusion reactions (28.1%) in RTX and infections in MMF (32.9%) and CYC (58.3%). SLEDAI and BILAG scores significantly decreased across groups. Primary endpoint (CRR) rates were similar: 40.6% (RTX), 48.7% (MMF), and 37.5% (CYC) (p=0.55), with no significant differences in GC sparing effects (-87.4%, -84.0%, -86.7%; p=0.78). Immune phenotyping showed higher class-switched memory B cells and plasmocytes in SLE vs. HCs. Naïve B cells, CM B cells, and plasmocytes disappeared after 26 weeks of RTX, remaining low up to 52 weeks in CRR cases, while CM B cells and plasmocytes increased in non-CRR cases. [Conclusions] RTX can be an effective treatment option for LN in real-world clinical practice.

ICW22-4

Early attainment of lupus low disease activity state and renal prognosis among patients with lupus nephritis

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Conflict of interest: None

[Objectives] Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE). A shorter time to reach lupus low disease activity state (LLDAS) has known favourable outcomes among SLE patients, but its utility in LN remains unclear. This study investigates the association between renal prognosis and time to LLDAS attainment. [Methods] Patients with biopsy-proven LN in 2010-2020 were included; those unable to reach LLDAS by the end of the follow-up period were excluded. They were routinely followed up to repeat blood tests and urinalysis. After the index LN, the first visit with LLDAS attainment was identified to calculate time-to-LLDAS. Any subsequent relapse confirmed by a renal biopsy was documented. Deterioration of renal function was assessed by doubling of serum creatinine level and chronic kidney disease (CKD) stage 3b. Associations between LLDAS and renal outcomes were tested. [Results] 159 patients were included in this study with a female-to-male ratio of 9:1. Most patients (72%) had proliferative LN (class III/IV+/-V). The median follow-up duration was 9.5 years. Patients with a longer time-to-LLDAS were associated with LN relapse (p=0.001) and higher CKD stages at the latest visit (p=0.007) but not baseline CKD status (p=0.344). After adjusting for baseline variables, including proteinuria, serology, serum creatinine, SLEDAI-2K, medications, time-to-LLDAS remained a significant predictor of LN relapse and renal function deterioration. For every year delay in LLDAS attainment, the risk of relapse increased by 27% (p=0.02); doubling of creatinine by 75% (p<0.001); CKD stage 3b by 42% (p=0.008). Time-to-LLDAS showed an area under ROC curve (AUC) of 0.73 in predicting doubling of creatinine and 0.71 in CKD3b. [Conclusion] Additional time to LLDAS attainment had negative associations with re-

nal outcomes. Early LLDAS attainment should be advocated in LN. Treatment intensification should be considered in patients who fail to attain the target timely.

ICW22-5

Safety and Efficacy Of Rituximab in Lupus Nephritis from a tertiary care centre

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Conflict of interest: None

Background: Current KDIGO and EULAR/ERA-EDTA guidelines recommend immunosuppressants including corticosteroids, cyclophosphamide or mycophenolate mofetil (MMF) as first-line agents for remission induction in lupus nephritis. However, with current induction regimens, <60% of class III to V patients with lupus nephritis achieve a complete response (1). Thus lupus nephritis is still in need of more effective therapeutic intervention. **Objectives:** Rituximab has been used off-label for various glomerular diseases. No Indian data is available to demonstrate the efficacy of rituximab in lupus nephritis. We evaluated rituximab as a potential therapeutic agent in lupus nephritis in Indian patients. **Methods:** Single centre, retrospective study, involving 126 patients with class III, IV or V lupus nephritis. Rituximab was given at a dose of 1 gram on days 1 and 15 with or without pulse methylprednisolone as induction agent. Patients with missing data are excluded in analysis. **Results:** 85 out of 113 (75%) patients achieved complete or partial remission with a sustained response in 82 out of 96 (85%) at 1 year. Mean steroid dose in prednisolone equivalent at 0, 3, 6, 12 months are 55, 19.95, 4, 55, 0.75 mg respectively. Significant reduction in other parameters like dsDNA, c3, c4, urine RBC, were recorded on treatment with rituximab. The complication rate was low with no severe infections or death. Subgroup analysis between 17 patients who received direct rituximab and those who received rituximab after treatment failure or relapse with either induction agents like cyclophosphamide and MMF didn't show any statistical difference in results including CKD, dialysis requirement or death. **Conclusions:** These results indicated the possible efficacy and safety of rituximab based regime with its potential to reduce the steroid requirement as well as achieving remission in treatment naïve and in patients who are refractory or relapse with standard agents.

ICW23-1

Dynamic functional and spatial transition of peripheral helper T cells in rheumatoid arthritis

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Conflict of interest: None

[Objectives] Peripheral helper T (Tph) cells play important pathogenic roles in autoimmune diseases. Tph cells are proposed to be the major B-cell helpers in inflamed joints of rheumatoid arthritis (RA). However, whether and how Tph cells are engaged in tissue inflammation remains unclear. [Methods] We performed multi-omics analyses of synovial CD4+ T cells from RA patients (n=10). Transcriptome, epigenome, TCR clonotype, and spatial transcriptome analyses at the single cell level, along with in vitro functional assays, were conducted. [Results] Tph cells consisted of two directly related subsets in RA: stem-like Tph (S-Tph) and effector Tph (E-Tph) cells. These two subsets differed in transcriptome, epigenome, B-helper capacity, spatial localization, and the encountering cells. S-Tph cells were endowed with a self-renewal capacity, which was dependent on TCF1. S-Tph cells were mainly found within tertiary lymphoid structures (TLSs) and colocalized with B cells. Consistently, S-Tph cells potently induced B cells to produce immunoglobulins. By contrast, E-Tph cells highly expressed genes associated with effector molecules, including IFN-g. Notably, the frequency of E-Tph cells, but not S-Tph cells, positively correlated with disease activity. E-Tph cells were found at the margins and outside of TLSs and were closer to proinflammatory macrophages and CD8+ T cells than B cells. Additionally, S-Tph and E-Tph cells robustly shared TCR clonotypes, and S-Tph cells were able to differentiate into E-Tph cells upon TCR stimulation and coculture with B cells, but not the opposite. [Conclusion] S-Tph cells play a central role in promoting Tph responses by undergoing self-renewal and seeding E-Tph cells. The major function of E-Tph cells is not to support antibody production but rather to augment the inflammation. Our study provides a rationale to target S-Tph cells for the treatment of autoimmune diseases with an expectation to reduce global Tph responses and TLS formation.

ICW23-2

Serum Cytokine-Based Clustering in DMARDs-Naïve Rheumatoid Arthritis and Distinct Cluster-Specific Cytokine Dynamics: A Multicenter RA Cohort Study

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Conflict of interest: None

[Objectives] To address the heterogeneity in rheumatoid arthritis (RA), we aimed to characterize the cytokine landscape of RA patients by clustering based on pre-treatment serum cytokine profiles and investigating cluster-specific cytokine dynamics as potential disease drivers and biomarkers. [Methods] Patients with newly diagnosed, DMARDs-naïve RA, registered in the multicenter RA registry "Three Arrow Study" were enrolled. Unsupervised clustering was performed using 13 serum cytokines measured at baseline. For each cluster, baseline characteristics, disease activity, and cytokine levels were evaluated, and correlations between changes in cytokine and disease activity over 24 weeks were assessed. [Results] Cluster analysis stratified 204 RA patients into four clusters (CL). CL1 was characterized by high arginase levels, while CL4 was marked by elevated levels of IL-4, TNFα, IL-1β, IFNγ, IL-12p40, and IL-23. CL3 showed moderate levels of these cytokines, and CL2 exhibited low levels across all cytokines. While inflammatory cytokine levels varied among clusters, no significant difference in baseline Clinical Disease Activity Index (CDAI) was observed. However, seropositivity for RF and anti-CCP antibodies was higher in CL4 and lower in CL1. CDAI at 24 weeks was similar across clusters, yet correlations between changes in serum cytokines and CDAI differed markedly by cluster. In CL4, moderate to strong positive correlations were found with IFNγ, IL-12p40, CXCL10, IL-1RA, and IL-10 (r=0.4-0.7), while CL1 showed a strong positive correlation only with IL-6 (r=0.74). In contrast, no correlation was observed between CDAI and serum cytokines in CL2 and CL3 (r=-0.2-0.1). [Conclusion] Pre-treatment serum cytokine clustering identified four subgroups associated with seropositivity rather than disease activity. Correlations between cytokine and disease activity changes varied by cluster, suggesting these cytokines as potential key factors in pathogenesis and biomarkers.

ICW23-3

Unveiling Predictive Parameters for Rheumatoid Arthritis Development in Arthralgia Patients: Insights from A Prospective Longitudinal Study

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Conflict of interest: None

Objective: To identify risk factors for the development of RA in individuals experiencing arthralgia. Method: 200 consecutive adults with arthralgia were enrolled from new referrals to our rheumatology clinic. Patients with synovitis or known arthritis were excluded. Follow-up assessments were conducted every 6 months, or sooner if symptoms worsened, for 2 years. The study endpoint was the development of RA according to the 2010 ACR/EULAR classification criteria. Baseline demographics, clinical parameters, serology, and acute phase reactant levels were compared between RA and non-RA groups. In addition, the classification score based on the 2010 ACR/EULAR criteria was utilised as a composite weighted score summarising the clinical presentation in the cohort, although the patients were deemed not fulfilling the mandatory criteria of having synovitis at baseline. Result: By May 2024, 104 patients were followed up for at least 1 year, with a median duration of 78 weeks (IQR: 58-97). Among these patients, 23 (22%) developed RA after a median follow-up time of 41 weeks (IQR: 25-52). Patients who developed RA had a significantly higher proportion of joint symptoms <1 year, difficulty making a fist, positive rheumatoid factor, anti-CCP antibodies, and elevated ESR and CRP at baseline. Multivariate logistic regression identified difficulty making a fist (OR 4.87, 95% CI: 1.40-17.04, p=0.013) and positive anti-CCP antibodies (OR 13.04, 95% CI: 3.74-45.44, p<0.001) as independent predictors for RA development. Meanwhile, patients who developed RA had significantly higher baseline classification scores compared to the non-RA group. Conclusion: Difficulty making a fist and positive anti-CCP antibodies are independent predictors of RA development. Patients who developed RA also exhibited significantly higher baseline scores on 2010 ACR/EULAR classification criteria. Early recognition of these variables and taking reference from the classification criteria score may aid in RA risk stratification.

ICW23-4

Analysis of macrophage subtype in the synovium of rheumatoid arthritis

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Conflict of interest: None

[Objectives] The relationship between the proportions of four subtypes of macrophages (M0, M1, M2, and M1/2) and inflammation in rheumatoid arthritis (RA) is currently unknown. Therefore, we compared the macrophage inflammatory phenotype in synovium from RA patients to those from patients with osteoarthritis (OA). [Methods] i) Histologic evaluation: The RA (n=5) and OA (n=6) patients' synovial membrane tissues were assessed for the degree of synovitis by the Krenn histopathological grading system. ii) Immunofluorescence analysis: Synovial membrane tissues paraffin section was incubated with iNOS (M1 macrophages) and CD163 (M2 macrophage). iii) Cell extraction: The postoperative synovial tissue was digested into single cells. iiii) Flow cytometry: Cells were incubated with fluorochrome-tagged monoclonal antibodies (CD11b, CD86, CD206) to characterize the phenotypes. [Results] i) The mean degree of synovial inflammation using the Krenn histopathological grading system was 6.4±1.9 (range 4-9) in RA and 2.2±1.1 (1-4) in OA, respectively. ii) Anti-iNOS and Anti-CD163 dual-positive cells were primarily in the synovial lining layers. iii) Single cells were successfully isolated from the patient's postoperative tissue. iiii) The proportions of M0, M1, M2, and M1/2 macrophages were shown. A comprehensive analysis of 5 inflamed RA cases and 6 less inflammatory OA cases revealed that RA synovium had a higher proportion of macrophages with both M1 and M2 phenotypes. In comparison, the proportion of M0 macrophages was relatively lower. [Conclusion] Our previous cell culture study showed an increased ratio of the M1/2 phenotype in type II inflammatory stimulation, suggesting the macrophage transition in synovial inflammation. Combined with the current research results in which the M1/2 phenotype was primarily located in the synovial lining layers, they may act as an anti-inflammation transition cell type and a cell barrier to protect the synovium from the inflamed joint fluid.

ICW23-5

Investigation of the Risk of Frailty Progression Based on 5-Year Data in Patients with Rheumatoid Arthritis -A Multicenter Observational Study T-FLAG-

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Conflict of interest: None

[Objectives] To examine the risk factors for non-frailty rheumatoid arthritis (RA) patients progressing to frailty. [Methods] A total of 304 RA patients available from the Japanese-Cardiovascular Study (J-CHS), a frailty criterion, from 2020 to 2024 and classified as non-frailty (J-CHS 0-3) in 2020 were included. Frailty progression events were recorded annually through 2024. Overall, 204 patients who did not experience frailty events were classified as the non-frailty progression group (n=204), while 100 patients who progressed to frailty were classified as the frailty progression group (n=100). The risk factors for frailty events over four years were analyzed using the Cox proportional hazards model. [Results] Compared with patients in the non-frailty progression group, patients in the frailty progression group were older (62.9 vs. 68.5 years, P <0.001) and had a longer duration of disease (9.1 vs. 14.2 years, P <0.001), lower rate of MTX use (74.4% vs. 56.1%, P=0.002), higher mean DAS28-ESR (2.40 vs. 2.77, P<0.001), higher HAQ-DI (0.17 vs. 0.45, P<0.001). Both groups had a high usage rate of b/tsDMARDs (34.3% vs. 42.0%, P=0.207). The risk factors for frailty events over four years included age≧65 years old (HR 1.86, P=0.014), duration of disease≧10 years (HR 1.64, P=0.021), DAS28-ESR <2.6 (HR 0.64, P=0.040), HAQ-DI≦0.5 (HR 0.45, P=0.001), and MTX use (HR 0.63, P=0.041 (Table 2). [Conclusion] It's important to use MTX as much as possible and aim for DAS and HAQ remission. However, we also need to be aware of the limits of relying on medication alone to prevent frailty.

ICW24-1

Single-cell RNA sequencing analysis of pregnancy in women with SLE: Immunological features associated with adverse pregnancy outcomes

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is associated with a high risk of adverse pregnancy outcomes (APO), which can have lasting effects on both the mother and the fetus. This study aimed to identify immunological features associated with APO in SLE pregnancies, using peripheral blood samples. [Methods] We performed single-cell RNA sequencing of peripheral blood mononuclear cells collected at 16-28 weeks of gestation from 31 pregnant women with SLE. [Results] There were 13 cases resulting in APO, including hypertensive disorders of pregnancy, fetal growth restriction, low birth weight, and preterm birth, and 18 without APO. Pregnancies with APO exhibited immunological alterations compared to those without APO. Type I interferon signaling pathway was upregulated in several monocyte subpopulations of the APO group ($p < 0.05$). Genes upregulated in monocytes of patients with APO were enriched in pathways associated with inflammatory cytokine production (FDR-corrected $p < 0.1$). Using a generalized linear mixed model, a higher proportion of naive $CD8^+$ T cells involved in T cell differentiation and activation was associated with the APO group (FDR-corrected $p < 0.05$). Additionally, partially differentiated $CD8^+$ T cells expressed certain chemokines and chemokine receptors that interact with those known to be expressed under inflammatory conditions of the placenta (FDR-corrected $p < 0.1$), suggesting that these $CD8^+$ T cells may migrate to the placenta and be involved in the development of pregnancy complications. [Conclusion] Pregnancies with APO exhibit qualitative changes in monocytes and quantitative changes in naive $CD8^+$ T cells as early as mid-pregnancy. These findings may be useful for early identification of high-risk pregnancies, enabling closer monitoring and timely intervention.

ICW24-2

Distinct roles and metabolic pathways of T-bet+CD11chigh atypical B cells (ABCs) compared to plasmablasts in patients with systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Objective] To elucidate the cellular metabolism in differentiation of ABCs and their relevance to SLE. [Methods] 103 newly-onset lupus patients were enrolled. ABCs in peripheral blood were evaluated by flowcytometry. The function and cellular metabolism of ABCs were assessed using human B cells. [Results] The proportion of ABCs in lupus patients was linked to active nephritis. A comprehensive serum cytokines analysis (IFN-α, IFN-β, IFN-γ, IFN-λ1, IL-2, IL-4, IL-6, IL-9, IL-10, IL-12, sBAFF) revealed increased levels of all cytokines compared to heathy controls, except for IL-4 and IL-9. Notably, IFN-γ and IL-6 were correlated with the proportion of ABCs. *In vitro* assay, ABCs were maximally induced when IgD^+CD27^- naïve B cells were stimulated with a combination of B cell receptor, CD40 ligand, IL-21, TLR9 ligand, and IFN-γ, which resulted in high levels of IL-6 production. By contrast, IgD^-CD27^+ class-switched memory B cells differentiated into plasmablasts (PBs) effectively, producing substantial amounts of IgG under the same condition. The fate of cell differentiation can be determined by the activity of various metabolic pathways in the cell. When comparing cellular metabolism between ABCs and PBs using an extracellular flux analyzer and electron microscopy, ABCs differentiation was dependent on glycolysis and was characterized by immature mitochondria. Conversely, PBs differentiation predominantly relied on oxidative phosphorylation (OXPHOS)-pathway. Consisted with these findings, glycolytic inhibitors suppressed proliferation and IL-6 production in ABCs, while selective inhibitors of OXPHOS had no impact on them. Finally, the expression of glycolytic markers in ABCs were elevated compared with other subsets in SLE patients. Of note, glucose transporter 1 expression was upregulated in patients with active nephritis. [Conclusions] ABCs, differentiated from naïve B cells by IFN-γ, rely on glycolysis and could be implicated in SLE pathogenesis through IL-6 production.

ICW24-3

Identification of Plasma Causal Proteins Linked to Macrophage Activation in Systemic Lupus Erythematosus: A Multi-Omics Approach

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Conflict of interest: None

Objective: This research seeks to elucidate plasma causal proteins related to Systemic Lupus Erythematosus (SLE), with a specific focus on those implicated in macrophage activation, utilizing a comprehensive multi-omics analytical framework. Methods: We employed two-sample Mendelian randomization (MR) analysis utilizing cis-protein quantitative trait loci (pQTL) data sourced from multiple centers, alongside SLE genome-wide association study (GWAS) data from the UK Biobank, to investigate the association between genetically determined plasma protein levels and the risk of SLE. Subsequently, we conducted MR analysis on a validation dataset from FinnGen and corroborated our findings through bulk RNA data analysis, single-cell data analysis, and Bayesian colocalization analysis. Furthermore, in vitro experimental validation was performed using THP-1-derived macrophage. Results: Through the analysis of pQTL data and SLE GWAS data, we identified 95 circulating plasma proteins associated with SLE. Further validation in a FinnGen external dataset confirmed 32 of these proteins. Combined with RNA data analysis, 10 proteins were further screened. Interestingly, bayesian colocalization analysis provided strong evidence supporting the colocalization of BTN2A1, INSIG1, NLRP1, and PDCD4 with SLE. Single-cell data analysis validated the expression of 9 proteins. In vitro THP-1 cell experiments using an SLE model confirmed the association of BTN2A1, HLA-A, NLRP1, and PDCD4 with macrophage activation. Conclusion: Through comprehensive multi-omics analysis, we identified 9 plasma causal proteins associated with SLE, including BTN2A1, INSIG1, NLRP1, PDCD4, HLA-A, CERS5, CANX, CCAR2, and NCL. The first four proteins were strongly colocalized with SLE. Besides, macrophage activation may be associated with BTN2A1, HLA-A, NLRP1, and PDCD4. These circulating plasma proteins may serve as potential predictive factors for SLE risk or therapeutic targets in SLE treatment.

ICW24-4

Choroid plexus volume estimated by magnetic resonance imaging as a novel marker for neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

[Objectives] The choroid plexus (CP) produces cerebrospinal fluid and, at least in lupus-prone mice, can serve as a migration site for circulating lymphocyte into the brain. Recent studies have suggested that CP enlargement may be a potential marker for neuroinflammation. This study aimed to correlate choroid plexus volume (CPV) and neuropsychiatric systemic lupus erythematosus (NPSLE). [Methods] This retrospective single-center observational study enrolled patients with SLE in the presence of neuropsychiatric symptoms who underwent enhanced magnetic resonance imaging (MRI). CPs were manually segmented on gadolinium-enhanced T1-weighted sequences, and CPV were estimated using SYNAPSE VINCENT. Patients with neuropsychiatric manifestations who received

additional immunosuppressive treatment after examining MRI findings were defined as having severe NPSLE (sNPSLE). Receiver operating characteristic (ROC) analysis was applied to determine the cutoff values of CPV for discriminating sNPSLE from the rest of SLE patients. [Results] A total of 42 patients were enrolled, with a median time (interquartile range) from SLE diagnosis of 50.4 (1.3-223.6) months. Twenty patients (47.6%) were clinically categorised as sNPSLE. Patients with sNPSLE showed significantly higher CPV than those without sNPSLE (mean±standard deviation 2.07±0.33 vs 1.62±0.39 mL, $P < 0.05$). No other cerebrospinal nor blood tests differed significantly between the two groups. ROC analysis indicated that a CPV > 1.76 mL was the optimal cutoff point for discriminating sNPSLE from the rest of SLE patients, with an area under the curve of 0.795, 85.0% sensitivity and 68.2% specificity. In five sNPSLE patients who underwent post-treatment MRI, CPV decreased significantly after therapy (2.34±0.36 vs 1.91±0.51 mL, $P < 0.05$) in parallel with the clinical response to the treatment. [Conclusion] CP enlargement was associated with severe neuropsychiatric manifestations in SLE and could be a potential marker for sNPSLE.

ICW24-5

Impact of belimumab on pregnancy in patients with Systemic Lupus Erythematosus: LOOPS Registry

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Conflict of interest: None

[Objectives] This study aimed to investigate pregnancy outcomes and the influence of belimumab (BEL) on pregnancy in patients with systemic lupus erythematosus (SLE). [Methods] We analyzed pregnancy outcomes (n=43, 56 cases) of patients with SLE treated in our department since BEL became available. The primary outcome was the live birth rate. [Results] The mean age at pregnancy was 30.4±4.5 years, and the mean SLEDAI score was 2.3±3.6. The live birth rate was 87.5% (49/56), with pregnancy complications occurring in 53.6% (30/56) of cases. Neonatal asphyxia was reported in 16.3% (8/49) of cases, and disease flares occurred in 35.7% (20/56) of cases. Multivariate analysis showed that the absence of hydroxychloroquine (HCQ) use during pregnancy was significantly associated with pregnancy complications ($p<0.01$), neonatal asphyxia ($p<0.01$), and disease flares ($p<0.01$). Among the 14 patients treated with BEL, six discontinued BEL in a planned manner, while three stopped it upon pregnancy confirmation. No significant differences were observed in the live birth rate, pregnancy complications, disease flares, or neonatal asphyxia between the planned discontinuation and other groups. All five patients who continued BEL due to a history of severe disease had live births. Among those who stopped BEL upon pregnancy confirmation, one had a miscarriage and two had disease flares requiring restarting BEL. In cases where BEL was continued during pregnancy or intentionally discontinued, no disease flare occurred, and GC dosage was lower compared to other cases. [Conclusion] HCQ use during pregnancy in patients with SLE may reduce pregnancy complications, neonatal asphyxia, and disease flares. Planned discontinuation of BEL may be possible after achieving disease control in patients aiming for pregnancy; however, patients with severe organ involvement may face risks of flare and should consider shared decision-making regarding BEL continuation.

ICW24-6

Hyperlipidemia is a risk factor for the development of osteonecrosis of the femoral head following methylprednisolone pulse therapy in systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Methylprednisolone (mPSL) pulse therapy is an essential option for patients with active systemic lupus erythematosus (SLE), but there is a risk of adverse events related to microcirculation disorders, including idiopathic osteonecrosis of the femoral head (ONFH). Excessive neutrophil extracellular traps (NETs) are involved in microcirculation disorders. mPSL pulse to lupus mice with hyperlipidemia elevated the serum levels of prenylcysteine oxidase 1 (PCYOX1), which produces hydrogen peroxide and farnesal, leading to an increase in circulating NETs. PCYOX1 is abundant in lipoproteins, especially in very low-density lipoproteins (VLDL). This study aimed to determine whether hyperlipidemia could be a risk factor for the development of ONFH following mPSL pulse in SLE. [Methods] SLE model mice were generated using imiquimod (IMQ) in congenic Apo E mutant mice (n=8), which exhibit a marked increase in VLDL. Five of them were given mPSL on days 39-41. Three were given PBS instead. BALB/c mice were treated similarly as controls (with mPSL pulse: n=6, without mPSL pulse, n=4). Peripheral blood was labeled with Sytox green and Gr-1, and circulating NETs were detected by flow cytometry. Pathological analyses were conducted to evaluate the tissue infiltration of NET-forming neutrophils and the development of ONFH. [Results] In IMQ-treated Apo E mutant mice that received mPSL, ONFH occurred with increasing PCYOX1 and NETs in circulation. Furthermore, the accumulation of NET-forming neutrophils was observed in the surrounding vasculature of the femoral head. In contrast, these findings were not evident in BALB/c mice. [Conclusion] mPSL pulse to lupus mice with hyperlipidemia increased PCYOX1, and probably through its effect, circulating NETs increased. The increase in circulating NETs may cause microcirculation disorders and be involved in the development of ONFH. Hyperlipidemia is considered as a risk factor for the development of ONFH following mPSL in SLE.

ICW25-2

Effects of secukinumab on enthesiophyte and erosion progression in psoriatic arthritis -a one-year double-blind, randomized, placebo-controlled trial utilizing high-resolution peripheral quantitative computed tomography

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Conflict of interest: None

[Objectives] To ascertain the effect of secukinumab (sek) on erosion and enthesiophyte progression in psoriatic arthritis (PsA) by high resolution peripheral quantitative computed tomography (HR-pQCT). [Methods] This was a one-year double-blind, randomized, placebo-controlled trial. Patients with erosion in the metacarpophalangeal joints (MCPJ) 2-4 were randomised in a 1:1 ratio to either the sek or placebo group. HR-pQCT of the MCPJ 2-4 were performed at baseline, week-24 and 1-year. [Results] Forty patients (age: 51.9±13.4 years, 20 [50%] male) were recruited. Thirty-four patients who completed study treatment were included in the per protocol analysis. The erosion volume at baseline, week-24 and week-48 revealed significant reduction in the sek group while no differences in the placebo group. There was a trend suggesting that fewer patients developed new-erosions in the sek group (one-erosion in one-patient) compared to the placebo group (six-erosions in five-patients) ($p= 0.078$). A significantly higher proportion of erosions with partial healing was observed in the sek group compared with the placebo group [51% vs

30%, p=0.029]. The enthesiophyte volume at baseline, week-24 and week-48 revealed significant differences in the sek group while no differences in the placebo group. While one (one-enthesiophyte in one-patient) and four enthesiophytes (four-enthesiophytes in three-patients) were newly identified in the sek group and placebo group respectively, the proportion of enthesiophyte progression was numerically higher in the placebo group than the sek group [40% vs 16%, p=0.114] at week 48. GEE results showed that the odds ratio (OR) for enthesiophyte progression in the sek group was 0.264 (95% CI: 0.080-0.878, p=0.030), while the OR for partial erosion healing in the sek group was 2.816 (95% CI: 1.109 to 7.153, p=0.029). [Conclusion] Secukinumab demonstrates a potential benefit in facilitating partial erosion repair and preventing enthesiophyte progression in PsA.

ICW25-3

Comparison of effectiveness and safety between TNF and IL-17-A inhibitors in the strategic treatment based on the peripheral blood helper T cells phenotyping for the treatment of psoriatic arthritis

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Conflict of interest: None

[Objectives] Head-to-heat direct comparison have shown the comparable efficacy of TNF-i and IL-17A-i against arthritis of PsA. On the other hand, IL-17A-i is more effective against skin lesions. In addition, the selection of bDMARDs according to PsA clinical phenotype was recommended as a highlight of the 2023 EULAR PsA recommendation update. We have shown that strategic use of bDMARDs based on peripheral blood helper T cell phenotypes leads to higher therapeutic effectiveness. We compared the effectiveness and safety of TNF-i and IL-17-i in each clinical phenotype when following our treatment strategy. [Methods] IL-17-i was administered to the activated Th 17 dominant type (IL-17A group, n=31), and TNF-i was administered to the activated Th1/Th7 hybrid or healthy control comparable type (TNF group, n=53). The primary endpoint was the achievement rate of MDA after 52 weeks, and the secondary endpoints were the DAPSA remission/low disease activity, PASI 100, retention rate, and adverse events. [Results] The overall MDA achievement rate with strategic treatment was 71.4% (60/84). The DAPSA-REM/LDA achievement rate was 59.5% (50/84)/76.2% (64/84). The PASI 100 achievement rate was 57% (48%). There were no significant differences in patient backgrounds. The retention rate was 83.0% (44/53 cases) in the TNF group and 96.8% (30/31 cases) in the IL-17 group (p=0.06). Adverse events occurred in 11.3% (6/53 cases) in the TNF group and 3.2% (1/31 cases) in the IL-17 group. The MDA achievement rate was 73.7/68.0% in the TNF/IL-17A group (p=0.63). The DAPSA remission/low disease activity achievement rate was TNF: 65.8/86.8%, IL-17A: 48/92.0%. The PASI100 achievement rates were 62% for TNF and 71.4% for IL-17A. [Conclusion] The strategic use of TNF/IL-17A inhibitors based on peripheral blood helper T cell phenotypes has been shown to provide equally high efficacy regardless of PsA clinical phenotype, potentially contributing to a high achievement rate of MDA, the treatment target.

ICW25-4

The Effect of Biologic Therapies on Serum Metabolic Biomarkers in Patients with Psoriatic Arthritis

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Conflict of interest: None

[Objectives] Since biologic therapies such as TNF inhibitors (TNFi) and IL-17 inhibitors (IL-17i) may affect the cardio-metabolic profile of patients with psoriatic arthritis (PsA), we assessed their short-term effects on serum metabolites in patients with PsA, and determined whether these metabolite changes differed across the drug classes. [Methods] A longitudinal cohort study was conducted in patients with PsA who initiated TNFi or IL-17i therapy. Serum samples prior to initiation of therapy, and three to six months after, were used to quantify 64 metabolic biomarkers using a Nuclear Magnetic Resonance targeted metabolomics panel, which comprised lipid particles, amino acids and various other metabolites. T-tests were used to compare differences in metabolite levels before versus after therapy within each drug class. Linear mixed effects models assessed the effect of each drug class on changes in metabolite levels adjusting for age, sex, lipid lowering drugs, diabetes, hypertension and menopause. [Results] 163 patients were analyzed between 2013 and 2021 (mean age 51 ± 12.6 years, 45.5% female). When comparing biomarkers between classes of medications, post- and pre-treatment levels differed significantly for alanine, glycine, histidine, citrate, creatinine and glycoprotein acetyls (GlycA), which is a marker of systemic inflammation. In models involving TNFi users, levels of alanine, glycine, phenylalanine, citrate and creatinine increased post-treatment, whereas acetate and GlycA decreased. In models involving IL-17i users, changes were observed among fewer biomarkers, with low-density lipoprotein (LDL) particle size increasing post-treatment, and levels of histidine and acetone decreasing. [Conclusion] Treatment with TNFi was associated with more changes in metabolite profiles than IL-17i, including changes associated with systemic inflammation (GlycA) and amino acids. The implication of these changes on long-term cardio-metabolic risk needs further research.

ICW25-5

Performance of the ASAS data-driven cut-offs for positive sacroiliac joint MRI typical of axial spondyloarthritis for discriminating axial involvement in patients with psoriatic arthritis

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Conflict of interest: None

[Objectives] The Assessment of Spondyloarthritis International Society (ASAS) data-driven cut-offs for sacroiliac joint (SIJ) magnetic resonance imaging (MRI) lesions characteristic of axial spondyloarthritis (axSpA) have demonstrated satisfactory performance for a long-term clinical diagnosis of axSpA. This study aimed to evaluate the performance of the ASAS-proposed cut-offs for active and structural SIJ lesions typical of axSpA in distinguishing axial involvement in psoriatic arthritis (PsA) patients. [Methods] Seventy-two consecutive PsA patients (67% male, aged 45±14 years) meeting the CASPAR classification criteria, regardless of the presence of back pain, were included. All patients underwent radiography of the pelvis and spine, as well as SIJ MRI, while 52 (72%) of 72 patients also underwent whole-spine MRI. The final diagnosis of axial psoriatic arthritis (axPsA) was ascertained by two experienced rheumatologists. One rheumatologist with expertise in imaging and one trained reader evaluated the radiography and MRI images. [Results] AxPsA was diagnosed in 27/72 (38%) patients, including 7 (26%) with non-radiographic axPsA. The proposed cut-offs for active sacroiliitis demonstrated high specificity (95.6%) but relatively low sensitivity (51.9%) in distinguishing patients with and without axPsA. When structural lesions of the SIJ were included in addition to active lesions, thesensitivity significantly improved (96.3% vs. 51.9%), though a modest decrease in specificity was noted (86.7% vs. 95.6%). Incorporating MRI spine lesions alongside SIJ lesions did not increase sensitivity or specificity further compared to assessing SIJ alone. [Conclusion] The ASAS-proposed cut-offs for identifying active and structural lesions of SIJ demonstrated satisfactory performance in discriminating axial involvement in PsA patients.

ICW26-1

Comparison of efficacy and safety of rituximab versus intravenous cyclophosphamide as a remission induction therapy in patients with severe ANCA-associated vasculitis in the Japanese multicenter REVEAL cohort study: analyses with inverse probability of treatment weighting

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Conflict of interest: None

[Objectives] This study aimed to investigate the effectiveness and safety of rituximab (RTX) as a remission induction therapy in severe AAV compared to intravenous cyclophosphamide (IVCY). [Methods] Microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) patients treated with systemic glucocorticoids and IVCY or RTX as initial remission induction therapy were extracted in multicenter REVEAL study between 2005 and 2024. They were diagnosed using the 2012 Chapel hill classification. We compared the effectiveness and safety outcomes between two groups. Effectiveness was evaluated by mortality, glucocorticoid (GC)-remission (i.e. Birmingham Vasculitis Activity score-remission plus a daily prednisolone dosage of <10 mg) rate, and relapse rate. Safety was also evaluated by the mortality due to severe infections. Selection bias was reduced to a minimum using propensity score-based inverse probability of treatment weighting (IPTW). [Results] Of the 397 MPA and GPA patients, 177 severe AAV patients were extracted. (IVCY group: N=132, RTX group: N=45) The median age, CRP, and BVAS of eligible patients were 73 years, 8.5 mg/mL, and 17, respectively. After adjustment by IPTW, there were no significant difference in baseline clinical characteristics between IVCY and RTX group. The 10-year survival rate was significantly higher in the RTX group compared to IVCY group. (P=0.04, log rank test) Also, GC-remission rate at 6 months was superior in RTX group (63%) compared to IVCY group (32%). (P=0.0008). Relapse rates were comparable between two groups. Regarding safety, there were 19 deaths due to severe infection in the IVCY group, but none in the RTX group. [Conclusion] In severe AAV, RTX remission induction therapy has superior effectiveness on mortality and GC-remission, and was associated with fewer infection-related death compared to IVCY treatment. These findings reveal the efficacy and safety of RTX remission induction therapy in a Japanese real-world practice.

ICW26-2

Association between peripheral blood immune phenotypes and the efficacy of rituximab in patients with ANCA-associated vasculitis with high disease activity: FLOW Study

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Conflict of interest: None

[Objectives] It remains unclear whether patients with antineutrophil cytoplasmic antibody-associated vasculitis (AAV) with high disease activity achieve better responses to remission induction therapy using either cyclophosphamide (CY) or rituximab (RTX). This study aimed to identify patient subgroups better suited for the treatment with either IV-CY or RTX. [Methods] Patients newly diagnosed with AAV enrolled in the FLOW study were included and their peripheral blood immune phenotypes were assessed using a standardized NIH/FOCIS protocol. Patients received remission induction therapy with either IV-CY (n=45) or RTX (n=124) in combination with high-dose glucocorticoids (GCs). The primary outcome was remission rates (defined as BVAS=0 and GC-free) at 52 weeks. [Results] There was no difference in patient background and the remission rate at 52 weeks between the IV-CY and RTX groups. No clinical signs or laboratory results were associated with remission. Immune phenotype analysis revealed that compared to healthy donors, patients with AAV had higher proportions of class-switch memory (CM) B cells and $IgD^{-}CD27^{-}$ (DN) B cells. No differences in immune phenotypes were observed between patients who achieved remission and those who did not. Cluster analysis identified three groups: Group 1, characterized by a high proportion of naïve CD4/CD8/B cells; Group 2, with a high proportion of CM B cells; and Group 3, with elevated CM B cell, DN B cell, and activated CD4 T cell numbers. Remission rates were higher in the RTX-treated patients in Group 2 (RTX: IV-CY=47:9 (%), p=0.04) and Group 3 (RTX: IV-CY=30:0 (%), p=0.04), with Group 2 achieving the highest rates of remission and GC discontinuation. [Conclusion] RTX may be more effective in patients with AAV exhibiting abnormal B cell differentiation, particularly those with low levels of activated $CD4^{+}$ T cells. Peripheral blood immune phenotype analysis may help in guiding treatment selection for patients with AAV with high disease activity.

ICW26-3

Real-World Efficacy and Safety of Avacopan in ANCA-Associated Vasculitis: Insights from the Multicenter REVEAL Cohort Study

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Conflict of interest: None

[Objective] Although Avacopan (AVC) has shown efficacy in clinical trials, real-world data on its use remains limited. We conducted a retrospective analysis of real-world clinical outcomes of AVC in patients with ANCA-Associated Vasculitis (AAV), utilizing data from the Kansai multicenter REVEAL cohort. [Methods] We enrolled 396 AAV patients, categorizing them by AVC use for newly diagnosed cases or relapse. Clinical data, including disease activity, relapse, mortality, and serious infection rates, were collected from medical records and analyzed using Fisher's exact test. Post-treatment glucocorticoid dosage was assessed via the Mann-Whitney test. We conducted a sub-analysis on AVC induction and maintenance therapies, with annual relapse rates in the maintenance group analyzed by Wilcoxon signed-rank test. [Results] In 53 patients treated with AVC (17 induction, 36 maintenance), baseline characteristics including other treatment were similar between AVC and non-AVC groups. Mortality and severe infection rates were significantly lower in the AVC group ($p < 0.0001$, $p = 0.0054$). In induction therapy, relapse rates were lower with AVC (29.4% vs. 42.1%, $p = 0.02$). Although disease activity showed no significant difference, glucocorticoid doses after 12 months were significantly lower in the AVC group (median [IQR], 4.5 mg [2, 9.25] vs. 9 mg [6, 11], $p = 0.003$). In maintenance therapy, relapse frequency and annual relapse rates were significantly reduced post-AVC (mean [SD], 0.3 [0.6] vs. 1.5 [1.4], $p < 0.0001$). AVC was temporarily discontinued due to adverse events (n = 8), with resumption in 4 cases. [Conclusion] This real-world analysis indicates that AVC use in AAV patients is associated with reduced mortality, severe infections, and relapse rates, alongside lower glucocorticoid doses. AVC showed a favorable safety profile, with temporary discontinuation manageable in some cases. These results empha-

size AVC's effectiveness as a treatment option in clinical practice.

ICW26-4

Recent glucocorticoid-sparing strategies lead to better prognosis for ANCA-associated vasculitis: Insights from the multicenter REVEAL cohort study

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Conflict of interest: None

[Objectives] This study aimed to comprehensively analyze clinical characteristics and treatment outcomes of microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA). In addition, we compared the prognosis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) over time using data from REVEAL cohort. [Methods] Patients diagnosed with AAV were enrolled in the cohort through June 2024. MPA was diagnosed based on Chapel Hill Consensus definitions; GPA was identified using Watts' algorithm or 2022 ACR/EULAR criteria; and EGPA met Lanham criteria, 1990 ACR classification criteria, or 2022 ACR/EULAR criteria. Of the 555 AAV patients registered, 460 newly diagnosed, treatment-naive cases were included in the analysis (MPA: 283, GPA: 66, EGPA: 111). [Results] Among AAV patients, MPA had significantly higher age, five-factor score, C-reactive protein, serum creatinine (Cr), and higher prevalence of myeloperoxidase-ANCA positivity at onset (all $P < 0.0001$). Although Birmingham Vasculitis Activity Score was initially highest in EGPA, no significant differences existed among groups at 12 months after onset. Vasculitis Damage Index also showed no differences at 12 and 24 months after onset. The 5-year survival rate for MPA was notably lower at 67.6% ($P = 0.000031$). Multivariable analysis among AAV patients identified age, Cr, infection-related hospitalizations, and diagnoses before 2018 (median diagnosis year) as factors significantly associated with mortality. Importantly, patients diagnosed after 2019 received lower glucocorticoid (GC) doses at 6, 12, and 24 months compared to earlier diagnoses (all $P < 0.0001$). In survivors, GC doses were lower than those in deceased patients at the same time points. [Conclusion] Although MPA remains associated with the highest mortality among AAV subtypes, the widespread adoption of GC-sparing strategies in recent years appears to have improved AAV prognosis.

ICW26-5

The Efficacy and Safety of Rituximab Maintenance Treatment for ANCA-associated Vasculitis: The Multicenter REVEAL Cohort Study

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Conflict of interest: Yes

[Objectives] Several randomized clinical trials have demonstrated the efficacy of rituximab (RTX) as a maintenance therapy for remission in ANCA-associated vasculitis (AAV). However, real-world data on RTX maintenance therapy, especially following RTX induction therapy, is limited. We aimed to evaluate the efficacy and safety of RTX maintenance therapy for AAV using a Japanese multicenter cohort (REVEAL cohort). [Methods] We enrolled patients with microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA) who were treated with RTX induction therapy. Clinical characteristics, laboratory data, and outcomes were obtained from medical records. The patients were divided into two groups based on whether or not they received RTX as maintenance therapy. Relapse, survival, and serious infections were assessed using Kaplan-Meier survival analysis and the log-rank test. Glucocorticoid dosage after treatment was evaluated using the Mann-Whitney test. [Results] A total of 57 patients were included (RTX maintenance: n = 18; without RTX maintenance: n = 39). Baseline clinical characteristics, including age, sex, and percentage of MPA, did not significantly differ between the two groups. Although relapse-free survival did not differ significantly between the groups ($p = 0.32$), glucocorticoid dosage at 12 months was significantly lower in the RTX maintenance group (median [IQR], 4.0 mg [3.0, 5.8] with RTX maintenance vs. 7.0 mg [6.0, 10.0] without RTX maintenance, $p = 0.01$). RTX maintenance therapy was associated with better survival ($p = 0.04$) and fewer serious infections ($p = 0.03$). [Conclusion] RTX maintenance therapy following RTX induction was associated with reduced glucocorticoid dosage, improved survival, and fewer serious infections. These findings underscore the efficacy and safety of RTX maintenance therapy in real-world settings.

ICW26-6

Autoantibody seroconversion and profound depletion of B cells in the bone marrow by CD19 CAR-T cell therapy in ANCA-associated vasculitis

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Conflict of interest: None

[Objectives] CD19 chimeric antigen receptor (CAR) T cells have shown success in other B cell-mediated autoimmune diseases, inducing rapid B cell depletion and durable remission, however data on ANCA-associated vasculitis (AAV) are limited. [Methods] We evaluated the efficacy and safety of autologous anti-CD19 CAR therapy (KYV-101, Kyverna Therapeutics) in severe, refractory PR3-ANCA+AAV. Bone marrow biopsies before and after CAR T cell therapy were conducted. [Results] CAR T cell therapy was administered in a 52-year-old man who had been suffering for 20 years from relapsing disease affecting multiple organs (lungs, kidneys, joints, skin, sinuses, eyes) and was being treated with various immunosuppressants. Despite continuous rituximab (RTX) treatment (10 years), he recently developed fever, weight loss, respiratory distress. RTX reinduction therapy resulted in only partial clinical improvement with persistent serologic activity, despite complete depletion of CD19+ and

CD20+B cells in peripheral blood. Following CAR T cell therapy, the patient developed mild CRS (Grade 1), managed with tocilizumab and neutropenia, resolving after filgrastim. No other safety events were observed. The initial bone marrow biopsy (54 days after RTX, before CAR T cell infusion), showed that, in contrast to peripheral blood, CD19+/CD20-B cells were still present. CD19+B cells primarily consisted of CD38hi transitional B cells and CD27hiCD38hi activated plasmablasts. In the second biopsy (48 days after CAR T cell infusion), no CD19+B cells could be detected, while CD138+plasma cells persisted both before and after therapy. PR3-ANCA levels rapidly decreased and the patient rapidly seroconverted 28 days after CAR T cell therapy and remained negative. IgG levels remained within the normal range. [Conclusion] In AAV, anti-CD19 CAR T cells induced complete CD19+B cell depletion in both peripheral blood and bone marrow, contrary to RTX, which completely depleted circulating but not bone marrow CD19+B cells.

ICW27-1

Single-cell analysis reveals the immune cell abnormalities underlying the clinical heterogeneity of systemic sclerosis

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Conflict of interest: Yes

[Objectives] Patients with systemic sclerosis (SSc) present with a wide range of organ manifestations. We aimed to elucidate the cellular diversity underlying the clinical heterogeneity of SSc, including important organ complications such as scleroderma renal crisis (SRC) and interstitial lung disease (ILD). [Methods] Peripheral blood mononuclear cells (PBMCs) were collected from 21 SSc patients without receiving immunosuppressive therapy and 6 age- and sex-matched healthy donors. The transcriptome and surface protein levels were measured simultaneously at the single cell level. Kidney biopsy samples were also obtained from SSc patients at the onset of SRC. Spatial transcriptome analysis was performed on kidney tissue from SRC patients using the CosMX platform. Principal component analysis (PCA) was used to classify SSc patients. Monocle 3 was used for trajectory analysis. [Results] Based on PCA of single cell gene and protein expression profiles, we found enrichment of monocyte subpopulations in SRC patients and T-cell subpopulations in patients with ILD. Differential abundance analysis revealed that $CD14^{+}$ monocytes highly expressing *EGR1* (CD14_EGR1) were specifically enriched in PBMC from SRC patients. In the representative case of SRC, *EGR1* expression levels in monocytes increased at the onset of SRC, and decreased after treatment. Trajectory analysis indicated that the CD14_EGR1 subset would differentiate into macrophages highly expressing *THBS1* (THBS1_Mac) in the diseased kidney. Spatial transcriptome analysis further revealed the formation of a fibrotic niche in the SRC kidney, composed of scattered tubular cells and various immune cells including the THBS1_Mac subset. [Conclusion] Skews in the PBMC gene expression are associated with SSc organ complications. Our data suggest that the novel CD14_EGR1 subset differentiates into the THBS1_Mac subset at the onset of SRC and is involved in the formation of the fibrotic niche.

ICW27-2

Deep Learning-Based Prediction of Interstitial Lung Disease in Systemic Sclerosis Using Multi-Modal Data Integration

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Conflict of interest: None

Objectives: Interstitial lung disease (ILD) is a leading cause of morbidity and mortality in systemic sclerosis (SSc), but early detection remains difficult. This study aims to develop a deep learning model that integrates high-resolution computed tomography (HRCT) features, extracellular vesicle (EV) miRNA profiles, and polygenic risk scores (PRS) to enhance ILD risk stratification and support early intervention. **Methods:** Data from the GENISOS, EUSTAR, and UK Biobank cohorts (n=2,000 SSc patients) were used, encompassing HRCT lung texture analysis, EV miRNA levels (e.g., miR-21, miR-155, let-7), and genome-wide association study-derived PRS. The model employed a multi-branch architecture: a convolutional neural network (CNN) for HRCT, a bidirectional long short-term memory (BiLSTM) network for miRNA time-series, and a gradient-boosted decision tree for PRS. Training utilized 80% of the data, with hyperparameter tuning via cross-validation, and performance was assessed on the remaining 20% using AUROC, AUPRC, and decision curve analysis. **Results:** The model achieved an AUROC of 0.81 (95% CI: 0.78-0.84) and an AUPRC of 0.78 (95% CI: 0.75-0.81) for predicting ILD within 18 months. It showed a significant improvement over clinical scoring systems ($p<0.05$), with a net reclassification improvement of 0.30. HRCT features accounted for 45% of the model's predictive strength, miRNA profiles for 35%, and PRS for 20%. Elevated miR-21 and decreased let-7 levels were associated with a 3.8-fold increased risk of rapid ILD progression (HR: 3.8, 95% CI: 3.1-4.9, $p<0.001$). Decision curve analysis indicated potential clinical benefit in guiding early ILD surveillance and intervention. **Conclusion:** This deep learning approach offers a promising tool for ILD risk stratification in SSc, supporting proactive patient management. Validation in diverse cohorts is needed to confirm its clinical utility.

ICW27-3

Esophagogastroduodenoscopy (EGD) Screening Practices and Findings in Patients with Systemic Sclerosis within a Large Urban Health System

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Conflict of interest: None

[Objectives] Systemic sclerosis (SSc) is a chronic autoimmune disease that affects esophageal function, increasing the risk of gastroesophageal reflux disease (GERD), Barrett's esophagus (BE), and esophageal adenocarcinoma (EAC). In the general population, BE is more common in men, with a U.S. incidence of 0.5-2%. Risk factors include GERD, older age, male sex, Caucasian race, obesity, and smoking. Since SSc primarily affects women (female-to-male ratio 5:1), it is unclear if women with SSc have the same protective effect against BE. There are no specific EGD screening guidelines for SSc patients. This study examines EGD screening prevalence and the incidence of GERD, BE, and EAC in SSc patients within a large healthcare system. [Methods] We conducted a cross-sectional chart review of SSc patients aged 18-75 at UCLA Health from October 1, 2014, to October 1, 2024. We assessed EGD screening and recorded diagnoses of GERD, BE, and EAC, with additional analyses by sex, race, and smoking status. [Results] Of 3,697 SSc patients included, 910 (24.6%) underwent EGD in the past decade. Most were female (86.9%), nonsmokers (97.6%), with an average age of 58, BMI of 24.6, and primarily identified as Caucasian or Asian. GERD was prevalent in 86.7%. The incidence of BE was 5.93%, slightly higher in males (6.78%) than females (5.81%). EAC was found in 7 patients (0.77%). [Conclusion] To our knowledge, this is the largest analysis of EGD screening in SSc patients to date. Despite high GERD prevalence and elevated risks for BE and EAC in SSc, only a quarter of UCLA SSc patients underwent EGD. BE and EAC rates were over three times higher than in the general population, highlighting the need for more rigorous screening. Similar BE rates in males and females suggest the protective effect seen in women may not apply to SSc patients, raising concerns about using general screening guidelines. Further research is needed to develop optimal screening strategies, especially for women with SSc.

ICW27-4

Clinical Relevance of Radial and Ulnar Artery Diameter Measurement Using Vascular Ultrasonography in Patients with Systemic Sclerosis

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Conflict of interest: None

[Objective] To assess the clinical relevance of radial and ulnar artery diameter measurements in assessing vasculopathy in patients with systemic sclerosis (SSc). [Methods] The medical records of SSc patients undergoing vascular ultrasonography (US) between November 2023 and March 2024 at our hospital were reviewed. The association between the occurrence of digital ulcers (DUs), internal organ complications and US findings (radial and ulnar artery diameter) was assessed by logistic regression analysis. [Results] Forty-seven patients with SSc (45 female) were included. The median age and disease duration were 74 years and 6.2 years, respectively. Thirty-one patients (66%) had interstitial lung disease, and nine (19%) had pulmonary hypertension (PH). Among them, twenty-one patients (45%) presented a history of DUs. The median diameters of the radial artery (RA) and ulnar artery (UA) were 1.72 mm and 1.05 mm, respectively; ulnar artery occlusion was observed in four patients (9%). RA and UA diameters significantly influenced the occurrence of DUs (odds ratio; 95% confidence interval, 8.12; 1.23-53.46, 18.86; 1.85-191.91, respectively). The cutoff value for UA diameter was 0.97 mm (AUC 0.724). UA diameter also significantly influenced the occurrence of PH (odds ratio; 95% confidence interval, 15.50; 1.06-226.88), with a cutoff value of 0.82 mm (AUC 0.721). [Conclusions] In SSc patients, measurement of UA diameter using vascular US enables straightforward screening for ulnar artery occlusion and serves as an indicator of broader vasculopathy, including DUs and PH.

ICW27-5

The Impact of Interstitial Lung Disease Severity on Health-Related Quality of Life in Systemic Sclerosis: Insights from Cross-Sectional and Longitudinal Analyses

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Conflict of interest: None

Objectives: This study aimed to investigate the impact of interstitial lung disease (ILD) on health-related quality of life (HRQoL) in systemic sclerosis (SSc) using the Short Form 36 (SF-36) questionnaire. **Methods:** Consecutive patients with SSc who visited our hospital from December 2020 to April 2024 underwent high-resolution computed tomography (HRCT), pulmonary function tests (PFTs), and the SF-36 questionnaire. Patients with SSc-ILD were assessed annually for PFTs and SF-36 scores. The severity of ILD was assessed using Goh's method. Progressive ILD was defined as a delta forced vital capacity (FVC) greater than 5% at the 3-year follow-up. **Results:** Among 64 patients (median age, 62 years; 3 men), 11 were diagnosed with extensive ILD, 21 with non-extensive ILD, and 32 had no ILD. Patients with extensive ILD demonstrated significantly lower median scores in the physical component summary (PCS), physical functioning (PF), and role physical compared to those without extensive ILD (all P <0.05). The extent of ILD was independently associated with decreased social functioning (β = -0.653, P = 0.02), while FVC% was correlated with PCS (β = 0.227, P <0.01) and PF (β = 0.336, P = 0.049) in multivariate analysis adjusted for age, sex, and skin score. Among the 17 patients who had follow-up SF-36 questionnaire at 3 years, patients with progressive ILD experienced a significantly greater median decline in PCS scores (-14.4, [IQR -17.6, -9.0]), compared to those without progressive ILD (3.30 [IQR -2.3, 9.5]) (P = 0.02). **Conclusion:** This study comprehensively assessed ILD, including its severity, and demonstrated that greater ILD severity was significantly correlated with increased physical and social impairment in SSc. Progressive ILD was associated with a pronounced deterioration in physical health status over time. Therefore, early diagnosis and timely intervention may be necessary to reduce the risk of deterioration in HRQoL in SSc, particularly those with progressive ILD.

ICW27-6

The role of soluble CD93 in the pathogenesis of skin fibrosis in systemic sclerosis

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Conflict of interest: None

[Objectives] CD93 is a transmembrane glycoprotein that is expressed mainly on endothelial cells. Soluble CD93 (sCD93) is released during inflammation. Serum sCD93 levels have been reported to increase in patients with Systemic Sclerosis (SSc). However, the role of sCD93 in the pathogenesis of SSc remains unclear. The present study aims to evaluate the involvement of sCD93 in skin fibrosis. [Methods] We measured serum sCD93 levels in SSc patients attending Ehime University Hospital, compared them with healthy controls, and analyzed their association with clinical data. We also induced skin fibrosis in wild-type and CD93$^{-/-}$ mice by administering bleomycin (BLM). As a control, phosphate-buffered saline (PBS) was administered. We evaluated the thickness and collagen proliferation of the dermis in the treated skin samples. *CD93* mRNA expression of the treated skin samples was analyzed by real-time qPCR. [Results] The serum sCD93 levels in SSc patients (n=10) were significantly higher than those in healthy controls (n=46) (median 186.2 vs 126.2 ng/mL, p=0.004), and were negatively correlated with the disease duration (rs=-0.79, p= 0.008). The dermal thickness and collagen proliferation were significantly suppressed in CD93$^{-/-}$ mice injected with BLM every other day for three weeks compared with their wild-type counterparts (median 199.2 vs 143.0 μm, p<0.001, 73.3% vs 53.2%, p<0.001, respectively). Real-time qPCR analysis revealed that expression levels of *CD93* mRNA in the skin of wild-type mice injected with BLM daily for three days were significantly elevated compared to those of PBS-treated mice. [Conclusion] We demonstrated the suppression of skin fibrosis in BLM-treated CD93$^{-/-}$ mice. The involvement of sCD93 in the early stage of pathogenesis of skin fibrosis in both humans and mice was suggested. To further elucidate the role of sCD93 in skin fibrosis, we are currently conducting RNA sequencing on RNA extracted from the skin of a mouse model with BLM-induced skin fibrosis.

ICW28-2

Heterogeneity of cytotoxic CD4+ T cell in centenarians

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Conflict of interest: None

[Objectives] The human immune system typically undergoes immunosenescence with age, including T cell population alterations. While these changes predispose many elderly individuals to malignancies and autoimmune diseases, centenarians tend to resist these age-related diseases. A previous single-cell RNA-seq analysis of peripheral blood mononuclear cell from centenarians revealed an increased proportion of cytotoxic CD4+ T cells (CD4CTLs) in supercentenarians compared to individuals under 100 years of age. However, the specific functions and populations of CD4CTLs remain unclear. This study aims to elucidate CD4CTL heterogeneity and identify novel cell types. [Methods] We analyzed 28 frozen peripheral blood T cell samples from individuals aged 72-114 years (8 healthy individuals under 100 years, 10 centenarians, and 10 supercentenarians) from the Centenarian Cohort. Single-cell isolation was performed using the 10x Genomics droplet-based method, and CITE-seq analysis was performed. After doublet removal using donor-specific hashtags and stringent quality control, we performed a weighted-nearest-neighbor (WNN)

method to integrate cell surface protein markers and transcriptome data. CD4CTLs clusters were identified and sub-clustered using both cell surface protein and transcriptome data. [Results] Analysis of 47,737 T cells from 28 samples yielded 5,431 CD4CTLs grouped into five subclusters. We identified 162 stably expressed genes (SEGs) within clusters (Log2 FC >0.5 and adjusted P-value <0.05). Among these SEGs, we identified cell surface protein markers that differentiate each cluster: such as chemokine receptors (e.g., CXCR3), cytokine receptors (e.g., IL6R, IL7R), and co-stimulatory molecules (e.g., CD28, PDCD1). [Conclusion] Our findings demonstrate heterogeneity of CD4CTLs and can contribute to the identification of longevity-associated CD4CTLs cell types. We plan to sort each cluster using cell surface markers identified in this study and conduct functional assays.

ICW28-3

Osteoarthritis-Driven Inflammatory Imprinting of Synovial Fibroblasts contributes to Gouty Arthritis Exacerbation through m6A modification of S100A4

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Conflict of interest: None

[Objectives] Patients with osteoarthritis (OA) face an elevated risk for the future development of gout; however, it remains enigmatic how the holistic chronic inflammatory milieu of OA contributes to gout exacerbation. Synovial fibroblasts (SFs) have been reported to acquire a memory-like phenotype under chronic inflammatory conditions to mediate arthritis remission, flare, and recurrence. This study was undertaken to examine whether SFs could be imprinted in osteoarthritic joints predispose to gout exacerbation. [Methods] Human SFs were collected from osteoarthritic and normal joints and then treated with monosodium urate (MSU). Phenotypic modifications were examined to assess their association with the inflammatory response to MSU crystals and their potential role in accelerating the crystallization process. Epigenetic and transcriptomic alterations in SFs were identified. Mice with or without synovial macrophage depletion were subjected to destabilization of the medial meniscus (DMM) surgery and injected with MSU to confirm the mechanisms in vivo. [Results] We demonstrated that OA-SFs exhibited enhanced inflammatory and fibrotic responses to MSU stimulation in vitro, which was dependent on METTL3/YTHDF2-mediated m^6A demethylation of FSP1/S100A4. And previous subjection to DMM rendered mice to develop more severe gout upon subsequent exposure to MSU, which was independent of synovial macrophages. Finally, local targeting METTL3/S100A4 obviously abolished gout exacerbation secondary to OA-induced inflammation in murine models. [Conclusion] Overall, our study uncovered that m^6A modification-mediated inflammatory imprinting of SFs under OA-associated joint inflammation is responsible for aggravated gout, suggesting potential cellular-level intervention and molecular targets for OA to prevent or alleviate subsequent development of gout.

ICW28-4

CD169 Expression on CD14+ monocytes is a Useful Marker for Assessing Type I Interferon Status in Pediatric Inflammatory Diseases

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Conflict of interest: None

[Background] Evaluation of type I interferons (IFNs) in rheumatic and inflammatory diseases is challenging because of their low concentration and rapid clearance in peripheral blood. Recently, we showed that CD169 (Siglec-1) expression was increased in $CD14^+$ monocytes ($CD14^+$Mo) after stimulating peripheral monocytes with IFN-α dose-dependently. Therefore, we assessed the feasibility of measuring expression of CD169 on monocytes as alternative markers for type I IFN status in various pediatric rheumatic and inflammatory diseases. [Methods] Data from flow cytometric analysis of surface CD169 on $CD14^+$Mo in peripheral blood were compared in patients with viral infections, bacterial infections, systemic lupus erythematosus (SLE), Sjögren's syndrome (SjS), juvenile dermatomyositis (JDM), Kikuchi-Fujimoto disease (KFD), juvenile idiopathic arthritis (JIA), Kawasaki disease (KD), and inflammatory bowel disease (IBD), and in healthy controls. We also conducted a time-series analysis of CD169 expression on monocytes in patients with KFD, anti-MDA5 antibody positive JDM, and SLE. In SLE patients, the correlation between various clinical data and CD169 expression on monocytes was also analyzed. [Results] Surface CD169 expression on $CD14^+$Mo was significantly increased in patients with viral infections, SLE, SjS, JDM and KFD, but not in patients with bacterial infections, JIA, KD, and IBD. The time-series analysis revealed that CD169 expression on $CD14^+$Mo decreased after the acute phase in KFD and anti-MDA5 antibody positive JDM patients but was observed even 2 years after onset in SjS and SLE patients. Furthermore, CD169 on $CD14^+$Mo in SLE patients was found to have a negative correlation with white blood cell count, lymphocyte count and C4 levels. [Conclusion] Analysis of CD169 expression on $CD14^+$Mo may be useful for rapid assessment of type I IFN status for differentiation of pediatric inflammatory diseases from type 1 IFN-mediated diseases.

ICW28-5

Combinatorial analysis identifies mesenchymal stromal cell (MSC) critical quality attributes that are sensitive to donor heterogeneity and variations in key processing parameters, which correlate with clinical outcomes

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Conflict of interest: None

[Objectives] Mesenchymal Stromal Cells (MSCs), known for their inflammation-regulating properties, face variability challenges hindering clinical and commercial success. Employing Design of Experiments (DoE) and desirability analysis, this study investigates donor heterogeneity and Critical Processing Parameters (CPPs) used to manufacture MSCs and assesses their dual impact on potency and expansion through surrogate critical quality attributes (CQAs). [Methods] We use DoE to evaluate input parameters such as donor heterogeneity, and CPP parameters (including MSC plating density, medium composition, and oxygen concentrations) across 13 bone marrow donors, including osteoarthritis (OA) patients from a clinical trial (NCT02351011). Exploring interaction effects between donors and CPPs, we focus on an 8-gene panel of anti-inflammatory/angiogenic genes, and cell expansion as CQAs. [Results] Desirability scores (DS) using a composite index of 8 genes and cell expansion metrics are calculated to determine the effectiveness of CPPs. Principal component analysis (PCA) unveils heterogeneity among 12 CPP combinations and 8 genes across 13 donors. Significant differences in PC1 scores emphasize donors' role in driving MSC gene expression. offline, CPP conditions drive MSC expansion, with human platelet lysate (hPL) or animal component-free (ACF)-supplemented CPPs exhibiting significantly higher cell expansion ($p<0.001$) than fetal bovine serum (FBS). We ranked MSC donors across CPP combinations by weighing DS using individual gene coefficient of variation (CV). [Conclusion] Our analysis revealed that 30% of CPP conditions resulted in desirable outcomes for both cell expansion and gene expression. These findings correlate with patient-reported improvements in pain and function, demonstrating the model's efficacy in evaluating MSC CQAs.

ICW29-1

Attenuation of immunogenicity after third booster of SARS-CoV-2 vaccines is associated with severe and critical outcome of COVID-19 in patients with autoimmune rheumatic diseases in omicron pandemic phase

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Conflict of interest: None

[Objectives] To assess the incidence of COVID-19 and evaluate the predictors of severe outcomes during the recent omicron pandemic phase. [Methods] This prospective observational study included consecutive AIRD patients treated with immunosuppressants who received three or more doses of mRNA vaccines. We measured neutralizing antibody titres and T-cell immunity responses using interferon (IFN) releasing assay

against SARS-CoV-2 to evaluate the humoral and cellular responses, respectively. The incidence of COVID-19 during the omicron pandemic phase (Jan. 2022 to Sep. 2024) was defined by positive antigen or PCR. Severe illness of COVID-19 was defined as hospitalization requiring oxygen support. [Results] A total of 462 patients with AIRD treated with immunosuppressive drugs were enrolled. The mean age was 57 years, and 71% of the patients were female. We assessed breakthrough SARS-CoV-2 infections during in 241 (52%) patients and 34 (7.3%) of them had severe disease. Logistic regression analysis revealed that the development of severe COVID-19 was associated with attenuated humoral response (neutralizing antibody titer < 10.7 IU/mL, AUC of 0.80 with sensitivity 76% and specificity 86%). Additionally, 5 of critical illness cases who required intensive care had negative of T-cell immunity response (IFN releasing assay antigen 1 < 0.5) even after third vaccination. On another front, this risk was reduced in patiehts who received 4 or more times of SARS-CoV-2 vaccination (hazard ratio 0.69, 95% CI 0.57-0.91). p=0.01). Attenuated both humoral and cellular response after third vaccination was associated with elder age (> 65 years old), glucocorticoid use (prednisolone > 7.5 mg/day), and the use of mycophenolate or rituximab. [Conclusion] Our results demonstrated attenuation of immunogenicity even after third vaccination against SARS-CoV-2 were associated with severe COVID-19 in AIRD patients in omicron pandemic phase. Repeated vaccine may prevent development of severe COVID-19.

ICW29-2

Single-cell transcriptome analysis revealed a distinctive subpopulation of CD8+ T cells expressing in Kawasaki disease patients with coronary artery involvement

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Conflict of interest: None

[Objectives] Kawasaki disease (KD) represents the prevalent etiology of pediatric heart disease, often engendering aneurysmal changes in morphology, followed by obstructive lesions within the coronary arteries. Increasing evidence delineates KD pathogenesis as a consequence of abnormal and imbalanced dynamics between innate and adaptive immunity. However, molecular mechanisms involved in changes in $CD8^+$ T cell function in KD remain unclear. [Methods] Here, characteristics of adaptive immune cells in KD was analyzed using single-cell RNA sequencing (scRNA-seq), and distinct immunophenotypic profiles of children with KD and coronary artery lesions (CAL) were elucidated. Comprehensive profiling of whole blood cells from two patients with acute KD, three KD patients with CAL, two febrile controls, and two healthy controls were performed. [Results] The most pronounced alterations in cell population and differentially expressed genes among adaptive immune cells were identified in $CD8^+$ T cells. Expression levels of PRDM1, CD69, and CCR7 in the tissue-infiltrating memory subpopulation in KD patients with CAL were found to increase compared to those in acute KD patients. Furthermore, clusters of $CD8^+$ T cells trajectories revealed distinct directions of differentiation in acute KD and KD with CAL. Interestingly, the differentiation modulator PRDM1, enriched in $CD8^+$ T cells of KD with developed CAL, significantly increased the expression of cytolytic enzymes, IFNG, and promoted stem-like features of proliferating ability, suggesting a dysregulated expansion of effector memory $CD8^+$ T cell subtypes involved in CAL pathogenesis. [Conclusion] The single-cell landscape of adaptive immune responses revealed distinctive patterns of differentiated $CD8^+$ memory T cells between children with KD with and without CAL development, which provides a potential target to assist in the differential therapeutics and diagnosis of Kawasaki disease with and without CAL formation.

ICW29-3

Evaluation of poor prognostic factors for cancer associated myositis: multi center MYKO cohort study

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Conflict of interest: None

[Objectives] To clarify the clinical characteristics and prognosis of patients with cancer associated myositis (CAM). [Methods] A retrospective evaluation was conducted on 487 patients diagnosed with idiopathic inflammatory myopathies (IIM) between January 2001 and April 2024 in multicenter MYKO cohort. Cancer-associated myositis was defined as cases where a malignancy was diagnosed within three years before or after the diagnosis of IIM, while all other cases were classified as the non-associated group. We compared the initial clinical symptoms, serological tests, treatments, and survival rates between them. [Results] Out of the 395 patients for whom pre-treatment clinical information was available, 65 (16.5%) were found to have coexisting malignancies. The most common malignancies were gastric cancer and breast cancer (11 and 10 cases, respectively). Among these, 38 cases (58.4%) were classified as CAM. Compared to the non-associated group, CAM patients were more likely to be older ($p < 0.001$), have a history of smoking ($p = 0.013$), a family history of malignancies within two degrees of relation ($p = 0.003$), and exhibit dysphagia ($p = 0.0013$). Additionally, CAM patients showed elevated serum CRP levels ($p = 0.016$). The presence of anti-TIF-1γ antibodies was significantly higher in CAM group ($p < 0.0001$). Regarding treatment, the rate of IVIG administration was significantly higher in CAM group ($p = 0.0059$), but the administration rates and dosage of PSL or IVCY were comparable between them. Overall, the CAM group had a significantly higher mortality rate compared to the non-associated group ($p = 0.0001$). [Conclusion] Patients who are older, have a history of smoking, exhibit dysphagia, have elevated CRP levels, and are positive for anti-TIF-1γ antibodies are at a higher risk of developing malignancies within three years before or after the diagnosis of IIM. These patients are also associated with a poorer prognosis, indicating the need for careful monitoring.

ICW29-4

Predictors of response to bDMARDs and tsDMARDs therapy in Psoriatic Arthritis: a Pilot Study on the role of musculoskeletal ultrasound

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Conflict of interest: None

[Objectives] This pilot study aimed to identify early predictors of therapy retention in patients with clinically active peripheral psoriatic arthritis (PsA) who initiated or switched to therapy with biologic and targeted synthetic disease-modifying antirheumatic drugs (bDMARDs and tsDMARDs). [Methods] Clinical and ultrasound (US) assessments were conducted at baseline (t0) and subsequently at 1 (t1), 3 (t3), and 6 (t6) months. US evaluations targeted joints/entheses according to PsASon-Score13 and the most clinically involved joint/enthesis/tendon or the two most clinically involved joints/entheses/tendons (MIJET and 2MIJET). After 6 months of follow-up, patients were divided into two groups based on drug retention, determined by the clinician's assessment of treatment efficacy (cResponder vs non-cResponder). Main endpoints were US changes in MIJET, 2MIJET, and GUIS (Global US Inflammation Subscore) derived from PsASon-13. [Results] Twenty-nine patients were enrolled, 22 cResponders and 7 non-cResponders at t6. In the comparison between cResponders and non-cResponders, GUIS variation significantly differed in Δt6-t0, while MIJET and 2MIJET variations were significant as early as Δt3-t0 and confirmed in Δt6-t0. The US response of MIJET and 2MIJET was faster in cResponder patients treated with JAKi compared to those treated with TNFi and IL-17/12-23i, significant in Δt1-t0. [Conclusion] Ultrasound imaging of clinically involved joint sites emerges as a valuable early predictor of therapy

response for predicting drug retention at 6 months in patients with psoriatic arthritis. Considering the impracticality of evaluating numerous joints included in the main composite US assessment scores, our results indicate that assessing only the most clinically involved joints can be equally valid in predicting therapy response.

ICW29-5

Successful treatment of myositis-associated, refractory interstitial lung disease by an interleukin 6 inhibitor

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Conflict of interest: None

[Objectives] Myositis-associated interstitial lung disease (ILD) is a potentially fatal disease despite the combination of therapy with glucocorticoids (GC) and immunosuppressants. Therefore, new therapies such as biological agents targeting a relevant cytokine are warranted. Janus kinase (JAK) inhibitors have become a treatment option, especially for anti-melanoma differentiation-associated gene 5 (MDA-5) positive cases, but there remained many issues, such as concerns about infection due to extensive cytokine suppression under high-dose GCs. We aimed to retrospectively examine the cases of myositis-associated ILD treated with an IL-6 inhibitor tocilizumab (TCZ). [Methods] We enrolled patients with myositis-associated ILD treated by TCZ at our medical center during 2019-23. [Results] Four female patients aged 43-84 years were identified. One patient was positive for MDA-5, and the other cases were positive for anti-aminoacyl-tRNA synthetase (ARS) antibody (one each for EJ, PL-7 and PL-12). The initial GC dose was 1 mg/kg/day (40-60 mg/day) of prednisolone and methylprednisolone (mPSL) pulse therapy was given except 1 case. They had polyarthritis and fulfilled the criteria for rheumatoid arthritis. Immunosuppressants included in the initial therapy were intravenous cyclophosphamide for 3 cases and tacrolimus for 2 cases, and mycophenolate mofetil for 1 case. TCZ (intravenous except for 1 case) treatment was started within 6 months of the initial treatments. All patients showed clinical and radiological improvement after TCZ without serious adverse events. Efficacy was most pronounced in the PL-12 positive case. She required 2 rounds of mPSL pulse therapy at onset, but after 3 months of TCZ administration, her PSL was reduced to 2 mg/day after 3 months of treatment, and her pulmonary function test improved to the normal range (%VC from 48.5% to 81.1% and DLco from 36% to 61%). [Conclusion] TCZ is likely to be an option for the treatment of myositis-associated, refractory ILD.

ICW30-1

New quantitative and qualitative analytical framework of scRNAseq data reveals the pathophysiology of systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is a complex autoimmune disease with unknown etiology. While we previously identified key gene signatures of SLE using bulk RNAseq from 27 immune cell types (*Cell* 2022), we failed to identify granular disease-relevant cell states within each cell type. Although single-cell RNA-seq (scRNAseq) can address this problem, recent studies depend on coarse cell-type level pseudobulk analysis, which cannot distinguish qualitative change (dysregulated gene expression) and quantitative change (cell state abundance within each cell type). This study aims to identify disease-relevant cell states of SLE and develop an analytical strategy to efficiently dissect quantitative and qualitative change at single-cell resolution. [Methods] We applied our framework to the largest-scale scRNAseq data of SLE with ~1.7 million cells from 301 donors. [Results] After the identification of 118 granular cell states in 25 cell types, we revealed that previously uncharacterized cell states such as *FAM13A*$^{+}$*ARID5B*$^{+}$ naive CD4^{+} T cells, *GZMK*$^{+}$ *GZMH*$^{+}$*HLA-DR*$^{+}$ effector memory CD8^{+} T cells, and *C1Q*$^{+}$ monocytes, expanded especially in active SLE. Next, our new statistical model successfully decomposed conventional pseudobulk-level differential expression into cell state abundance signature genes (quantitative change) and dysregulated signature genes (qualitative change) at single-cell level. Intriguingly, while these two signatures showed different immunological pathway enrichment patterns, stratified LD score regression revealed that SLE-GWAS signals were enriched in both signatures. Finally, integrative analysis with 137 cell surface markers successfully identified the key surface markers of disease-relevant cell states, which enabled us to perform in-depth functional characterization of these subpopulations. [Conclusion] Our approach can provide new insight into analytical pipelines for single-cell data and contribute to a better understanding of SLE pathogenesis.

ICW30-2

Ktrans (Dynamic contrast enhanced-MRI); a novel imaging evaluation method for the diagnosis of Neuropsychiatric Systemic Lupus Erythematosus -LOOPS Registry-

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Conflict of interest: None

[Objective] The primary pathologies in Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) involve vascular endothelial cell damage and increased permeability of the blood-brain barrier (BBB). Dynamic contrast-enhanced MRI (DCE-MRI) K^{trans} imaging can assess BBB permeability by measuring the volume transfer constant of contrast agents from the intravascular to the extravascular space. This study aimed to evaluate the utility of K^{trans} imaging in diagnosing NPSLE in patients with SLE. [Methods] We included 104 SLE cases (mean age 45.3 years, 85.6% female, mean disease duration 88 months) from our SLE cohort (LOOPS registry) who consented to participate in the NPSLE study and underwent DCE-MRI between March 2019 and December 2023. We retrospectively analyzed the characteristics of K^{trans}-positive cases. [Results] (1) Of the 104 SLE cases, 34 (32.6%) met the criteria for NPSLE, including 25 with focal manifestations, 5 with diffuse manifestations, and 4 with peripheral nervous system involvement. Additionally, 15 cases (14.4%) had non-NPSLE neuropsychiatric symptoms, including bipolar disorder, glucocorticoid-induced psychiatric disorders, and other conditions. (2) Among the 104 cases, 32 were K^{trans}-positive, including 21 NPSLE cases (65.6%). In the K^{trans}-positive group, focal manifestations were notably high, while peripheral nervous system involvement was negative in all cases (p=0.0082). (3) Among the 15 cases with non-NPSLE neuropsychiatric symptoms, 14 were K^{trans}-negative, with one exception being a patient with active NPSLE (p=0.0288). (4) No significant differences were found between K^{trans}-positive and -negative groups in other clinical parameters, including ds-DNA antibodies, complement, spinal fluid protein, IgG index, spinal fluid IL-6, and white matter lesions on MRI. [Conclusion] Our findings suggest that K^{trans} imaging may aid in diagnosing focal NPSLE manifestations and help exclude non-NPSLE neuropsychiatric symptoms by assessing BBB permeability.

ICW30-3

Factors Associated with Early Glucocorticoid Dose Tapering in Young Newly Diagnosed Systemic Lupus Erythematosus Patients: A Case-Control Study Using the PLEASURE-J Cohort

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Conflict of interest: None

[Objectives] In systemic lupus erythematosus (SLE) patients, it is recommended to taper glucocorticoids to 5 mg or less in prednisolone (PSL) equivalent. This study exploratively examines factors associated with early tapering to PSL ≦5 mg following new onset of SLE. [Methods] This case-control study was conducted using the PLEASURE-J registry. The study population included newly diagnosed SLE patients aged 16-40 years who were initially prescribed glucocorticoids at a dose of >5 mg PSL equivalent with 2-year follow-up. Patients achieving tapering to PSL ≦5 mg at follow-up end were categorized as the successful tapering group, while others formed the control group. Sixteen potential factors at baseline associated with PSL dose tapering were evaluated, including age, sex, SLEDAI-2K score, organ involvement, initial treatment. Crude odds ratios and 95% confidence intervals were estimated using univariate logistic regression analysis. Multivariate analysis was performed for age, sex, SLEDAI-2K score, organ involvement, low C3 level, initial glucocorticoid dose, immunosuppressant use, and hydroxychloroquine use to estimate the adjusted odds ratios and 95% confidence intervals. [Results] Of 152 eligible patients, 88 were in the successful tapering group and 64 were in the control group. The median age was 24 years (21-31 years) in the successful tapering group and 25 years (21-30 years) in the control group, with proportion of females of 88.6% and 90.6%, respectively; the median SLEDAI-2K scores at diagnosis were 16 (9.8-22) and 17 (10-23), respectively. Univariate analysis showed a positive association of successful tapering with cytopenia ($p = 0.047$) and a negative association with arthritis ($p = 0.011$). Multivariate analysis confirmed a negative association with arthritis ($p = 0.014$). [Conclusion] The presence of arthritis at diagnosis may be a potential predictive factor for difficulty in tapering glucocorticoid dose to ≦5 mg PSL equivalent in the early disease course.

ICW30-4

Impact of organ damage on pregnancy outcomes, and the progression of organ damage during pregnancy in pregnant with systemic lupus erythematosus

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Conflict of interest: Yes

[Objectives] Organ damage in systemic lupus erythematosus (SLE) is linked to increased mortality, making early disease control and glucocorticoid tapering essential to prevent further damage. However, its impact on pregnancy outcomes in SLE remains unclear. The use of certain immunosuppressants is contraindicated during pregnancies, often requiring discontinuation of some immunosuppressants and glucocorticoid escalation, potentially increasing the risk of SLE flare or glucocorticoid-induced organ damage. This study investigates the effect of organ damage on pregnancy outcomes and the progression of damage during pregnancy. [Methods] We retrospectively studied SLE patients who delivered at our institution, stratified by the presence of organ damage using the SLICC-ACR Damage Index (SDI). Pregnancy outcomes and SDI progression during pregnancy were compared between groups, and associated factors were analyzed. [Results] Among 48 pregnancies, 8 cases (16.7%) had organ damage at pregnancy diagnosis. These patients had significantly higher rates of PROMISSE adverse preganancy outcomes (APOs) (62.5% vs 7.5%, $p = 0.002$), preterm delivery (50% vs 14.7%, $p = 0.082$), and lower birth weights (2145.00 [1526.50, 2744.00] g vs 2738.00 [2429.00, 3008.50] g, $p = 0.053$). Logistic regression model analysis revealed that organ damage was significantly associated with increased risk of PROMISSE APOs (OR 20.6, 95% CI 3.22-131, $p = 0.001$). No SDI progression occurred despite five flare-ups during pregnancy. [Conclusion] The presence of organ damage in pregnancies complicated by SLE is associated with an increased risk of PROMISSE APOs, underscoring the need for pre-pregnancy risk assessment. On the other hand, appropriate pregnancy planning can help mitigate the progression of organ damage during pregnancy in SLE patients.

ICW30-5

Impact of early belimumab induction on rapid glucocorticoid reduction in new onset systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Glucocorticoid (GC) is a critical treatment option for systemic lupus erythematosus (SLE). However, long-term use is associated with numerous side effects and an increased risk of organ damage and mortality, necessitating early dose reduction. Although several studies have addressed the achievement rate of GC reduction in SLE, there is limited information regarding the risk and protective factors involved. This study aims to fill that gap. [Methods] We conducted a retrospective analysis of medical records for SLE patients who received follow-up care at our hospital between April 2006 and April 2024. We included patients with new-onset SLE treated at our center, and those requiring prednisone (PSL) >20 mg/day to manage initial symptoms. We addressed the time to achieve PSL ≦7.5 mg/day and PSL ≦5 mg/day and its risk and protective factors. [Results] Of the 537 patients diagnosed with SLE, 106 met the inclusion criteria. The median initial induction dose of GC was 50.00 [30.00, 75.00] mg/day, which was reduced to 7.50 [5.00, 10.00], and 5.00 [3.00, 7.62] mg/day at weeks 26, and 52, respectively. By week 52, 78.1% of patients achieved PSL ≦7.5 mg/day, and 63.8% achieved PSL ≦5 mg/day. Cox proportional hazards model analysis indicated that early induction with belimumab was associated with an increased rate of achieving PSL ≦7.5 mg/day and PSL ≦5 mg/day (early belimumab exposure: achieving PSL ≦7.5 mg/day: HR 4.05, 95% CI 1.95-8.38, $p < 0.001$; achieving PSL ≦5 mg/day: HR 1.92, 95% CI 0.92-3.99, $p = 0.082$). Positivity for anti-Sm antibodies was associated with a decreased likelihood of achieving PSL ≦5 mg/day (HR 0.48, 95% CI 0.27-0.85, $p = 0.013$). No organ manifestations, including lupus nephritis and neuropsychiatric SLE, were related to the rate of achieving PSL ≦7.5 mg/day or PSL ≦5 mg/day. [Conclusion] The use of belimumab was associated with an increased likelihood of achieving GC reduction in patients with new-onset SLE.

ICW31-1

Association between clinical efficacy and hydroxychloroquine concentration in Japanese patients with Rheumatoid arthritis

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Conflict of interest: None

[Objectives] To evaluate the association between serum concentrations of hydroxychloroquine (HCQ) and its derivatives and clinical efficacy in Japanese patients with rheumatoid arthritis. [Methods] Patients with active RA despite conventional synthetic disease-modifying antirheumatic drugs were recruited, and HCQ was administered for 24 weeks in addition to the prior treatment. Serum concentrations of HCQ, desethylhydroxychloroquine (DHCQ), desethylchloroquine (DCQ) and bisdesethylchloroquine (BCQ) were measured at weeks 0, 4, 8, 12, 24, and 36. Association between each serum concentration and achievement of American College of Rheumatology (ACR) 20/50/70 was analyzed. [Results] Forty nine patients whose sera were available were included in the analysis. The mean age was 63, and 45 patients were female. Forty three patients (88%) were treated with concomitant methotrexate. The mean DAS28 at baseline was 4.4, and 27 patients (55.1%) achieved ACR20 at week 24. The serum concentrations of HCQ, DHCQ, DCQ and BCQ reached plateau at week 4 and remained at the stable levels during the 24 weeks. The concentrations of HCQ, DHCQ, DCQ and BCQ at week 24 was higher in patients who achieved ACR20 than in those who did not. Receiver operating characteristic curve (ROC) revealed the cut-off concentrations of HCQ, DHCQ, DCQ and BCQ to predict the ACR20 achievement were 0.55 μg/mL, 0.26 μg/mL, 0.078 μg/mL and 0.044 μg/mL, respectively. Furthermore, higher serum concentrations of DHCQ and BCQ were also associated with the achievement of ACR50 and ACR70, while those of HCQ and DCQ were not, suggesting DHCQ and BCQ are more related with clinical effectiveness of HCQ for rheumatoid arthritis. Serum concentrations of HCQ, DHCQ, DCQ and BCQ were not associated with the incidence of infections and infestations or gastrointestinal disorders. [Conclusion] Serum concentrations of HCQ and its derivatives are associated with clinical effectiveness of HCQ in Japanese patients with rheumatoid arthritis.

ICW31-2

Disease activity of rheumatoid arthritis correlates with insomnia, depression, and fatigue: AMED RA IoT prospective observational study

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Conflict of interest: Yes

[Objectives] Patients with rheumatoid arthritis (RA) often complain of sleep disturbances, depression, and fatigue in addition to joint symptoms. The aim of our study was to elucidate the prevalence of insomnia, depression, and fatigue in patients with RA and the relationship between its rate and RA disease activities. [Methods] Patients with RA who were able to complete the questionnaire were prospectively included in the study. The Athens insomnia scale (AIS) was used for insomnia, the patient health quetionnaire-9 (PHQ-9) for depressive symptoms, and the brief fatigue inventory (BFI) and the functional assessment of chronic illness therapy-fatigue (FACIT-F) for fatigue. The disease activity score 28-CRP (DAS28), clinical disease activity index (CDAI), and simplified disease activity index (SDAI) were used for disease activity of RA, and health assessment questionnaire-disability index (HAQ-DI) for functional assessment. [Results] A total of 107 patients (17 men, 90 women) of RA were included. The median age was 55 years. The median DAS28-CRP was 2.9, median CDAI was 10.2, median SDAI was 10.2, median HAQ-DI was 0.5, and median RA duration was 82 months. A median AIS score was 6, and 91 patients (85%) had insomnia. The AIS score was positively correlated with DAS28 (p=0.03), CDAI (p=0.03), SDAI (p=0.03) and HAQ-DI (p=0.03). A median PHQ-9 score was 6, and 14 patients (13%) were depressed (PHQ-9 score ≧10). The PHQ-9 score was positively correlated with DAS28 (p<0.01), CDAI (p<0.01), and SDAI (p<0.01). With regard to fatigue, 91 patients (85%) were rated as having severe fatigue (BFI score ≧7). The BFI score was positively correlated with DAS28 (p<0.01), CDAI (p<0.01), SDAI (p<0.01), and HAQ-DI (p<0.01). The FACIT-F scores were positively correlated with DAS28 (p<0.01), CDAI (p<0.01), SDAI (p<0.01), and HAQ-DI (p=0.01). [Conclusion] In patients of RA, 85% of patients had insomnia and fatigue. Insomnia, depression, and fatigue were correlated with disease activity of RA.

ICW31-3

Differentiating Clinical and Serological Profiles of ICI-induced Arthritis and Cancer bearing Rheumatoid Arthritis treated with ICI

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Conflict of interest: None

[Objective] The primary aim was to compare overall survival (OS) between cancer patients with immune checkpoint inhibitor-induced arthritis (ICI-IA) and those with pre-existing rheumatoid arthritis undergoing ICI therapy (RA-ICI). The secondary aim was to clarify the clinical profiles of ICI-IA compared to RA-ICI. [Methods] One-year survival from ICI induction was analyzed using the log-rank test, adjusting for immortal time bias due to the time-dependent nature of ICI-IA. A 200-day landmark analysis focused on patients who developed ICI-IA within 200 days. [Results] Among 38 patients, 15/16 (94%) of ICI-IA and 15/22 (68%) of RA-ICI were alive at 200 days. Of the 15 ICI-IA, 9 (60%) developed arthritis within 200 days, resulting in 24 patients (ICI-IA, n=9; RA-ICI, n=15) included in the landmark analysis. Baseline characteristics of ICI-IA and RA-ICI groups were as follows: The median age was 67 vs. 73 years, with a male predominance of 89% vs. 67%, non-small cell lung cancer prevalence of 33% vs. 53%, and combination therapy with anti-PD (L) 1 and anti-CTLA4 antibodies in 11% vs. 0%, respectively. The median one-year survival was lower in RA-ICI compared to ICI-IA (50%, [95%CI 22.2-72.6] vs. 100%, [95%CI NA]; log-rank test, p<0.001). Arthritis onset tended to be delayed in ICI-IA (103.4±65.7 days) compared to 6 (10%) of RA-ICI whose activity increased after ICI treatment (39.8±32.9 days). Pre-treatment serum data revealed significantly lower IgA levels in ICI-IA compared to RA-ICI (225.3±116.5 vs. 393.2±178.7 mg/dL, p=0.012). IgG (1063.3±381.4 vs. 1561.7±636.9 mg/dL, p=0.06) and IgM (42.8±13.2 vs. 97.9±40.3 mg/dL, p<0.001), were comparable. [Conclusion] Despite potential biases, ICI-IA patients appeared to exhibit better cancer prognosis than RA-ICI patients, indicating a distinct pathophysiology. These findings could inform the development of tailored treatment strategies and monitoring practices based on the type of arthritis during ICI treatment.

ICW31-4

Fourth-generation CD19-targeted chimeric antigen receptor T-cell therapy in difficult-to-treat rheumatoid arthritis

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Conflict of interest: None

[Objectives] To examine the efficacy and safety of a new, autologous,

~~fourth-generation CD19-targeted chimeric antigen receptor (CAR) T-cell that secretes antibodies against IL-6 and TNFα (CD19/aIL-6/aTNFα) in the treatment of difficult-to-treat (D2T) rheumatoid arthritis (RA) patients. [Methods] Three patients with D2T RA, were infused with a new fourth-generation CD19/aIL-6/aTNFα CAR-T cells after standard conditioning treatment. The expansion of CAR-T cells and proportion of CD19+ B cells in circulation was examined. Disease activity indexes, including DAS28-CRP, CDAI and SDAI were evaluated during follow-up. Synovitis in knee joints was assessed by Power Doppler ultrasound (PDUS). [Results] After infusion, CD19/aIL-6/aTNFα CAR-T cells rapidly expanded in vivo, peaking on day 9 in patient 1 and 3 and on day 11 in patient 2. CD19+ B cells vanished from the patients' peripheral blood after 3 days in patient 1 and 7 days in patient 2 and 3. DAS28-CRP decreased from 4.67 to 2.59 in patient 1, 4.04 to 2.18 in patient 2 and 4.61 to 1.50 in patient 3 at 12 weeks post-CAR-T-cell infusion. Consistent with clinical improvement, RA-associated autoantibodies significantly decreased over a 3-month period. Rheumatoid factor (RF) disappeared in all three patients. Anti-cyclic citrullinated peptide (CCP) antibody was disappeared in two patients and significantly decreased in patient 3. Moreover, improvement of synovitis was further confirmed by PDUS of the knee joints. In all three patients, peripheral B cells were reconstituted at 60, 90 and 90 days respectively. Notably, CAR T-cells infusion was well tolerated and no cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS) or immune effector cell-associated hematotoxicity (ICAHT) occurred. [Conclusion] Our data show the feasibility of a fourth-generation CAR T-cell treatment approach in D2T RA with amelioration of inflammation and reduction of autoantibodies.~~

ICW31-5

The Role of Financial Toxicity in Predicting Long-Term Disease Progression and Functional Decline in Rheumatoid Arthritis Patients: A Multi-Layer Structural Equation Modeling Approach

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Conflict of interest: None

Objectives: Financial toxicity can harm chronic disease management, but its effects on RA progression and functional decline are unclear. This study evaluates how financial stress influences RA disease activity and impairment over time, guiding strategies to reduce financial barriers in patient care. Methods: Data from 2,562 RA patients with 10-year longitudinal follow-up from the US National Data Bank for Rheumatic Diseases were analyzed. Financial toxicity was assessed using measures of out-of-pocket costs, medical debt, and income loss. Disease progression was tracked through changes in Clinical Disease Activity Index (CDAI) and Health Assessment Questionnaire Disability Index (HAQ-DI) scores, while structural equation modeling (SEM) assessed effects on disease outcomes mediated by treatment adherence (medication possession ratio), mental health (Patient Health Questionnaire-9), and healthcare utilization. Model fit was determined using Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), and Root Mean Square Error of Approximation (RMSEA), with significance at $p<0.01$. Results: Financial toxicity accelerated significantly RA progression, with a direct effect of $\beta = +0.43$ CDAI/year (99% CI: +0.31 to +0.55, $p<0.001$) and worsening functional status ($\beta = +0.27$ HAQ -DI/year, 99% CI: +0.18 to +0.36, $p<0.001$). Indirect pathways showed that lower medication adherence contributed an additional 0.21 points/year in CDAI worsening (99% CI: +0.14 to +0.28, $p< 0.001$), while 29% of the relationship with functional decline was mediated by mental health deterioration (99% CI: 20% to 37%, $p<0.001$). The SEM model indicated a strong fit (CFI = 0.95, TLI = 0.93, RMSEA = 0.04), confirming the robustness of the findings. Conclusion: Financial toxicity significantly accelerates RA progression and functional decline, directly and via treatment adherence and mental health. Addressing financial barriers may improve clinical outcomes by supporting adherence and psychological well-being.

ICW32-1

The Deficiency of Deltex1 Impairs Human Regulatory T cell Function and is Associated to High Disease Activity in Primary Sjögren's Syndrome

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Conflict of interest: None

[Objectives] Deltex1 is a transcriptional target of NFAT that promotes T cell anergy. However, its impact on the function of regulatory T cells (Tregs), which play a key role in the pathogenesis of primary Sjogren's syndrome (pSS), remains unknown. [Methods] Deltex1 mRNA levels in T cells were measured by quantitative reverse transcription polymerase chain reaction. The mean fluorescent intensity (MFI) of Tregs-associated molecules and the cytokine positivity of CD4+ FoxP3+ Tregs were analyzed by flow cytometry. The suppressive function of both Deltex1-knockdown and wild-type (WT) human Tregs were assessed through in vitro assays. Systemic disease activity and symptoms in patients with pSS were assessed using the ESSDAI and ESSPRI. [Results] Deltex1 expression in T cells was significantly lower in pSS patients than in age- and sex-matched healthy controls ($p < 0.001$). Additionally, Deltex1 mRNA levels in T cells showed a negative correlation with fatigue scores on the visual analog scale, as well as with the ESSDAI and ESSPRI (all $p < 0.05$). Furthermore, the mean fluorescent intensity (MFI) of inhibitory molecules, including PD-1, CTLA-4, TIM-3, and LAG-3 on Tregs, as well as the percentage of interferon-r+, interleukin (IL)-4+, and IL-17A+ Tregs, were significantly higher in the low Deltex1 group (Deltex1/GAPDH $< = 0.02$) compared to the high Deltex1 group (Deltex1/GAPDH > 0.02) ($p < 0.05$). At last, we found that Deltex1-knockdown expanded Tregs inhibited the proliferation of stimulated CD4+ CD25- T cells less effectively than WT expanded Tregs. At a1:10 ratio of Tregs to Tresp, siCtrl Tregs were able to suppress 51.8% of Tresp proliferation, while siDTX1 Tregs exhibited a reduced suppression rate of only 33.6% ($p = 0.023$). [Conclusion] The deficiency of Deltex1 impairs the suppressive function of Tregs and may contribute to high disease activity in pSS, suggesting its potential as a therapeutic target for this autoimmune disease.

ICW32-2

The presence of the SSA-specific T cells in the salivary glands of SjS patients

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Conflict of interest: Yes

[Objectives] Sjögren's syndrome (SjS) is an autoimmune disease characterized by lymphocytic infiltration of exocrine glands and the appearance of serum anti-SSA antibodies. We analyzed the antigen specificity of B cells infiltrating the salivary glands of this disease and found that approximately 30% of the infiltrated cells produced disease-specific autoantibodies. Since affinity maturation occurred in these autoantibodies and ectopic lymphoid structures were often observed in lesions of SjS, we hypothesized that T cells with the same antigen specificity may help B cells. The aim of this study was to determine the antigen specificity of T cells in salivary glands in SjS. [Methods] We performed single-cell gene expression and TCR analysis of salivary glands from seven anti-SSA antibody-positive SjS patients. More than 100 TCRs of CD4 T cells enriched in the lesions were expressed in TCR reporter cells to create a lesion-derived TCR reporter library. Lymphoblastoid cell lines (LCLs) were generated from the peripheral blood of each patient using EBV. LCLs and TCR reporters were cocultured with SSA-derived peptides to determine whether the TCRs responded to SSA. [Results] Ten different TCRs reacted with SSA-derived peptides, and the HLA alleles and peptide sequences corresponding to each TCR were identified; the HLAs to which the TCRs reacted were not only DR, but also DQ and DP. The autoreactive TCR reporter could react with monocytes phagocytosed with immune complexes con-

taining SSA, indicating that the identified peptides can be naturally processed and presented in vivo. Primary CD4 T cells from healthy individuals with forced expression of autoreactive TCRs could also reactive to the corresponding HLA/peptide complexes, indicating that the identified TCRs are functional. [Conclusion] SSA-specific T cells were identified in the salivary glands of SjS patients, indicating that T and B cells cooperate to response against SSA at the site of the lesion.

ICW32-3

Presence and Clinical Significance of Anti-SMN Antibodies in Patients with Rheumatic Musculoskeletal Diseases

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Conflict of interest: None

[Objectives] Anti-SMN (Survival of Motor Neuron) antibodies often coexist with anti-U1-RNP antibodies and are found in patients with rheumatic musculoskeletal diseases (RMDs), especially in MCTD. However, few studies have explored their characteristics and clinical significance. The study aims to confirm the presence of SMN-specific antibodies and to determine their clinical significance in RMD patients. [Methods] His-tagged SMN complex (SMN1, Gemin2-8, UNRIP) and GFP-fused U1-RNP complex (SNRNP70k, SNRPA-G) were co-overexpressed in 293T cells, and immunoprecipitation was performed with monoclonal anti-GFP antibodies. SMN specific antibody were detected by western blotting (WB) and immunofluorescent staining. The titers of anti-SMN antibodies were measured using recombinant SMN complex-bound magnetic beads and FACS, in serum samples from 827 patients with RMDs, including 91 RA, 217 SjS, 190 SLE, 30 MCTD, 126 SSc, 72 IIM, 76 AAV, and 148 others, as well as 81 healthy controls. [Results] SMN complex was immunoprecipitated with U1-RNP complex, confirming the binding of the two protein complexes. WB with patient serum revealed the presence of SMN-specific antibodies. The immunofluorescent staining with fluorescent-labeled SMN complex revealed the presence of anti-SMN antibody-producing cells in lymph nodes. With a cut-off of 1000 MFI (median fluorescence intensity), 36.7% of MCTD, 11.1% of SLE, 4.1% of SjS, and 2.4% of SSc patients were positive, while no healthy controls tested positive. Anti-SMN-positive MCTD patients had a higher prevalence of interstitial lung disease (10/11 [90.9%] vs. 7/19 [36.8%], $p = 0.013$). [Conclusion] This study confirms the presence and clinical significance of anti-SMN antibodies in RMDs, especially in patients with MCTD and interstitial lung disease.

ICW32-4

Pro-inflammatory Role of TLR2+ CD8+ T Cells in Primary Sjögren's Syndrome

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Conflict of interest: None

[Objectives] This study aims to identify abnormal gene expression in CD8+ T cells in primary Sjögren's syndrome (pSS) and explore their role in pSS pathogenesis and hyperactivation. It also investigates the pro-inflammatory function of CD8+ T cells, providing a foundation for future targeted therapies. [Methods] The RNA transcriptome of CD8+ T cells was analyzed to identify key genes and pathways related to the pathogenic mechanisms of CD8+ T cells. Differential gene expression was validated using RT-PCR. CD8+ T cells were isolated and cultured in vitro, and their morphology and organelle status were examined by electron microscopy. Flow cytometry, ELISA, RT-PCR, and WB were used to assess the impact of key genes on the morphology and function of CD8+ T cells. [Results] RNA-Seq analysis identified 725 differentially expressed genes in CD8+ T cells from pSS patients, with 481 upregulated and 244 downregulated. GO and KEGG analyses linked these genes to inflammatory and immune pathways, with key genes like TLR2 and CYBB significantly upregulated. TLR2+ CD8+ T cells were elevated in pSS patients. In vitro, TLR2 ligands increased inflammatory cytokine secretion but had minimal impact on cytotoxicity. Electron microscopy showed increased mitochondrial numbers and density, indicating higher energy consumption. Seahorse analysis revealed enhanced respiration rates and ROS levels, and Western blot confirmed TLR2 activation of the NF-κB pathway, promoting inflammation. [Conclusion] This study demonstrates that CD8+ T cells exhibit significant pro-inflammatory activity in patients with pSS, particularly through the abnormal upregulation of TLR2, which activates the NF-κB pathway in CD8+ T cells, promoting their activation and inflammatory response. These findings provide potential therapeutic targets for pSS treatment.

ICW32-5

The Role and Mechanism of Peripheral Helper T Cells in Renal Injury of Sjögren's Syndrome

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Conflict of interest: None

[Objectives] To investigate the expression of Tph cells in the blood and renal tissues of pSS-TIN patients and their correlation with clinical features. The study also aims to explore Tph cells' role in renal pathology, B cell differentiation, antibody secretion, recruitment, and related chemokine pathways. [Methods] Peripheral blood samples from 60 pSS-TIN patients and 20 healthy controls were analyzed using flow cytometry to detect Tph cells, B cell subpopulations, and age-associated B cells (ABC). IHC and IF techniques assessed the distribution of T, B, and Tph cells in renal tissues. Tph cells from healthy and pSS-TIN patients were co-cultured with glomerular mesangial and tubular epithelial cells to study their interactions and migration. Cytokine and chemokine levels were measured to evaluate Tph cell pathogenicity on HMC and HK2 cells. Western blot and RT-PCR analyzed fibrosis, autophagy, and apoptosis. [Results] Flow cytometry revealed significantly higher Tph and CX3CR1+ Tph cell levels in pSS-TIN patients, likely related to renal lesion recruitment. B cell subpopulations, including ABCs, double-negative, Naïve, and Switched memory B cells, were also increased, while IL-21 levels were elevated, potentially linked to CX3CR1+ Tph cells. Immunohistochemistry and immunofluorescence confirmed increased CD4+, CD8+, CD19+ cells, and CD4+PD1+CXCR5- T cells in renal tissues. CX3CL1 expression in renal tissues suggests CX3CR1+ Tph cells contribute to renal pathology by recruiting B cells. [Conclusion] Tph cells are significantly elevated in the peripheral blood of pSS-TIN patients and correlate with disease severity, suggesting their key role in pathogenesis. Additionally, increased B cell subpopulations, including ABCs, double-negative, Naïve, and Switched memory B cells, highlight B cell activation in pSS-TIN. CX3CR1+ Tph cells likely contribute to renal damage by migrating to renal tissues and recruiting B cells.

ICW33-1

Transcriptomic Profiling of Synovial Macrophage Subtypes in Knee Osteoarthritis

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Conflict of interest: None

Objective: Macrophages are abundant in the synovial membrane, yet their specific roles in osteoarthritis (OA) pathology remain unclear. This study characterizes synovial macrophage subtypes in knee OA and evaluates their transcriptomic profiles across disease stages. **Methods:** Knee

synovial tissue samples of early-stage (Kellgren-Lawrence [KL]=1, n=5) and advanced-stage (KL=3/4, n=4) radiographic knee OA patients were analyzed using single-nucleus RNA sequencing (snRNA-seq) to identify macrophage subtypes and their transcriptomic profiles. Subcluster identities were also cross-referenced with published datasets. Gene ontology (GO) analysis was conducted to identify putative biological processes and pathways. **Results:** snRNA-seq data revealed that macrophages are the predominant immune cells in the synovium of both early and advanced knee OA. We identified seven distinct macrophage subclusters with unique transcriptomic profiles; Cluster_0 (top 2 transcriptomic profiles: PDE3A, TPRG1), Cluster_1 (FRMD4B, SLC9A9), Cluster_2 (TTN, STAB1), Cluster_3 (TMTC2, VCAN), Cluster_4 (SFMBT2, BNC2), Cluster_5 (MEF2C, ANKRD44), and Cluster_6 (KAZN, EBF1). Interestingly, Clusters 0, 3, and 4 were enriched in advanced-stage OA, while clusters 1, 2, and 5 were dominant in early OA. Mapping our data to published data suggests that TREM2+ Cluster 0 may be the most prominent subset in advanced OA, while FOLR2-high, LYVE1+ Cluster 1 may be prevalent in early-stage OA. GO analysis indicated association of Cluster_0 with TGF-β signaling and GTPase activity regulation, whereas Cluster_1 was associated with immune response regulation, cytokine production, and MHC II complex assembly. Currently, flow cytometry and multiome analysis is being employed to confirm the identify of each identified cell subtype and their roles in OA. **Conclusion:** This study reveals diverse synovial macrophage subtypes with unique transcriptomic profiles during distinct stages of knee OA and may play a key role in OA pathology.

ICW33-2

Identification of BHLHE40 as a critical mediator of extracellular matrix regulation and synovial fibrosis during knee osteoarthritis

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Conflict of interest: None

[Objectives] Knee osteoarthritis (KOA) is a joint disease impacting various tissues, including the synovium. Our initial studies identified two populations of fibroblasts, DPP4+ and ITGB8+, primarily found in synovium of early (KLI) and advanced (KLIII/IV) stage radiographic KOA, respectively. This study sought to identify fibroblast subsets mediating ECM regulation and synovial fibrosis during KOA. [Methods] Synovia from patients with early and advanced stage radiographic KOA were subjected to bulk RNA sequencing (KLI; n=6, KLIII/IV; n=8), single nuclei (sn) RNAseq (KLI; n=5, KLIII/IV; n=4) and flow cytometry (healthy; n=5, KLI; n=10, KLIII/IV; n=14). Computational and bioinformatics analyses identified cell (sub) types and differentially expressed genes, which were analyzed for pathway involvement and putative transcriptional regulators. BHLHE40 siRNA studies were conducted on human KOA synovial fibroblasts cultures followed by Nanostring analysis using an ECM and fibrosis gene Panel (over 700 genes). BHLHE40 conditional knock out (CKO) mice were generated and subjected to the destabilization of the medial meniscus (DMM) KOA model. [Results] Bulk RNAseq analysis showed advanced-stage vs. early-stage KOA synovia had greater expression of matrisome-annotated genes. SnRNAseq and computational analyses identified DPP4+ and ITGB8+ cells as key fibroblast subsets enriched with ECM-related pathway genes. Next, BHLHE40 was identified as a key upstream transcriptional regulator enriched in ITGB8+ fibroblasts, putatively targeting 20 of 24 ECM-related DEGs. BHLHE40 expression was increased in ITGB8+ vs. DPP4+ fibroblasts from OA synovia from humans and mice. Finally, loss of BHLHE40 induced severe synovial fibrosis in vivo, and increased fibrosis-related gene expression in human OA synovial fibroblasts, suggesting a crucial role of BHLHE40 in limiting synovial fibrosis. [Conclusion] BHLHE40 is a potential key mediator of ECM regulation and synovial fibrosis in KOA pathogenesis.

ICW33-3

Transcriptomic Differences in Adipocytes, Macrophages and Endothelial Cell Populations of Infrapatellar Fat Pads from Patients with Knee Osteoarthritis

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Conflict of interest: None

Objective: Knee osteoarthritis (KOA) is the most common form of arthritis. The infrapatellar fat pad (IFP) is the largest FP within the knee; however, its role in KOA is not well understood. Using single-nucleus RNA sequencing (snRNA-seq), we previously showed that major cell types contributing to the IFP include fibroblasts, macrophages, adipocytes and endothelial cells, each with multiple subclusters (PMID 39375009). We also identified transcriptomic differences in fibroblasts by OA, sex and BMI and metabolomic differences by BMI. In this study, we investigated if macrophages, adipocytes and endothelial cells exhibit transcriptomic differences in the IFP based on OA, sex and BMI. **Methods:** IFPs were obtained [n=21] and nuclei were subjected to snRNA-seq on an Illumina NextSeq 550 using the 150bp high output sequencing kit. Data was processed using Cell Ranger and clusters were annotated by canonical markers, with differential gene expression testing determining gene signatures. Major cell types were independently clustered to identify subclusters present. **Results:** Clustering analysis identified subsets of macrophages (4 subclusters), adipocytes (4 subclusters) and endothelial cells (5 subclusters), each with unique transcriptomic profiles. We also determined transcriptomic differences within each cell type comparing KOA-IFP vs control, female vs male KOA-IFP, and obese BMI vs normal BMI KOA-IFP. Pathway enrichment analysis identified pathways related to inflammation, metabolism and cellular communication enriched within each cell type, respectively, by KOA status. **Conclusions:** Using snRNA-seq, we identified transcriptomic differences within adipocyte, macrophage and endothelial cell subsets in IFP by KOA, sex and BMI. Our ongoing efforts will help characterize the role and function of identified cell subsets in KOA pathogenesis. We are now focused on using Multiome analysis to identify gene regulatory networks impacting the function of cell subtypes during KOA pathogenesis.

ICW33-4

Mid- to long-term clinical and radiological assessment of a short, titanium, porous plasma-splayed flat-tapered cementless femoral stem: An 8- to 12-year follow-up study

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Conflict of interest: None

[Objectives] Short cementless stems offer advantages such as bone-stock preservation and minimally invasive insertion. Despite encouraging short- to midterm outcomes, the long-term clinical and radiological implications of short, titanium, and porous plasma-sprayed flat-tapered stems remain unclear. [Methods] A retrospective review of 138 primary total hip arthroplasties, conducted between 2010 and 2015 in 130 patients, with a minimum 8-year follow-up was performed. Patients with Dorr type A or B

femora were included. Clinical and radiographic results, complications, and survival rates were evaluated. [Results] A total of 102 hips (94 patients) were reviewed with complete clinical and radiographic data at a minimum 8-year follow-up (mean, 9.5 years). The modified Harris hip score significantly improved from a mean preoperative value of 40.1 to 97.8 at the final follow-up, with 91% of the hips achieving a score of ≧ 90. In the original cohort of 138 hips, none underwent revision surgery for symptomatic loosening. Perioperative complications occurred in eight hips, including femoral fractures, postoperative dislocation, subcutaneous abscess, and transient thigh pain. Radiographically, femoral stem alignment was predominantly neutral in 86% of the hips in the anteroposterior plane. No hip exhibited radiolucency > 1 millimeter, and no subsidence > 2 mm was observed. Bone ingrowth fixation was observed in all 102 hips. Stress shielding around or below the lesser trochanter occurred in 58% of hips. Kaplan-Meier survival analysis indicated a 100% survival rate at eight, 10, and 12 years for stem revision or radiological instability. [Conclusion] The short, titanium, porous, plasma-sprayed, flat-tapered cementless stem exhibited excellent mid- to long-term results in primary total hip arthroplasties with Dorr type A or B femora, comparable with those of other short cementless and standard-length stems.

ICW33-5

Systematic profiling of osteoarthritic chondrocytes identifies senescence gene signature for prediction of disease progression

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Conflict of interest: None

[Objectives] Systemic gene profiling of osteoarthritic chondrocytes is expected to aid in improving our knowledge underling pathogenesis of diseases and providing clues to therapeutic strategy. Thus, the aim of the current study is to analyze the transcriptomic profiling of osteoarthritic chondrocytes for defining the major pathways involved in the progression of disease using clinical and experimental samples. [Methods] The bulk and scRNA-seq data from public databases of chondrocytes from clinical and experimental OA samples. For in vivo analysis, anterior cruciate ligament transection was performed on the left knee of mice to induce OA process. The knee joints were harvested at different time points and subjected to histopathological examination. Moreover, senescence was induced in chondrocytes using doxorubicin or etoposide and their responses were analyzed using bulk RNA-seq. [Results] Bulk RNA-seq data of mouse and rat DMM model demonstrated that instability model promoted the expression of genes involved in cellular senescence and P53 signaling pathways in chondrocytes in the early stage of disease. Senescent chondrocytes were observed in the joint as early as 2 weeks after surgery. Likewise, bulk RNA of human OA knee of patients undergoing arthroplasty revealed the upregulation of genes involved in P53 signaling pathway and inflammation. The scRNA-seq exhibited a distinct subset of osteoarthritic chondrocytes expressing gene signatures of inflammation and cellular senescence. On the other hand, bulk RNA-seq of stimulated chondrocytes with doxorubicin or etoposide revealed the upregulation of genes involved in cellular senescence and the p53 signaling pathway. [Conclusion] Our findings indicate that regulating p53 signaling activity in chondrocytes could be a key strategy in managing OA progression, potentially leading to the development of novel therapeutic approaches. Targeting cellular senescence represents a promising approach for prevention of OA progression.

ICW33-6

The Efficacy and Safety of Autologous Adipose-Derived Mesenchymal Stem Cells in Patients with Knee Osteoarthritis Therapy: A Systematic Review and Meta-Analysis

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Conflict of interest: None

[Objectives] This study aimed to evaluate the efficacy and safety of autologous adipose-derived mesenchymal stem cells (ADMSCs) for knee osteoarthritis (OA) therapy. [Methods] PubMed, ScienceDirect, and Google Scholars were used to retrieve studies investigating ADMSCs for knee OA treatment. All published articles were searched from inception to September 2024. A clinical trial and randomized controlled trial were included. The outcomes were visual analog scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and adverse events (AEs). The effect sizes of mean differences (MDs), a fixed-effects model, and 95% confidence intervals (CI) were calculated using RevMan 5.4 software. Cochrane risk of bias tool was used to assess the quality of studies. [Results] Seven studies were retrieved, of which four were eligible for meta-analysis with a total of 208 participants. The treatment group significantly reduced VAS scores (MD= -1.54, 95% CI [-1.97, -1.11], p= <0.00001) compared with the control group. Subgroup analyses respecting the time of follow-up on VAS scores (6 months, MD= -2.89, 95% CI [-3.45, -2.33], p= 0.00001; 12 months, MD= -0.84, 95% CI [-1.37, -0.31], p= 0.002) revealed that the treatment group yielded a significant improvement than the control group. The treatment group significantly improved WOMAC pain (MD= -6.52, 95% CI [-7.92, -5.11], p= <0.00001) and stiffness scores (MD= -2.63, 95% CI [-3.32, -1.95], p= <0.00001). The heterogeneity was not found across analyses. Most AEs were transient pain and mild edema, which were relieved spontaneously. No serious AEs were found. All included studies have a low risk of bias. [Conclusion] ADMSCs were found to have significantly better outcomes than the control group. This therapy has been proven to be effective and safe for knee OA. Future studies must address the strategy to translate this treatment into clinical application, such as administration routes, doses, and other AEs.

ICW34-1

The influence of the region and distribution of swollen lymph nodes on the clinical signs and course of Castleman's disease and TAFRO syndrome: a multicenter retrospective observational study

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Conflict of interest: None

[Objectives] Castleman's disease (CD) and TAFRO syndrome (thrombocytopenia, edema, fever, bone marrow fibrosis, and organomegaly) present with lymphadenopathy in various regions and a variety of clinical symptoms. In this study, we investigated whether the region and distribution of swollen lymph nodes are predictive factors for the clinical symptoms, course, and severity of these diseases. [Methods] This was a multicenter retrospective cohort study of 332 patients with CD and TAFRO syndrome who were followed-up at 11 facilities in Japan between 1995 and 2022. Diagnosis was based on Japanese diagnostic criteria and classified according to histopathological classification of lymph nodes and clinical subtypes (iMCD-TAFRO, iMCD-IPL, iMCD-NOS, and TAFRO syndrome). The patients were divided into four groups according to the region and distribution of the swollen lymph nodes (no swollen lymph nodes, single region, and one or both sides of the diaphragm), and the severity was evaluated using the CHAP and TAFRO syndrome severity scores. [Results] In the 321 cases analyzed, there was no significant association between severity or prognosis and the region or distribution of swollen lymph nodes, regardless of the presence of TAFRO symptoms. TAFRO symptoms had high inflammatory responses regardless of the area and distribution of swollen lymph nodes, and iMCD patients had high IgG levels regardless of the area and distribution of swollen lymph nodes. In contrast, the frequency of hepatosplenomegaly was higher in patients with a larger

area of swollen lymph nodes. [Conclusion] In CD and TAFRO syndrome, it is difficult to adequately assess the severity and clinical features based on the area and distribution of swollen lymph nodes alone, and a comprehensive evaluation is necessary to understand the clinical signs and prognosis.

ICW34-2

Questionnaire-based nationwide survey on the safety of azathioprine in Japanese patients with rheumatic diseases: a cross-sectional study

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Conflict of interest: None

[Objectives] Azathioprine (AZA) is an established treatment for rheumatic diseases. However, real-world data on its safety in Japanese patients are limited. This study aimed to assess the real-world use and safety of AZA in treating rheumatic diseases in Japan. [Methods] We conducted a nationwide, questionnaire-based survey. Questionnaires were distributed to 1,163 facilities, including university hospitals and the Japan College of Rheumatology educational hospitals. Of these, 170 facilities (14.6%) responded. Adverse events (AEs) were classified into three grades (grade 1, grade 2, and grade 3 or higher [grade ≧ 3]) according to the Common Terminology Criteria for Adverse Events. [Results] A total of 1,943 patients with rheumatic diseases who began AZA treatment between November 2000 and September 2023 were included. Of these, 33.9% experienced AEs, including hepatobiliary disorders (13.9%), gastrointestinal disorders (10.4%), blood and lymphatic system disorders (9.3%), infections and infestations (5.1%), and skin and subcutaneous tissue disorders (2.4%). The rates of AZA discontinuation due to AEs and AZA resumption were 71.6% and 9.4%, respectively. The incidence of grade ≧ 3 AEs was 2.7% and varied by disease type. Of the 1,028 patients (52.9%) who underwent *NUDT15* genetic testing, those with the Arginine (Arg)/Arg or Arg/ Histidine genotypes had the lowest frequency of AEs (39.1%), whereas all patients with the Cysteine (Cys)/Cys genotype experienced AEs. Multivariate analysis revealed that older age (odds ratio [OR]: 2.47; 95% confidence interval [CI]: 1.32-4.59) and systemic lupus erythematosus (SLE) (OR: 2.31; 95%CI: 1.09-4.87) were associated with an increased risk of grade ≧ 3 AEs. [Conclusion] This study provides evidence of AZA-related AEs in Japanese patients with rheumatic diseases. The incidence of AZA-related AEs was relatively high, with grade ≧ 3 AEs occurring more frequently in patients aged > 65 years and those with systemic lupus erythematosus.

ICW34-3

Comparative efficacy of mepolizumab 100 mg, mepolizumab 300 mg and benralizumab 30 mg in eosinophilic granulomatosis with polyangiitis (EGPA): a monocentric retrospective observational study

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Conflict of interest: None

Objectives: Mepolizumab, targeting IL-5, and benralizumab, targeting IL-5α receptor, are effective in EGPA treatment. This study aimed to assess and compare them in a monocentric real-life cohort. **Methods:** We included EGPA patients (2022 ACR/EULAR criteria) treated with benralizumab 30 mg/8w, mepolizumab 100 mg/4w, or mepolizumab 300 mg/4w. Clinical, functional, and biological data were compared. Remission was defined as a BVAS=0 and prednisone (PDN) dose <=4 mg/day. **Results:** We included 61 patients exposed to 77 treatment lines (n=33 benralizumab, n=31 mepolizumab 300 mg, n=13 mepolizumab 100 mg). Demographic and clinical characteristics were comparable, except for severe asthma in benralizumab and mepolizumab 100 mg groups (p<0.001). At 12 months, BVAS significantly decreased in benralizumab (p<0.001) and mepolizumab 300 mg (p=0.022), but remained stable for mepolizumab 100 mg. Eosinophils reduced throughout follow-up, with benralizumab as the most depleting (p<0.001). Benralizumab patients showed significant FEV1 and FeNO improvement (p=0.012 and p<0.001), and mepolizumab 300 mg patients showed quality-of-life improvement (p<0.001) per AAV-PRO questionnaire. PDN intake decreased significantly for mepolizumab 300 mg and benralizumab, with PDN discontinuation at 6 months (mepolizumab 300 mg: 56%; benralizumab: 46%), and mepolizumab 300 mg led to shorter PDN discontinuation time (log-rank p=0.006). No serious adverse events led to discontinuation; main reason for discontinuation was secondary failure, mainly due to persistent ENT symptoms in the benralizumab group (p=0.001). **Conclusions:** Mepolizumab 300 mg showed superior drug survival, faster PDN discontinuation, and improved quality of life. Anti-IL-5/Ra biologics effectively improved respiratory symptoms, reduced PDN intake and eosinophils, with benralizumab being the most effective for eosinophil depletion. Persistent ENT symptoms were the primary reason for discontinuation, especially in benralizumab-treated patients.

ICW34-4

Polyangiitis overlap syndrome: a rare clinical phenotype with high relapse risk and unique features

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Conflict of interest: None

[Objectives] Polyangiitis overlap syndrome, characterized by coexistence of giant cell arteritis and ANCA-associated vasculitis (AAV) in a patient, is a rare clinical phenotype with unknown characteristics and prognosis. This study aims to elucidate the clinical features and prognosis of this syndrome. [Methods] We retrospectively reviewed patients with polyangiitis overlap syndrome who visited our institution from 2012 to September 2024. We collected information from their medical charts. Immunohistochemical staining for CD20 was performed on the temporal artery biopsy samples. [Results] Out of 61 GCA and 152 AAV, 7 patients were diagnosed with polyangiitis overlap syndrome. Median age of onset was 63 years (range 54-75), and 28.6% were female. Fever was the most frequent symptom in all, and headache was present in 5. Involved large vessels were temporal arteritis in 4 and aortitis in 5. No patients had a complication of polymyalgia rheumatica. Interestingly, B-cell infiltration was prominent in the tissues of temporal arteritis. Regarding co-existing AAVs, granulomatosis with polyangiitis was the most common in 4, followed by microscopic polyangiitis in 2 and eosinophilic granulomatosis with polyangiitis in 1. AAV-related manifestations included renal involvement in 5, pulmonary lesions in 4, and multiple mononeuropathy in 4. As remission induction treatment, high-dose glucocorticoids with or without steroid pulse therapy were administered in all patients, with cyclophosphamide in 4 patients and tocilizumab in 2 patients, leading to remission in all but one patient. However, during the observation period (median duration of 66 months, range 5-137), 5 patients relapsed (71.4%) with AAV manifestations, and 1 patient died of infection. [Conclusion] Our present study revealed that polyangiitis overlap syndrome is a high-risk clinical phenotype for relapse, highlighting the necessity of establishment of optimal remission maintenance treatment.

~~ICW34-5~~

~~**The Role of Aikune Gymnastics in Cognitive Dysfunction Management Among Senile Osteoporosis Patients**~~

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~~Conflict of interest: None~~

~~The aim of the study was to evaluate the effect of the Kazakh physical exercise system "Aikune" on the dynamics of cognitive dysfunction indicators in patients with senile osteoporosis. Methods: 25 patients with senile osteoporosis (attending Aikune gymnastics sessions 3 times per week~~

~~for 45 minutes, mean age 67.6 years, 20 females (80%), 5 males (20%), 10-year absolute FRAX risk for major bone fractures - 16.8%, proximal femoral fracture - 5.8%) underwent testing at baseline and after 6 months of follow-up using the 6-CIT test (Brooke, Bullock version, 1999), an adapted modification of the reading comprehension test (Daneman, Carpenter, 1980), grip strength measurement using a DK-50 mechanical dynamometer, and the IPAQ questionnaire for physical activity assessment. Results were compared with a control group of 25 age- and sex-matched patients who did not participate in gymnastics sessions. All patients received ibandronic acid 150 mg orally once monthly, calcium 500 mg and cholecalciferol 400 IU orally twice daily. Results: After 6 months of observation, positive dynamics were noted not only in significant muscle strength gain according to hand dynamometry (from 21.2 to 24.8 kg (by 10.1%)), physical activity by IPAQ (from 9.2 to 12.4 points (by 34.8%)), but also in improvement of cognitive dysfunction indicators (reduction in 6-CIT from 17.3 to 9.4 points (by 45.7%)), and reading comprehension (from 32.5 to 0.5 % (by 49.1%)). Conclusion: Kazakh Aikune gymnastics is effective not only as a rehabilitation intervention that increases physical activity and muscle strength but also as a means of improving cognitive impairment in patients with senile osteoporosis.~~

ICW35-1

Investigation of a biomarker to predict for rapidly progressive interstitial lung disease with anti-melanoma differentiation-associated gene 5-positive dermatomyositis

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Conflict of interest: None

[Objective] Rapidly progressive interstitial lung disease (RP-ILD) is a fatal complication associated with anti-melanoma differentiation-associated gene 5 (MDA5)-positive dermatomyositis (MDA5-DM). Prediction of developing RP-ILD is crucial due to its high mortality rate. Herein, we investigated the risk factor of RP-ILD with MDA5-DM. [Methods] We analyzed the immunophenotype by flow cytometry and transcriptome by RNA-sequencing of 26 immune cell subsets from patients with MDA5-DM patients. We referred "RP-ILD" as radiological interstitial changes with progressive dyspnea and hypoxemia within 3 months after the onset of respiratory symptoms. Transcriptomes were analyzed between RP-ILD and non-RP-ILD by differentially expressed genes (DEGs) with edgeR and gene set variation analysis (GSVA). [Results] Seven patients with MDA5-DM, including three with RP-ILD and four with non-RP-ILD, were enrolled. Myeloid dendritic cells exhibited a larger number of DEGs that met the threshold of FDR < 0.05, and the DEGs included CLNK, CADM1, and XCR1. GSVA scores of mDC from RP-ILD patients showed that interferon-γ pathway tended to be higher. Also, flow cytometric analysis revealed that the number and ratio of $CD141^+$DC was higher in RP-ILD patients. Further, univariate logistic regression model with Firth penalization clarified that the number of $CD141^+$DC was a risk factor for RP-ILD (Odds ratio, 1.064; 95%CI: 1.002-1.606, p=0.036). [Conclusions] $CD141^+$DC could be a biomarker to predict developing RP-ILD and might play a key role in the pathogenesis of MDA5-DM.

ICW35-2

GPX4 downregulation induces platelet ferroptosis and activation in systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Ferroptosis is a recently discovered type of regulated necrosis and glutathione peroxidase 4 (GPX4) has been recognized as a key enzyme that protects against ferroptosis. However, the role of platelet GPX4 in systemic lupus erythematosus (SLE) has not been explored. In this study, GPX4 levels in platelets were measured and the correlation with clinical features were analyzed. [Methods] Platelet GPX4 protein expression was detected by Western blot and immunofluorescence in 37 SLE patients and 23 healthy controls. Clinical data were recorded at time points of blood sampling. Platelet activation was analyzed by flow cytometry, LDH release by LDH release assay and plasma oxidized DNA levels by a general 8-OHdG ELISA kit. GPX4 inhibitors and agonists were used to evaluate the effect of GPX4 on platelet ferroptosis and activation. [Results] Patients with SLE had significantly decreased expression of platelet GPX4 enhanced lipid peroxidation and increased percentage of platelet activation as compared with healthy controls. Furthermore, levels of platelet GPX4 were negatively correlated with SLEDAI-2K score, 24-hour urine protein and oxidized DNA. Low GPX4 expression were associated with skin and joint involvements of SLE patients. Inhibiting GPX4 induced platelet ferroptosis and activation. Interestingly, GPX4 agonists can protect SLE platelets from ferroptosis and activation. [Conclusions] These findings confirmed that downregulated GPX4 protein in platelets of SLE patients negatively correlated with plasma oxidized DNA, SLE disease activity and 24-hour urine protein. The activation of GPX4 mitigated platelet ferroptosis and activation in SLE, indicating a potential involvement of GPX4-related platelet ferroptosis in the development of SLE. Hence, activating GPX4 could represent a promising avenue for the development of novel SLE therapies.

ICW35-3

Soluble TNFRII in Lupus Nephritis as a Biomarker of Disease Activity and Treatment Response

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Conflict of interest: None

Objectives: To assess sTNFRII as the biomarker of LN disease activity and treatment response. Methods: SLE patients (n=91, F: M=85:6) satisfying the ACR/EULAR 2019 criteria were enrolled. Patients with active disease (SLEDAI>4) were subcategorized as - Active Nephritis (AN); & active disease without nephritis (Active Non-Renal; ANR). All patients gave baseline serum and urine samples. AN patients were followed up for 12 months and 3 monthly serum and urine samples were collected. Blood and urine samples from Healthy Controls (HC; n=30) and Disease Controls (DC) (patients with active rheumatoid arthritis - n=30) were taken at baseline for comparison. Soluble TNFRII was measured using commercially available ELISA kits. Urinary values were normalized for creatinine excretion. Non-parametric tests were used for analysis. A p-value <0.05 was considered significant. Results: Among SLE patients (63 as AN and 28 as ANR), baseline urinary TNFRII (uTNFRII) was significantly higher in AN group as compared to ANR, HC and DC ($p<0.05$) groups. Baseline uTNFRII showed good correlation with urinary protein: creatinine ratio ($r=0.5$; $p<0.001$), rSLEDAI ($r=0.4$, $p<0.05$), SLEDAI ($r=0.3$, $p<0.05$) and sTNFRII ($r=0.5$; $p<0.001$). Similarly, baseline sTNFRII was significantly higher in AN group as compared to ANR, HC and DC ($p<0.05$). At baseline, sTNFRII also showed good correlation with urinary protein: creatinine ratio ($r=0.5$; $p<0.001$), rSLEDAI ($r=0.4$, $p<0.05$) and SLEDAI ($r=0.4$, $p<0.05$) Both sTNFRII and uTNFRII could differentiate between AN and ANR groups (ROC analysis - sTNFRII (AUC=0.8), uTNFRII (AUC=0.6), C3 (AUC=0.6), C4 (AUC=0.37) and anti-ds DNA antibodies (AUC=0.64). On follow-up, both uTNFRII and sTNFRII showed significant decrease in AN group at 3, 6, 9 and 12 months as compared to baseline levels. Conclusions: Urinary and serum sTNFRII help differentiate between patients with and without renal involvement. With treatment, their levels decrease and correlate with decreasing renal disease activity.

ICW35-4

Hepatocyte Growth Factor as a Driver of Inflammatory Amplification and Therapeutic Resistance in Rheumatoid Arthritis

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Conflict of interest: Yes

[Objectives] Our previous multi-omics studies investigating anti-tumor necrosis factor (TNF) inhibitors and abatacept have shown that serum hepatocyte growth factor (HGF) levels may serve as a biomarker for predicting poor response to these therapies in patients with rheumatoid arthritis (RA). However, the precise mechanisms by which HGF influences therapeutic outcomes remain elusive. This study aimed to elucidate the mechanistic role of HGF in the pathophysiology of RA and treatment resistance. [Methods] Plasma HGF concentrations were measured in 66 RA patients using the Luminex Discovery Assay (R&D Systems). Expression levels of HGF and its receptor, c-Met, were evaluated in synovial tissues from patients with RA and osteoarthritis using immunostaining. The effects of HGF on synovial fibroblasts isolated from RA synovial tissue, as well as on human monocytes, were examined through RNA sequencing, immunostaining, and quantitative PCR. [Results] Compared to healthy controls, RA patients exhibited significantly elevated plasma HGF levels (P=0.0003), which strongly correlated with Disease Activity Score 28-ESR (DAS28-ESR) (r=0.367, P=0.002). Immunostaining demonstrated robust HGF expression in RA synovial tissues, primarily by monocytes and synovial fibroblasts, while c-Met expression was restricted to synovial fibroblasts. RNA sequencing indicated that HGF stimulation upregulated key inflammatory markers, including IL-6 and HGF itself, in synovial fibroblasts. In addition, Toll-like receptor (TLR) 4 or 5 activation led to increased HGF expression in human monocytes, suggesting a potential role in inflammation amplification. [Conclusion] HGF appears to act primarily on synovial fibroblasts, potentially driving a vicious cycle of IL-6-mediated inflammatory amplification loop that may contribute to therapeutic resistance in RA. These findings imply that targeting the HGF-c-Met pathway could represent a novel strategy for mitigating treatment refractoriness in RA.

ICW36-1

CD4 positive effector memory T cells re-expresses CD45RA (TEMRA) in rheumatoid arthritis (RA) pathogenesis and the role of IL-6 in its differentiation

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Conflict of interest: Yes

[Objective] To explore abnormal lymphocyte differentiation in RA patients and assess cell functionality. [Methods] We conducted comprehensive immunophenotyping of RA patients' blood using multi-color flow cytometry and investigated factors contributing to abnormal cell differentiation in vitro. [Results] Analysis of 533 RA patients without b/tsDMARDs usage showed abnormal T cell differentiation compared to healthy controls, particularly increased $CD4^+$ TEMRA. Whole transcriptome analysis of isolated $CD4^+$ TEMRA cells ($CD4^+CCR7^-CD45RA^+$) revealed high expression of cytotoxic molecules and markers of cellular senescence. Additionally, analysis of the T cell receptor (TCR) repertoire sequencing revealed that $CD4^+$ TEMRA cells exhibit reduced diversity in both the α and β chains of their TCR. TCR of regulatory T cells (Tregs) are known for self-reactivity, and hydrophobic amino acids in TCR are associated with self-antigen recognition. Analyses showed these amino acids were prevalent in the TCR of $CD4^+$ TEMRA cells. Furthermore, a comparison of the TCRs of Tregs and $CD4^+$ TEMRA cells showed a high degree of homology. However, subsequent analysis showed a minimal presence of Tregs within the $CD4^+$ TEMRA population. These indicated that the $CD4^+$ TEMRA are characterized by oligoclonal expansion and autoreactivity. In vitro, stimulation of naïve T cells with TCR led to the differentiation of $CD4^+$ TEMRA, which displayed senescence markers (p16, CD57) and cytotoxic molecules. Telomere shortening was observed in these $CD57^+$ cells, confirming their senescence. Adding IL-6 during TCR stimulation enhanced $CD4^+$ TEMRA differentiation, an effect negated by tocilizumab. Conversely, IFN-γ, IL-12, and IL-17 had no impact on differentiation. In RA patients, treatment with IL-6 inhibitors significantly reduced p16 expression in T cells, corroborating these findings. [Conclusions] IL-6 contributes to RA pathogenesis by promoting cellular senescence and driving the differentiation into $CD4^+$ TEMRA.

ICW36-2

Exploration of Flare Risk Factors Based on Strategic Dose Reduction Protocols of Biologic Agent

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Conflict of interest: Yes

[Objectives] The purpose of clinical trial is to examine the outcomes of prolonged dosing intervals or withdrawal of biologic agents (bDMARDs) in stable rheumatoid arthritis (RA) patients in a real-world clinical setting. It also aims to evaluate predictors of flares associated with drug tapering. [Methods] In patients with RA who have maintained low disease activity (LDA) for at least six months. The study included RA patients who were in remission at the time of obtaining informed consent and were not taking glucocorticoids (GCs). Patients were divided into two groups: 1. **Continuation Group (C group)**: Patients who continued their usual treatment without tapering. 2. **Tapering and Discontinuation Group (TD group)**: Patients who tapered bDMARDs over the course of one year and then discontinued the medication. The primary outcomes analyzed were the maintenance of LDA and the risk factors associated with disease flare during the two-year follow-up period. [Results] A total of 499 patients who met the eligibility criteria were included in the study, of which 71 patients underwent drug tapering. There was no significant difference in flare rates during the prolonged dosing intervals phase between the TD and C groups (73.0% vs. 95.4%). However, once the medication was discontinued in the TD group, there was a significantly higher rate of flare compared to the C group (47.6% vs. 95.5%, p=0.0003). Risk factors for flare included the presence of serum autoantibodies such as rheumatoid factor and anti-citrullinated protein antibodies, as well as higher baseline grey scale scores in joint ultrasound examinations. [Conclusion] These findings suggest that careful consideration should be given when discontinuing bDMARDs in RA patients, especially those with identified risk factors, such as ultrasound findings of the joints and the presence of serum autoantibodies. However, it may be possible to prolong the dosing interval if the decision is based on a thorough evaluation of risk factors.

ICW36-3

Exploration of Macrophage-Derived Cytokines/Chemokines predictive for radiographic progression in DMARD-naïve patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To investigate predictive value of biomarkers in 13 macrophage-derived cytokines/chemokines for radiographic progression during one year of initial treatment in DMARD-untreated patients with rheumatoid arthritis (RA). [Methods] This is a post-hoc study using data from a

multicenter cohort study conducted in Hiroshima from June 2018 to March 2022: Three Arrow Study. 13 biomarkers (IL-12p70, TNFα, IL-6, IL-4, IL-10, IL-1β, Arginase, TARC, IL-1RA, IL-12p40, IL-23, IFN-γ, IP-10) were measured by the LEGENDplex Human Macrophage/Microglia Panel in sera at initiating first DMARD treatment obtained from 170 patients. They were treated according to T2T strategy. Radiographic progression during one-year treatment was evaluated by changes in modified total Sharp score (ΔmTSS). Relationship between the biomarkers and ΔmTSS were assessed using Pearson's correlation coefficient and multiple regression analysis. [Results] Among the 170 patients (mean age 64.7 years, 62.4% female, 67.5% anti-CCP2 positive, 72.4% RF-positive), 88.8% (n=151) initially treated with MTX, and 18.2% (n=31) received either biological agents or JAK inhibitors during the first year. In the overall cohort, IL-1β and IFN-γ levels positively correlated with ΔmTSS (IL-1β: r=0.16, p=0.04; IFN-γ: r=0.17, p=0.03), however these associations were not significant in multivariate analysis. In anti-CCP2-positive patients, TNFα, IL-4, IL-1β, IL-12p40 and IFN-γ levels were positively correlated with ΔmTSS (TNFα: r=0.20, p=0.03; IL-4: r=0.25, p=0.009; IL-1β: r=0.28, p=0.003; IL-12p40: r=0.19, p=0.04; IFN-γ: r=0.27, p=0.03), and multivariate analysis confirmed TNFα, IL-1β, and IL-12p40 were significant (TNFα: p=0.001, IL-1β: p=0.005, IL-12p40: p=0.002). No significant correlations were observed in anti-CCP2-negative patients. [Conclusion] In anti-CCP2-positive untreated RA patients, pre-treatment levels of TNFα, IL-1β, and IL-12p40 were predictive markers for radiographic progression.

ICW36-4

Thermographic assessment of patients with rheumatoid arthritis: a comparison with ultrasound-detected power Doppler and grey-scale joint inflammation at the knees

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Conflict of interest: None

[Objectives] To compare thermal imaging (TI) and ultrasound (US) for joint inflammation assessment at the knees of patients with rheumatoid arthritis (RA). [Methods] TI parameters (maximum (Tmax), average (Tavg) and minimum (Tmin) temperatures) at the anterior (ANT), lateral (LAT) and medial (MED) knee aspects were correlated with US power Doppler (PD) and grey-scale (GS) joint inflammation (scored 0-3 at the supra-patellar recess) using the Spearman's correlation coefficient. The ability of TI in identifying (a) US PD score>0 and (b) GS score≧2 were studied using receiving operating characteristic (ROC) curve analysis. 30 each of Tmax, Tavg and Tmin from the baseline thermograms were re-read (>2 weeks apart) for intra-rater reliability testing using intra-class correlation coefficient (ICC) analysis. [Results] This cross-sectional study (n=95 RA patients) included 570 thermograms (3 aspects per knee) and 190 knees scanned by US. All TI parameters at the 3 aspects of the bilateral knees correlated significantly with US PD and GS scores (rho ranged from 0.21 to 0.43, P<0.05 (for PD) and 0.27 to 0.49, P<0.01 (for GS). Area under the ROC curves (AUCs) for TI parameters in identifying PD score>0 and GS score≧2 ranged from 0.63 to 0.82 and 0.65 to 0.82, respectively. For PD, TI parameters with (a) AUC>0.70 to 0.80: Right ANT (Tmin and Tavg) and Tmax (LAT and MED); Left Tmin and Tmax (all 3 aspects for both) and LAT Tavg and (b) AUC>0.80: Left Tavg (ANT and MED). For GS, TI parameters with (a) AUC>0.70 to 0.80: Right ANT (Tmin, Tmax and Tavg) and LAT (Tmax and Tavg); Left Tmin and Tmax (all 3 aspects for both) and (b) AUC>0.80: left Tavg (all 3 aspects). The ICC values (Tmax, Tavg and Tmin) at the knees were high (0.997 to 0.999). [Conclusion] For the first time, TI was shown to help discriminate both US PD status (positive versus negative) and GS joint inflammation severity at the RA knees. TI appears promising and requires further validation in independent RA cohorts.

ICW36-5

The safety of folic acid supplement in rheumatoid arthritis patients on methotrexate

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Conflict of interest: None

[Objectives] Methotrexate is commonly used as a disease-modifying drug for rheumatoid arthritis (RA), but its inhibition of dihydrofolate reductase can lead to folate deficiency. As a result, it is standard clinical practice to prescribe folic acid alongside methotrexate. However, there is no consensus on the appropriate frequency and dosage of folic acid supplementation or on the comorbidities that may arise from its use. This study aims to compare the incidence of major adverse cardiovascular events (MACE) in RA patients receiving high versus low doses of folic acid alongside methotrexate. [Methods] RA patients using methotrexate without baseline MACE were recruited from a citywide database in Hong Kong between 2006 and 2015 and followed until 2018. The primary outcome was the first occurrence of MACE. Cox regression and inverse probability treatment weighting (IPTW) analyses with time-varying covariates were used to assess the association between folic acid dosage and MACE, adjusting for demographics, traditional cardiovascular risk factors, inflammatory markers, and antirheumatic drug use. [Results] A total of 8,405 RA patients on methotrexate were identified, with a median follow-up of 9 years (IQR: 5 years) and a mean age of 56.0 years (SD: 13.5). Of these, 6,854 (78.5%) were female, and 504 (6.0%) developed MACE. Among the cohort, 2,967 patients (35.3%) received >=5 mg of folic acid daily, while 5,438 (64.7%) received 0-<5 mg. Univariate analyses showed that elevated ESR and CRP levels, and the use of folic acid >=5 mg daily were associated with a significantly higher risk of MACE. The IPTW Cox model with generalized boosted modelling indicated that a higher folic acid dose was associated with increased MACE risk (C-reactive protein model: HR 1.66; erythrocyte sedimentation rate model: HR 1.77; both $p < 0.001$). [Conclusion] High doses of folic acid are linked to a dose-dependent increase in MACE risk among RA patients.

ICW37-1

Change in disease activity and autoantibody titers after COVID-19 vaccination in rheumatoid arthritis: Real-world data from KURAMA cohort

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Conflict of interest: Yes

[Objectives] This study aimed to assess whether COVID-19 vaccination leads to increased autoantibody production or worsens disease activity in patients with rheumatoid arthritis (RA). [Methods] RA patients without a history of COVID-19 infection who had been regularly followed at our hospital since before the pandemic, were surveyed about their vaccination status. We compared the mean rheumatoid factor (RF) titer and Clinical Disease Activity Index (CDAI) after 4/12/2024 (the date of COVID-19 vaccination started) between vaccinated and unvaccinated patients. We also analyzed RF titers and CDAI within 30 days of vaccination from the first to the third dose. Subgroup analyses were performed based on vaccine doses and types (Pfizer-BioNTech vs. Moderna). The null hypotheses were that vaccination and vaccine types do not change RF and CDAI. [Results] A total of 693 RA patients were contacted, and 440 valid responses were received. Of these, 387 patients had been vaccinated against COVID-19, while 53 had not. The total number of vaccinations was 1,964 (Pfizer-BioNTech: 1,587; Moderna: 333; unknown/other: 44). Of the vaccinated patients, 331 (87.6%) were RF-positive. The mean RF titers in unvaccinated and vaccinated patients were 153.2±323.4 and 102.5±214.1 IU/mL, and CDAI was 6.06±5.15 and 4.64±4.09 (mean±SD), respectively. In vaccinated patients, there were no differences in RF and CDAI from prevaccination to the third postvaccination. Subgroup analyses showed that no significant differences were found between Pfizer-BioNTech and Moderna vaccines (RF: 104.2±217.5 vs 105.8±177.4; CDAI: 4.72±5.25 vs. 5.81±6.37). All comparisons failed to reject the null hypothesis. [Conclusion] COVID-19

vaccination did not affect autoantibody titers or disease activity in RA patients.

ICW37-2

Serum Inflammatory Markers and Disease Activity Scores Are Associated with TNF-alpha and IL-6-Induced Osteoclasts, but Not with RANKL-Induced Osteoclasts in Peripheral Blood Monocytes from Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Objectives] We have reported that stimulation of human peripheral blood monocytes (PBMs) with TNF-α and IL-6, the major inflammatory cytokines in rheumatoid arthritis (RA), induces differentiation of osteoclasts (OCs) *in vitro*. We also have shown that the number of TNF-α and IL-6-induced OCs differentiated from PBMs in RA patients positively correlated with the modified total Sharp score, while that of RANKL-induced OCs did not. The present study aims to: 1) clarify the association between clinical indicators and OCs induced by TNF-α and IL-6 or RANKL; 2) evaluate the effects of the JAK inhibitor (JAKi) filgotinib (FIL) on these OCs; 3) identify the presence of these OCs in areas of bone erosion in RA patients. [Methods] PBMs from 18 RA patients were stimulated with TNF-α and IL-6 or RANKL. Tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells were quantified as osteoclasts. We analyzed the numbers of OCs induced by these cytokines before and after 24 weeks of treatment with FIL. Tibial bones from 5 RA patients were stained with TRAP and immunohistochemically with anti-MMP-3 or anti-RANK antibodies. [Results] The number of TNF-α and IL-6-induced OCs differentiated from PBMs in RA patients showed significant positive correlations with serum levels of CRP, ESR, and MMP-3 as well as with DAS-28-ESR, SDAI, and CDAI, whereas that of RANKL-induced OCs did not. After 24 weeks of treatment with FIL, the number of TNF-α and IL-6-induced OCs differentiated from PBMs significantly decreased compared to that before the treatment, on the other hand, that of RANKL-induced OCs did not change. The number of $MMP\text{-}3^{+}$ $RANK^{-}$ OCs as markers for TNF-α and IL-6-induced OCs was significantly higher than that of $MMP\text{-}3^{-}$ $RANK^{+}$ OCs as markers for RANKL-induced OCs in the areas of bone erosion in RA patients. [Conclusion] TNF-α and IL-6-induced OCs may contribute to bone destruction in patients with RA, and targeting these OCs could lead to new therapeutic strategies such as JAKi.

ICW37-3

Decoding the Synovial Metabolomic Fingerprint of Rheumatoid Arthritis Subtypes: A Machine Learning Approach to Identify Treatment-Specific Metabolic Pathways and Predict Drug Responsiveness

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Conflict of interest: None

Objectives: Rheumatoid arthritis (RA) is heterogeneous, complicating treatment outcomes. Metabolomic profiling may help classify RA subtypes and predict drug responses. This study aims to develop a machine learning model using synovial fluid metabolomics to classify RA subtypes and identify metabolic pathways linked to responsiveness for methotrexate, TNF inhibitors, and JAK inhibitors. Methods: Synovial fluid from 1,198 RA patients in the Accelerating Medicines Partnership Rheumatoid Arthritis network was analyzed. Patients were classified as responders or non-responders based on EULAR criteria after 6 months on various therapies, including methotrexate, TNF inhibitors, and JAK inhibitors. LC-MS identified 4,856 metabolites, and data integration included clinical, genetic, and histological information to improve model accuracy. A machine learning pipeline with XGBoost and neural networks, using cross-validation and SHAP for feature interpretation, was employed. Performance was assessed via AUROC, balanced accuracy, and F1-score. Results: The model achieved an AUROC of 0.87, with 82.3% balanced accuracy in predicting treatment response across different RA subtypes. Key predictors included elevated kynurenic acid (OR: 3.92, 95% CI: 3.41-4.51), reduced lactate (OR: 2.78, 95% CI: 2.41-3.22), and dysregulated arachidonic acid metabolism (OR: 3.18, 95% CI: 2.70-3.74). Non-responders to TNF inhibitors showed increased biosynthesis of pro-inflammatory eicosanoids, while JAK inhibitor non-responders displayed abnormal purine metabolism patterns, suggesting distinct metabolic signatures associated with drug resistance. The inclusion of genetic and histological data significantly improved the model's predictive power ($p<0.001$), indicating the added value of multi-omics integration. Conclusion: This metabolomics-based approach provides a novel framework for predicting RA treatment outcomes, emphasizing kynurenic and arachidonic acid metabolism as potential therapeutic targets.

ICW37-4

Propensity Score-Matched Analysis of Clinical Parameters Between Rheumatoid Arthritis Patients Treated with bDMARDs and tsDMARDs in NinJa 2022

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Conflict of interest: None

[Objectives] Real-world evidence regarding rheumatoid arthritis (RA) patients treated with disease-modifying antirheumatic drugs (DMARDs), especially with targeted synthetic (ts)DMARDs, provides valuable insights for clinical practice. [Methods] Data from the NinJa 2022 database were analyzed. A propensity score (PS) was generated using independent variables as follows: age, sex, disease duration, class, stage, and RF titer. PS-matched comparison of clinical parameters was performed between RA patients treated with biological (b)DMARDs and tsDMARDs. For the tsDMARD group, patients treated with tofacitinib and baricitinib were included. Statistical analyses were conducted using R software, with a significance threshold set at $p < 0.05$. [Results] RA patients treated with abatacept (ABA, n=557), TNF inhibitors (TNFi, n=1143), IL-6 inhibitors (IL-6i, n=939), and JAK inhibitors (JAKi, n=415) were included in the analysis. In the post-matched comparison of CDAI scores between ABA/JAKi and IL-6i/JAKi, significant differences were observed (ABA: 6.13 vs. JAKi: 5.03, $p=0.016$; IL-6i: 6.84 vs. JAKi: 5.02, $p<0.001$). In contrast, no significant difference was found in CDAI scores between TNFi and JAKi (TNFi: 5.21 vs JAKi: 5.01, $p=0.632$). Regarding patient-reported outcomes (PROs), a significant difference in Patient Global Assessment (PGA) scores was noted between IL-6i and JAKi-treated patients (IL-6i: 2.69 vs. JAKi: 2.18, $p=0.017$). Additionally, the glucocorticoid (GC) doses (daily PSL dose, mg/day) were significantly lower in JAKi-treated patients compared to those treated with ABA and IL-6i (ABA: 3.57 vs. JAKi: 2.94, $p=0.026$; IL-6i: 3.64. vs. JAKi: 2.94, $p=0.015$). [Conclusion] In the NinJa 2022 dataset, JAKi-treated patients exhibited lower disease activity scores and required lower GC doses compared to those treated with ABA and IL-6i. These real-world data provide valuable evidence to guide the clinical decision-making process when selecting DMARDs for RA treatment.

ICW37-5

Developing a Rheumatology Skilled Nurse Training Program in a Private Tertiary Hospital in the Philippines

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Conflict of interest: None

[Objectives] In the Philippines, there is a disparity in the number and distribution of rheumatologists in the country, creating an unmet need of

providing holistic care for patients with rheumatologic conditions. Several studies have demonstrated that rheumatology skilled nurses impact treatment of patients positively by ensuring patient centered care. This study aims to describe and assess a training developed, based on the Asia-Pacific Initiative for Rheumatology Nurse Education, that was used to educate nurses in a tertiary private hospital in the Philippines. [Methods] A formal three session training was conducted among nurses. Trained nurses completed pre- and post-evaluation. Significance of change in scores was assessed by paired t-test control for each session. [Results] The training consisted of separate sessions on rheumatoid arthritis, spondyloarthropathies and cognitive behavioral therapy. Each session consisted of didactics in the morning and patient encounters in the afternoon. The training was attended by 38 nurses. Majority of participants worked in the out-patient department and had limited or no rheumatology experience. Upon paired t-test of pre-test and post-test scores of each session at 95% confidence interval, a statistically significant difference in test scores was observed. All participants found the training relevant to their daily practice and 87% found the patient sessions to be most helpful to their learning experience. [Conclusion] This training series is an effective tool which can provide motivated nurses with the necessary skills to become rheumatology skilled nurses. The next session will be a clinical skills exam for those who completed all trainings. They will eventually serve as the core training faculty to facilitate training of future rheumatology skilled nurses in the country. This program is key in creating a holistic approach in the treatment of patients with rheumatic diseases.

ICW38-1

Distinct clinical features associated with Cancer associated myositis with Anti-TIF1g positivity - results from a multicentre longitudinal cohort

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Conflict of interest: None

[Objectives] Autoantibody against transcription intermediary factor 1-gamma (TIF1g) is common in cancer-associated myositis (CAM). The characteristics of anti-TIF1g positive CAM evaluated were using data from a regional idiopathic inflammatory myopathy registry (MyoHK). [Methods] MyoHK is a longitudinal observational cohort collecting data from IIM patients from 8 rheumatology centers in Hong Kong. Data was reviewed from 2004-2023. CAM was defined by cancer within 3 years of IIM diagnosis (before or after). Patients with unknown myositis specific antibody (MSA) were excluded. Demographic, clinical, and serological factors were compared between CAM patients with and without anti-TIF1g positivity. MSA was determined by commercial immunoblot assays. [Results] Among 567 IIM patients in the cohort, 94 patients had CAM. 83 patients were analyzed after excluding 11 patients for unavailable MSA. 42 patients (50.6%) were positive for anti-TIF1g, followed by negative MSA in 10 patients (24.4%), anti-SAE1 in 8 patients (19.5%) and non-Jo1 antisynthetase Ab (17.1%) in 7 patients. 45 cancers were detected upon cancer screening at IIM diagnosis. More nasopharyngeal cancer was observed in patients with anti-TIF1γ (16 vs 7, p=0.03) while breast cancer was less common (3 vs 8, p=0.097). No patient with anti-TIF1g CAM had colorectal cancer (0 vs 6, p=0.01). CAM patients positive for anti-TIF1g were more commonly male (47.6% vs 26.8%, p=0.05) and had dermatomyositis (76.2% vs 36.6%, p<0.001), while arthritis (2.4% vs 22.0%, p=0.006) and interstitial lung disease (0% vs 29.3%, p<0.001) were less common. There was a trend towards increased mortality in anti-TIF1g positive cancer patients (23 vs 14, p=0.059). [Conclusion] Distinct cancer patterns were observed with anti-TIF1g positivity. Vigilant screening for NPC should be considered in anti-TIF1g-positive patients from prevalent regions. The difference in cancer pattern might have pathogenic implications and warrants further study.

ICW38-2

The association between phosphatidylserine dependent antiprothrombin antibodies (aPS/PT) and clinical domain scores in the 2023 ACR/EULAR classification criteria for antiphospholipid syndrome

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Conflict of interest: None

[Objectives] Antiphospholipid syndrome (APS) is an acquired thrombophilia in the presence of antiphospholipid antibodies (aPL). The new 2023 ACR/EULAR APS classification criteria (2023 APS criteria) classify patients according to the six clinical and two laboratory domains. The clinical domains were established by the new criteria committee members using a questionnaire that was focused on the clinical manifestations related with aPLs. They weighted the likelihood of each item based on the results of the surveillance. In this study, we aimed to correlate each aPL to the clinical domain score described in the 2023 APS criteria. [Methods] This cross-sectional study comprised our 80 patients with thrombotic APS based on the 2006 Sapporo/Sydney classification criteria. Lupus anticoagulant (LA), serum anti-cardiolipin antibody (aCL IgG/IgM), anti-β2GPI antibody (aβ2GPI IgG/IgM), and anti-phosphatidylserine/prothrombin complex antibody (aPS/PT IgG/IgM) were measured and assessed for the relationship between clinical scores. The profiles of aPL and clinical characteristics of the patients were collected from medical reports. Triple positive aPL was defined as the presence of LA, aCL, and aβ2GPI. All patients were scored for the clinal domains of the 2023 APS criteria at the time of medical record check-up. [Results] The median clinical score of the patients was 4 (IQR: 3-6). The prevalence of aPL was as follows: LA 74 (93%), aCL 50 (63%), aβ2GPI 42 (53%), triple positive aPL 43 (53%) and aPS/PT 56 (70%). Patients with positive aPS/PT had significantly higher clinical scores compared to those without aPS/PT (median (IQR): 6 (4-8) vs 4 (3-6), p<0.0001). No significant associations were observed between clinical scores and other evaluated aPL. [Conclusion] In APS patients, the presence of aPS/PT is associated with higher clinical scores in the 2023 APS criteria, suggesting that aPS/PT feasibly contributes to the better recognition of APS.

ICW38-3

Enhanced senescence-associated secretory phenotype signature in active giant cell arteritis

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Conflict of interest: Yes

[Objectives] Giant cell arteritis (GCA) is an autoimmune vasculitis predominantly affecting the elderly. This study aimed to elucidate the characteristic transcriptome pattern of peripheral blood in patients with GCA, especially active disease. [Methods] Whole blood samples were collected from GCA patients and age/sex-matched healthy controls (HC), and RNA-sequencing was performed. The subjects were categorized into three groups: GCA at initial onset/relapse (GCA_I/R), GCA in a stable state (GCA_S), and HC. Gene Set Enrichment Analysis (GSEA) was conducted to comprehensively assess the upregulation or downregulation of biological pathways in each group. Gene Set Variation Analysis (GSVA) was also employed to calculate and compare the signature score of each pathway across the three groups. By deconvolution, the proportion of each immune cell type was estimated. [Results] Samples of 32 GCA (7 GCA_I/R and 25 GCA_S) and 14 age/sex-matched HC were analyzed. GSEA and GSVA revealed that the E2F targets gene signature was significantly lower in GCA_I/R compared to GCA_S or HC (p<0.05). In contrast, the inflammatory response gene signature was significantly elevated in GCA_I/R, com-

pared to GCA_S or HC. Notably, the senescence-associated secretory phenotype (SASP) gene signature, including genes such as *MMP9* and *PLAUR*, was highest in GCA_I/R, compared to GCA_S and HC. The SASP signature negatively correlated with the E2F targets gene signature (ρ= -0.654, p=1.65×10^{-5}). Deconvolution analysis revealed that the estimated proportions of $CD16^+$ monocytes and neutrophils were significantly higher in GCA_I/R and positively correlated with SASP gene signature. [Conclusion] Senescent cells often secrete pro-inflammatory factors, known as the SASP, which are associated with aging-related inflammatory conditions. Active GCA exhibited an enhanced SASP, which may contribute to the pathogenesis of GCA and represent a potential novel therapeutic target.

ICW38-4

Unremarkable nailfold capillary abnormalities at baseline predict a poor prognosis in patients with anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objectives] Anti-MDA5 antibody-positive dermatomyositis (MDA5-DM) is known to be associated with interstitial pneumonia and has a poor prognosis. Methods to distinguish between good and poor prognosis groups need to be developed. In a previous report, we reported that the NVC score, which is calculated by evaluating nailfold capillary abnormalities, is inversely correlated with MDA5 antibody titers. The purpose of this study was to re-examine the results by adding additional cases and to clarify whether the same results can be obtained and whether the NVC score is associated with prognosis. [Methods] This study included patients who visited Hiroshima University Hospital between April 2018 and May 2024 and were diagnosed with MDA5-DM. Among these, patients who underwent nailfold video-capillaroscopy (NVC, Optipix capillaroscopy) at baseline and were treated with glucocorticoids and immunosuppressants were included (including previously reported cases). NVC scores are the sum of the scores for the eight fingers, which were calculated on a nine-point scale, including the sum of the enlarged capillaries, giant capillaries, and hemorrhages. [Results] 22 patients were enrolled in this study. 12 were female (54.5%). The mean age was 55.0±12.5 (S.D.). 18 patients (81.8%) survived to discharge. The mean MDA-5 antibody titer was 2522±1671 (S.D.), and the mean NVC score was 21.9±12.7 (S.D.). There was an inverse correlation between MDA5 antibody titer and NVC (R^2=0.50, p=0.0002). The median NVC score for survivors was 24.5 (IQR: 13.25-32.5), while the median score for deceased patients was 11 (1-16). The NVC score was significantly higher in survivors (Wilcoxon signed-rank test p=0.04). [Conclusion] There was an inverse correlation between NVC score and MDA5 antibody titer at diagnosis, with more deaths in patients with low NVC scores and no deaths in patients with high NVC scores.

ICW38-5

Exploring effect of yoga and standard therapy on corticomotor functions and pain relief in fibromyalgia patients: A Randomized Controlled Trial

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Conflict of interest: None

Background & Objectives: Fibromyalgia is a chronic widespread musculoskeletal pain syndrome which has no permanent cure till date. Patients besides excruciating pain, suffer from severe fatigue, morning stiffness, sleep problems and brain fogging. We aimed to study the effect of yoga therapy on pain status and corticomotor function in fibromyalgia patients. Methods: We have recruited 107 fibromyalgia patients in the randomized controlled trial with yoga therapy and standard therapy groups. Pain assessment using Visual Analogue Scale score, Pain Catastrophizing Scale and quantitative sensory testing was done. Quality of life (QoL) was assessed using WHO-QoL questionnaire. Musculoskeletal activity was assessed using sit and reach box. Corticomotor function was recorded using Transcranial Magnetic Stimulation. Glutamate and cortisol levels were also estimated using ELISA. Results: We have found a significant reduction in the pain on both objective and descriptive outcomes in yoga therapy arm as compared to the standard therapy arm. A significant increase in the pressure pain thresholds of fibromyalgia patients after yoga therapy was reported. Quality of life of the patients allocated to receive yoga therapy had also improved significantly. Musculoskeletal performance assessed for forward flexion and range of motion were improved post yoga. Standard therapy group didn't show any significant change. Corticomotor parameters, like resting motor threshold and motor evoked potential showed significant change from the baseline only after yoga therapy. We have also found a significant change in the serum level of glutamate in yoga group after intervention. Conclusion: Yoga therapy can improve pain and quality of life of fibromyalgia patients. It can also help patients in ameliorating corticomotor functions and brain excitability.

ICW39-1

Two-decade trends in clinical remission rates among rheumatoid arthritis (RA) patients treated with molecular targeted therapies: Insights from the FIRST registry

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Conflict of interest: Yes

[Objective] To evaluate the changes over time in the effectiveness of b/tsDMARDs for treating RA. [Methods] In our RA registry (FIRST registry), we analyzed the proportion of RA patients achieving CDAI remission one year after starting b/tsDMARDs in Phase II of the EULAR recommendations. [Results] Since the approval of the first TNF inhibitor in Japan in 2003, 2916 RA patients naive to b/tsDMARDs were included. Over the years, patient backgrounds had shifted, with increasing age and shorter disease duration. The remission rate in 2005 was 16.3%, which rose to 27.1% by 2009 and further to 31.2% in 2011. This upward trend continued to 2013, reaching a peak of 39.9%. However, from 2015, the remission rates stabilized at around 37.2% and 35.6%, followed by a decline to 28.7% starting in 2021. Multivariate analysis highlighted higher MTX doses and absence of glucocorticoids as predictive of remission, along with a lower initial CDAI. Additionally, JAK inhibitors were more effective than other b/tsDMARDs. Annual analysis of these factors in patient backgrounds showed that in 2005, the average dose of MTX was low at 6.9 mg/w, with a high rate of concomitant glucocorticoid use at 48.8%. By 2013, the MTX dose had increased to 12.9 mg/w, and the rate of concomitant glucocorticoid use had decreased to 23.5%, while concomitant MTX use peaked at 84.0%. However, by 2021, the MTX dose decreased to 12.0 mg /w, and the rate of concomitant MTX use also declined to 71.6%. Disease activity at the start of treatment was high in 2005 with a CDAI of 33.6 but decreased by 2013 to a CDAI of 24.8. Regarding b/tsDMARDs, the introduction of IL-6 inhibitors in 2008, CTLA4-Ig in 2010, and JAK inhibitors in 2013 corresponded with improved remission rates. Post-2020, however, the use of JAK inhibitors diminished, likely influencing the drop in remission rates observed. [Conclusions] Optimizing MTX use remains essential, alongside the discovery of new molecular targets to address unmet needs in treatment.

ICW39-2

Mortality and Medical Utilization in Rheumatoid Arthritis Associated Interstitial Lung Disease: A Real-World, Large-Scale Retrospective Study Comparing Tocilizumab and Rituximab

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Conflict of interest: None

[Objectives] To investigate the mortality and medical utilizations in patients with rheumatoid arthritis associated interstitial lung disease (RA-ILD) receiving tocilizumab compared to rituximab. [Methods] A retrospective cohort study was conducted using the TriNetX database within the US collaborative network, covering the period from January 2011 to June 2024. The study included the patients diagnosed with RA-ILD and who received new prescription for tocilizumab or rituximab. The primary outcome was all-cause mortality, while secondary outcomes included hospitalization, high oxygen demand, and respiratory failure. Hazard ratios (HRs) and Cox regression analyses were employed to evaluate these outcomes. [Results] Out of 50,746 RA-ILD patients, 1,058 patients were selected per treatment cohort (tocilizumab and rituximab). Tocilizumab demonstrated a comparable risk of all-cause mortality to rituximab (HR 0.853, 95% CI: 0.705-1.031). For secondary outcomes, the tocilizumab cohort demonstrated a lower risk of hospitalization (HR 0.837 95% CI: 0.736-0.952) and respiratory failure (HR 0.814 95% CI: 0.697-0.950) than the rituximab cohort. The subgroup analyses exhibited consistent results for patients treated within 18 months of RA-ILD diagnosis. [Conclusion] This study highlights that both tocilizumab and rituximab present similar mortality risks in RA-ILD patients, with tocilizumab potentially reducing hospitalization and respiratory failure risks. These findings highlight the importance of individualized treatment considerations for RA-ILD in clinical practice.

ICW39-3

Comparable Improvement in Work Productivity in Patients with Rheumatoid Arthritis Treated with Reduced Dose or Maximum Tolerated Dose of Methotrexate in combination with Adalimumab: analysis of subpopulation from the MIRACLE trial

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Conflict of interest: Yes

[Objectives] This study aims to compare the improvement in work productivity between maximum tolerated dose or reduced dose of methotrexate in combination of adalimumab. [Methods] Patients who visited Keio University Hospital and participated in the MIRACLE trial were included in the analyses. Work productivity was assessed with the work productivity and activity impairment (WPAI) questionnaire. The improvement in WPAI was compared between the reduced dose or maximum tolerated dose of methotrexate groups. [Results] A total of 61 patients were included in the analysis. The mean age was 59.7±17.3 years and 80.3% were female. All patients were treated with methotrexate monotherapy during the first 24 weeks. After 24 weeks, patients who achieved remission continued maximum tolerated dose until week 48 (ARM-1, N=24), and patients who did not achieve remission were randomized to the continued methotrexate dose group (ARM-2, N=13) or reduced methotrexate dose group (ARM-3, N=13), with an initiation of adalimumab. At baseline, 57% were employed, and work time missed due to RA (absenteeism) was 14.2% and impairment at work (presenteeism) was 41.2%. At week 24, absenteeism became almost none, while presenteeism was still 22.1%. Patients who did not achieve remission at week 24 had higher impairment of presenteeism at week 24 compared to those who achieved remission at week 24 (42.7% vs 8.1%, P=0.001). After week 24, presenteeism continued to improve, and ARM-2 and ARM-3 showed comparable improvement (22.5% vs 16.0% at week 48, P=0.69). In all patients irrespective of working status, activity impairment improved from 48.0% at baseline to 12.3% at week 48. The improvement in activity impairment was also comparable in ARM-2 and ARM-3. [Conclusion] Work productivity was impaired in patients with active RA. Reduced dose of methotrexate with concomitant adalimumab contributed comparable improvement in work productivity to continued dose.

ICW39-4

Selection of the Optimal Treatment for Interstitial Lung Disease Associated with Rheumatoid Arthritis from the FIRST Registry

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Conflict of interest: None

[Objectives] This study aimed to clarify the efficacy and safety of biologic disease-modifying antirheumatic drugs (bDMARDs) for interstitial lung disease associated with rheumatoid arthritis (RA-ILD) in a real-world clinical setting. [Methods] Patients with RA-ILD diagnosed at our hospital who required therapeutic intervention due to worsening of ILD in respiratory symptoms or radiological findings before induction of conventional synthetic DMARDs (csDMARDs) or bDMARDs were enrolled (csDMARDs n=40, bDMARDs n=135). The rates of acute exacerbations of ILD (AE-ILD), pulmonary function test (PFT), computed tomography (CT) scores (quantitative scoring by two radiologists), and adverse events at 52 weeks were compared using the inverse probability of treatment weighting with propensity score (PS-IPTW). [Results] After adjustment for PS-IPTW, patient background showed no significant difference. The rate of AE-ILD was higher in the csDMARDs group (13.0% vs. 2.1%, p= 0.003). PFT and CT scores worsened at 52 weeks in the csDMARDs group ($p<0.001$), but not in the bDMARDs group. The incidence of infection was higher in the bDMARDs group (p=0.012). Among the bDMARDs groups (TNF inhibitor [TNFi n=35], Cytotoxic T-lymphocyte Antigen-4 Immunoglobulin [CTLA4-Ig n=45], IL-6 receptor inhibitor [IL-6Ri n=55]), PFT worsened in the TNFi group ($p<0.001$), remained unchanged in the CTLA4-Ig group, and improved in the IL-6Ri group at 52 weeks ($p<0.001$). The factor associated with worsening forced vital capacity (FVC) was identified as usual interstitial pneumonia (UIP) pattern in multivariate analysis, and FVC improvement rate in patients with UIP was higher in the IL-6Ri group (p=0.017). The incidence of all adverse events was lower in the CTLA4-Ig group (p=0.044). [Conclusion] CTLA4-Ig and IL-6Ri were more effective in patients with RA-ILD. IL-6Ri showed greater efficacy than other bDMARDs for patients with UIP, whereas CTLA4-Ig may be more suitable for those at high risk of adverse events.

ICW39-5

Impact of interstitial lung disease on drug retention of biologics in patients with rheumatoid arthritis -data from the IORRA cohort

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Conflict of interest: Yes

[Objectives] We investigated the impact of interstitial lung disease (ILD) on drug retention of biologic disease-modifying antirheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA) using a large-scale, real-world registry in Japan. [Methods] This study included patients with RA who were enrolled in the IORRA cohort and initiated bDMARDs between 2003 and 2020. Patients without chest computed to-

mography (CT) data were excluded. The index month was the month of the first bDMARD prescription after IORRA enrollment. Baseline was determined by the IORRA survey prior to the index month. Reasons for drug discontinuation were classified into ineffectiveness, adverse drug reactions (ADR), non-ADR, and remission. Overall drug retention included discontinuations due to ineffectiveness and ADR. Retention rates at 12 months were calculated using the Kaplan-Meier method, and hazard ratios (HRs) were calculated using the Cox proportional hazards model adjusted for baseline confounders (age, sex, disease duration, seropositivity, methotrexate [MTX], and glucocorticoid [GC]). [Results] A total of 906 patients were included; 151 (16.7%) had ILD. At baseline, the mean age was 53.4 years, 804 patients (88.8%) were female, and the mean disease duration was 10.1 years. Patients with ILD were older, had a higher proportion of seropositivity, higher GC use, and lower MTX use compared to those without ILD. The overall drug retention rates were 76.3% for ILD and 84.4% for non-ILD. Reasons for discontinuation were ineffectiveness (n=67), ADR (n=85), non-ADR (n=24), and remission (n=3). Discontinuation rates due to ineffectiveness were 11.7% (ILD) vs. 7.3% (non-ILD), and due to ADR were 13.5% (ILD) vs. 9.0% (non-ILD). Adjusted HRs (95% CI) of drug discontinuation associated with ILD were 1.56 (1.02, 2.37) for overall, 1.81 (0.95, 3.45) for ineffectiveness, and 1.40 (0.80, 2.44) for ADR. [Conclusion] ILD was associated with lower drug retention of bDMARDs in patients with RA.

Workshop

W1-1

Analysis of Risk Factors for Exacerbation in Patients with Rheumatoid Arthritis and Interstitial Pneumonia

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Conflict of interest: None

[Objectives] Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) has a poor prognosis, with factors like methotrexate (MTX) use thought to impact RA-ILD exacerbation, though these remain debated. This study examines RA-ILD patients at our institution to identify new risk factors for ILD exacerbation. [Methods] A retrospective analysis was conducted on 126 RA-ILD patients with records and chest CTs between April 2012 and July 2024. Exacerbation was defined as requiring hospitalization and steroids > 0.5 mg/kg of prednisolone. [Results] The cohort (mean age 68.8, 66 male) had 22 patients with exacerbations. Multivariate analysis showed no significant exacerbation risk for age (p=0.51), male gender (p=0.059), or smoking (p=0.22). However, a UIP pattern (p=0.038) and RF positivity (p=0.029) were significant. MTX use was not linked to exacerbation (p=0.15), while non-exacerbated patients more commonly used sulfasalazine (SASP) (p=0.0010). [Conclusion] MTX use was not associated with higher exacerbation rates, while SASP use correlated with lower exacerbation rates in RA-ILD patients at our institution.

W1-2

A Study on the Prognosis of Rheumatoid Arthritis Patients with Bronchiectasis

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) can coexist with bronchiectasis (BE), complicating treatment due to infection risks. It is unclear whether patients with RA-associated BE (RA-BE) have a worse prognosis than those with non-RA BE. This study analyzes the prognosis of RA-BE patients compared to non-RA BE patients at our hospital. [Methods] A retrospective study was conducted on 763 BE patients followed for at least six months who underwent chest CT between January 2012 and August 2023. RA patients were defined as those receiving at least one DMARDs or steroid. Exacerbation was defined as a worsening of respiratory symptoms requiring a treatment change. [Results] We identified 731 non-RA BE patients and 32 RA-BE patients. No significant differences were found in age at BE diagnosis, gender, BMI, smoking rates, or macrolide use. Exacerbation rates within three years were 31.9% for non-RA BE and 36.5% for RA-BE, with no significant difference (p=0.47). In multivariate analysis, no significant differences were found for gender, age, or medication use; however, smoking rate (p=0.015) and cavitary lesions (p=0.055) were linked to increased risk of exacerbation. [Conclusion] In our hospital, there was no significant difference in exacerbation rates between RA-BE and non-RA BE patients.

W1-3

Efficacy of Tocilizumab for acute respiratory distress syndrome associated with connective tissue disease

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Conflict of interest: None

[Objectives] Acute respiratory distress syndrome (ARDS) associated with connective tissue disease (CTD-ARDS) is a critical organ lesion with no established treatment. This study aimed to analyze the prognostic fac-

tors of CTD-ARDS and clarify the efficacy of molecular targeted therapies for CTD-ARDS. [Methods] We enrolled CTD-ARDS patients in our institute diagnosed between 2019 and 2023. Prognostic factors were explored using the Cox proportional hazards models. The observation period was set until August 2024 and death was defined as the event. [Results] Twelve CTD-ARDS patients (8 females, 67%) including 4 (33%) with rheumatoid arthritis (RA). Age was 74 [65-79] years (median [interquartile range]), KL-6 was 1645 [644-4110] U/mL. High-dose glucocorticoid (GC) was administered in 11 patients (92%) and tocilizumab (TCZ) in 5 patients (42%). In univariate analysis, TCZ treatment significantly reduced the risk of death (HR: 0.44, 95%CI: 0.17-0.93, p=0.029). Similar results were observed in multivariate analysis, including factors such as age, sex, ARDS disease activity, and RA diagnosis (HR: 0.33, 95% CI: 0.11-0.82, p=0.015). [Conclusion] Our study showed that tocilizumab treatment may improve the prognosis of CTD-ARDS, regardless of age, ARDS disease activity, or type of CTD.

W1-4

Predictive Factors of Worsening in Interstitial Lung Disease Associated with Connective Tissue Disease Treated by Nintedanib

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Conflict of interest: None

[Objective] Nintedanib (NTB), an anti-fibrotic agent, has become available for the treatment of connective tissue disease-associated interstitial lung disease (CTD-ILD). This study aimed to analyze the clinical course of CTD-ILD during NTB treatment and identify predictive factors of CTD-ILD worsening. [Methods] CTD-ILD who started NTB treatment between 2022 and 2023 in our institute were enrolled. ILD worsening was defined as a ≧10% decline in %VC and predictive factors were explored using logistic regression analysis. [Results] We enrolled 22 CTD-ILD including 16 females (76%), with a mean age of 58 [50, 74] years old. (median [interquartile range]) 12 patients (57%) exhibited a UIP pattern and 11 patients (52%) had systemic sclerosis (SSc). At the time of NTB initiation, %VC was 71 [60, 78] % and KL-6 was 879 [491, 1270] U/mL. In multivariate analysis, baseline %VC was identified as a significant predictive factor of CTD-ILD worsening (OR 1.18, 95%CI 1.01-1.58, p=0.031). With a cutoff value of 74.5% (AUC: 0.923) for the two-group comparison, only the group with %VC ≦74.5% showed ILD worsening (0% vs. 75%). [Conclusion] In the clinical course of CTD-ILD, initiating NTB when %VC is maintained at or above 75% may reduce the risk of CTD-ILD worsening.

W1-5

Long-term Prognosis of Pulmonary Arterial Hypertension Associated with Connective Tissue Disease Treated with Combination Therapy of Pulmonary Arterial Hypertension Specific Drugs

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Conflict of interest: Yes

[Objectives] Pulmonary arterial hypertension associated with connective tissue disease (CTD-PAH) has shown improved survival with the combination of PAH specific drugs. We aimed to clarify the long-term prognosis of CTD-PAH based on the numbers of PAH specific drugs administered. [Methods] CTD-PAH diagnosed between 1976 and 2023 in our institute were enrolled. Based on the number of PAH specific drugs administered, CTD-PAH were categorized into four groups: untreated, monotherapy, dual-therapy, and triple-therapy. Long-term survival was compared among groups using the Kaplan-Meier curve. [Results] We enrolled 139 CTD-PAH including 124 females, with age of 52 [39, 62] years old. CTD-PAH included 68 patients with SSc and 48 with SLE/MCTD. PVR was 4.9 [3.3, 8.6] WU, and the WHO Fc was I/II in 75, III in 44, and IV in 16. CTD-PAH were divided as follows: untreated, 38; monotherapy, 74; dual-therapy, 17; and triple-therapy, 10. There was a significant difference in survival among groups (p=0.039). The survival rates (3-year, 10-year, 20-year) were better in the triple-therapy (100%, 85%, 50%) compared to the dual-therapy (85%, 60%, 35%). [Conclusion] PAH specific drugs improve long-term survival in CTD-PAH. Moreover, for short-term outcomes, triple therapy appears to be an effective option.

W1-6

The Benefit of Intensive Screening for Malignancies in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Purpose] Malignancies are a leading cause of death in rheumatoid arthritis (RA) patients. This study aimed to clarify the usefulness of intensive malignancy screening when initiating molecular-targeted therapies (b/tsDMARDs) in RA patients. [Methods] We enrolled RA patients visited our institute between 2019 and 2023. We compared outcomes between the routine screening (RS) group, received symptom-based examinations, and the intensive screening (IS) group, underwent neck-pelvic CT, high-resolution lung CT, and fecal occult blood tests (FOBT) when initiating b/ts DMARDs. Tumor staging followed the TNM classification. [Results] Among 4614 RA patients, 4466 were in the RS group and 148 in the IS group. New malignancies were detected in 71 RS group patients (1.6%) and 6 IS group patients (4.1%), with the IS group showing a significantly higher diagnosis rate (p=0.04). In the RS group, 34% were diagnosed at Stage IV, resulting in 12 malignancy-related deaths. In contrast, the IS group had no Stage IV diagnoses or deaths. The IS group's malignancies included 2 colorectal cancer cases and 2 lymphoma cases, suggesting a utility for neck-pelvic CT and FOBT. [Conclusion] The IS when initiating of b/tsDMARDs in RA patients may contribute to early cancer detection and improved survival outcomes.

W2-1

Safety and Efficacy of Subcutaneous Ianalumab (VAY736) for up to 68 Weeks in Patients with Systemic Lupus Erythematosus: Results from Phase 2 Study (Encore presentation)

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Conflict of interest: Yes

[Objectives] Ianalumab is a fully human IgG1 monoclonal antibody with a dual mechanism of enhanced B-cell depletion (ADCC) and BAFF-R blockade. This multi-center, randomized, parallel-group phase 2 trial. [Methods] Patients were randomly assigned in a 1:1 ratio to receive either ianalumab 300 mg q4W or placebo, open-label period where all patients received ianalumab until W52. Follow-up assessments were conducted until W68. The primary endpoint was the proportion of patients achieving GC reduction and SRI-4 at W28. The secondary endpoint was the GC+SRI-4 response rate at W52. [Results] Overall, 67 patients were enrolled. At W28, the proportion of patients achieving the SRI-4+GC response was 44.1% for those treated with ianalumab and 9.1% for those receiving placebo. At W52, the response rates were 45.5% for patients switching from ianalumab to ianalumab and 40.6% for those switching from placebo to ianalumab. Longer exposure to ianalumab or placebo resulted in further improvements in BILAG flare, SRI-6, SRI-8, DORIS, LLDAS, and serum levels of complement and autoantibodies. There were no unexpected or new safety concerns during the follow-up period at W68. [Conclusion] Ianalumab was well-tolerated, and data suggests longer exposure up to 1 year provides further benefits in patients with active SLE.

W2-2

Long-term effects of tacrolimus and mycophenolate mofetil on renal function in patients with SLE -A study using ANSWER-SLE cohort-

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Conflict of interest: Yes

[Objective] To clarify the long-term effects of tacrolimus (TAC) and mycophenolate mofetil (MMF) on renal function in SLE patients. [Methods] Renal function (eGFR, serum Cre, and their change ratio) was retrospectively examined 12 and 24 months after the start of observation in SLE patients who received TAC or MMF. [Results] At the start of observation, renal function was lower in the MMF group compared to the TAC group (TAC group/MMF group; eGFR 82.7/78.4: p=0.0235, serum Cre 0.74/0.85: p=0.0002). The change ratio in serum Cre at 24 months was higher in the TAC group than in the MMF group (0.0618/0.0307: p=0.0443). Further analysis was performed using eGFR 60 at the start of observation as the cut-off value. In patients with eGFR<60, renal function at the start of observation was lower in the MMF group than in the TAC group (eGFR 45.5/40.6: p=0.0017, serum Cre 1.28/1.60: p=0.0001) unlike patients with eGFR>60. The change ratio in eGFR was lower in the TAC group than in the MMF group (0.0558/0.1389: p=0.0411), and the change ratio in serum Cre was lower in the TAC group than in the MMF group (-0.0767/0.0054: p=0.0391). [Conclusion] In SLE patients, especially those with impaired renal function, MMF may have a better long-term effect of renal protection than TAC.

W2-3

Long-term Efficacy and Safety of Cyclophosphamide and Tacrolimus Combination Therapy for Lupus Nephritis as remission induction therapy

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Conflict of interest: None

[Objective] To investigate the long-term efficacy and safety of pulsed cyclophosphamide (pCYC) and tacrolimus (TAC) for lupus nephritis (LN) as remission induction therapy. [Methods] We retrospectively examined patients treated with pCYC or pCYC+TAC or mycophenolate mofetil (MMF) in addition to prednisolone (PSL) escalation following three years. Complete remission (CR) was defined as a urine protein/creatinine (Cr) ratio of less than 0.5 g/gCr, normalization of serum Cr (sCr), or an increase in sCr within 10% of the pretreatment value, and no further PSL escalation. Histology, ISN/RPS 2003; and LOCF as missing values. [Results] 100 cases were in the following groups: 1) pCYC (41), 2) pCYC+TAC (29), and 3) MMF (30, including with TAC): Age, 40 (30-49) years; male: female, 15:85; disease duration, 4.4 (0.5-126.4) months; sCr, 0.77 (0.63-1.07) mg/dl; proteinuria, 2.68 (1.2-5.5) g/gCr. Class III 24 (mixed 7); IV, 66 (22); V, 3; unknown, 7; the initial PSL, 0.98 (0.87-1.05) mg/kg. CR at 2/3 years was 57.5%/52.5% for group 1), 87.1%/80.7% for group 2), and 66.7%/73.3% for group 3), p<0.05, Kruskal-Wallis test, respectively. There were no significant signals as adverse events. [Conclusion] pCYC +TAC showed a higher remission rate than pCYC or MMF, and tolerability even in the long term.

W2-4

Clinical efficacy and patient-reported outcomes (PROs) in anti-Ro/Sjögren's Syndrome-Related Antigen A (SSA) antibody-positive (+) patients (pts) with active systemic lupus erythematosus (SLE) treated with deucravacitinib, a first-in-class, oral, selective, allosteric tyrosine kinase 2 inhibitor, in the phase 2 PAISLEY trial (Encore presentation)

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Conflict of interest: Yes

[Objectives] This subgroup analysis of the phase 2 PAISLEY trial (NCT03252587) assessed efficacy and PROs with deucravacitinib in anti-Ro/SSA+ pts with SLE. [Methods] Pts who were anti-Ro/SSA+ at baseline were included in this post hoc analysis (placebo [PBO], n=48; deucravacitinib 3 mg BID, n=52; 6 mg BID, n=46; 12 mg QD, n=42). Clinical outcomes of SRI (4) and BICLA and PROs for pain and fatigue were assessed at wk 48. [Results] Response rates with deucravacitinib (3 mg BID, 6 mg BID, 12 mg QD) were increased vs PBO for SRI (4) (65.4%, 43.5%, 54.8% vs 33.3%, respectively) and BICLA (51.9%, 32.6%, 42.9% vs 25.0%); mean pain and fatigue scores were improved with deucravacitinib vs PBO (change from day 1: pain, -1.8, -2.0, -2.7 vs -1.1; fatigue, -5.6, -6.2, -8.3 vs -3.5). Pts receiving deucravacitinib had numerical improvements in mean pain and fatigue scores at wk 48 vs PBO, and more pts reported score improvements greater than or equal to the respective minimal clinically important differences. [Conclusion] Improvements in efficacy and PROs with deucravacitinib vs PBO in anti-Ro/SSA+ pts with active SLE were consistent with the overall PAISLEY population. Given the similarities between Sjögren's disease (SjD) and SLE, these findings warrant investigation of deucravacitinib in SjD.

W2-5

Deconvolution of transcriptomics changes in patients treated with deucravacitinib, a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor, reveals novel mechanistic effects of TYK2 inhibition in systemic lupus erythematosus (SLE) (Encore presentation)

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Conflict of interest: Yes

[Objectives] In this study, gene set enrichment and cellular deconvolution analyses were performed on RNA-sequencing data from patients with SLE treated in the PAISLEY trial (NCT03252587). [Methods] Linear mixed-effects models for Differential Expression for Repeated Measures in R were used for pharmacodynamic and differential gene expression analyses. Single-sample gene set enrichment analysis (ssGSEA) was performed using public predefined gene modules from MSigDB Hallmark and BloodGen3. xCell was used to digitally portray the blood cellular heterogeneity landscape. [Results] Compared to placebo, 73, 122, and 392 genes were differentially modulated by deucravacitinib 3-mg twice-daily (BID), 6-mg BID, and 12-mg once-daily groups, respectively, at week 32 (adjusted $P < 0.05$). ssGSEA and cellular deconvolution identified SLE-relevant gene sets modulated by deucravacitinib, including interferon-regulated genes. Gene sets representing naive and memory B lymphocytes were increased, while plasma cell modules were reduced. Deconvolution revealed normalization of dendritic cell populations and increased regulatory T-cell gene sets with deucravacitinib. [Conclusion] RNA sequencing revealed expected and novel gene expression changes in patients with SLE treated with deucravacitinib.

W2-6

Safety, Biomarker Response, and Efficacy of E6742, a Dual Antagonist of Toll-Like Receptor 7 and 8, in a First-in-Patient, Randomized, Double-Blind, Phase1/2 Study in Systemic Lupus Erythematosus (Encore presentation)

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Conflict of interest: Yes

[Objectives] The safety, pharmacokinetics (PK), biomarker response, and efficacy of E6742, a novel small molecular with selective TLR7/8 dual antagonist, were assessed in this Phase 1/2, randomized, double-blind, placebo-controlled study in SLE (NCT05278663). [Methods] Active SLE patients received E6742 100 mg, 200 mg or placebo twice daily for 12 weeks. [Results] A total of 12 patients (8 for E6742 100 mg, 4 for placebo) were enrolled in the cohort 1 and subsequently 14 patients (9 for E6742 200 mg, 5 for placebo) were enrolled in the cohort 2. E6742 demonstrated a favorable safety profile and was well tolerated. After oral administration, plasma concentrations of E6742 increased in dose dependent manner. The interferon gene signature (IGS) and production of proinflammatory cytokines after ex-vivo challenge with a TLR 7/8 agonist were decreased by E6742 treatment. Dose-dependent improvements in the British Isles Lupus Assessment Group-based Composite Lupus Assessment response were observed at Week 12 in the E6742 (37.5% for 100 mg; 57.1% for 200 mg) and placebo (33.3%) groups. [Conclusion] E6742 had a favorable safety profile and was well tolerated, with IGS responses, proinflammatory cytokines responses and sufficient efficacy signals in patients with SLE.

W3-1

Identification of factors associated with belimumab retention in systemic lupus erythematosus: The ANSWER-SLE Cohort Study

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Conflict of interest: None

[Objectives] Approved in Japan in 2017 for systemic lupus erythematosus (SLE), belimumab (BLM) has limited real-world data on its retention and safety. This study evaluates BLM retention in SLE patients and identifies factors influencing its persistence. [Methods] Data from 354 SLE patients who initiated BLM between April 2017 and December 2023 were analyzed. Baseline data included age, sex, disease duration, organ complications, anti-dsDNA/anti-Sm antibody positivity, hypocomplementemia, glucocorticoid dose, immunosuppressant co-use, SLEDAI, and SLE Damage Index. BLM retention rates at 1 and 5 years were assessed. [Results] Median age was 43 years (33-52); median disease duration was 12 years (4-19), and 88.4% were female. The average glucocorticoid dose dropped from 9.3 mg/day to 6.5 mg/day after one year. The mean SLEDAI score declined from 6.4 to 3.8. BLM retention rates were 88% in 1 year and 74% at 5 years. Lupus nephritis (LN) was associated with a higher 5-year retention rate (94% vs. 69%, P=0.004) and remained a significant factor after age and sex adjustment (HR=0.25, 95% CI: 0.09-0.69). [Conclusion] Higher BLM retention in SLE cases with LN suggests LN as a key factor for BLM persistence.

W3-2

Evaluation of the Rate of Achievement of Glucocorticoid Discontinuation in Patients with Systemic Lupus Erythematosus Concomitant with Belimumab and Investigation of Predictive Factors

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Conflict of interest: None

Objective: To identify predictors of achieving GC discontinuation (GC free) in systemic lupus erythematosus (SLE) patients treated with belimumab (BEL). Methods: SLE patients treated with BEL for at least 1-year were included. We collected clinical information retrospectively up to the 5 years. In patients who achieved GC free, clinical characteristics at the time of BEL initiation and factors contributing to GC free achievement by Cox proportional hazard model were analyzed. Results: After 37.5 [12-60] (median [range]) months of observation, 38 of 142 patients (26.8%) achieved GC free, and the time to GC free was 16.5 [2-53] months. Patients who achieved GC free had significantly higher rate of combined HCQ (84.2% vs 65.4%, P=0.037) and arthritis (36.8% vs 16.4%, P=0.009). In multivariate analysis, the combined HCQ (hazard ratio (HR) 2.682, 95% confidence interval (CI) 1.107-6.498, P=0.029) and presence of arthritis (HR 2.240, 95%CI 1.151-4.358, P=0.018) was significantly associated with achieving GC free. Conclusions: The combined HCQ and presence of arthritis was a factor for achieving GC free. These results, together with the benefit of the HCQ combination in patients with BEL, suggest that BAFF hyperactivity may be related to the pathogenesis of arthritis in SLE.

W3-3

Treatment with Belimumab in Patients with Systemic Lupus Erythematosus: A Single-Center Observational Study

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Conflict of interest: None

[Objectives] We aimed to investigate the use of belimumab in patients with systemic lupus erythematosus (SLE). [Methods] The clinical data of consecutive patients with SLE who were newly treated with belimumab from 2018 to 2024 at our institution were retrospectively reviewed. [Results] 41 consecutive SLE patients who received belimumab were investigated. 37 patients (90%) were female, the age at the time of belimumab initiation was 17-68 years (median 42 years), the disease duration was 0-37 years (median 16 years), and the dosage of prednisolone (PSL)-equivalent glucocorticoid (GC) was 4-30 mg/day (median 10 mg/day). Hydroxychloroquine and immunosuppressants were used concomitantly in 24 (59%) and 35 patients (85%). The formulation of belimumab was intravenous drip in 11 patients and switched to subcutaneous injection in 7 patients. 14 patients (34%) discontinued belimumab, and 3 patients discontinued after only one infusion. 11 patients discontinued after receiving a second infusion or later, and the treatment period was 0-46 months. After initiating belimumab, the PSL-equivalent GC dosage was reduced in 30 patients (85%) by a median of 5 mg. [Conclusion] Belimumab was well tolerated, and the GC dosage was reduced in the majority of patients who continued to receive the drug.

W3-4

A survey of the use of belimumab for lupus nephritis and the factors influencing the renal outcomes

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Conflict of interest: None

[Objectives and Methods] In clinical practice, belimumab (BEL) is being used in combination with the standard of care for patients with mild lupus nephritis (LN) that does not meet the inclusion criteria of the BLISS-LN trial. In this study, we investigated the relationship between background characteristics at the start of BEL and renal outcomes in LN patients who had received belimumab treatment, regardless of the severity or duration since the onset of LN. [Results] A total of 28 patients with LN who were treated at our hospital, had a urine protein >150 mg/gCr at the start of BEL, and were followed for one year were included in the study. There was no significant difference in the major renal outcomes at 12 months whether baseline urine protein level was <1 g/gCr or not, nor in the duration from renal biopsy to the strat of BEL. In the group that achieved complete renal response at 12 months, there was a trend toward a higher estimated glomerular filtration rate and a higher proportion of patients without tacrolimus at baseline. [Conclusion] In LN patients receiving BEL at our institution, there was no significant difference in renal outcomes at 12 months based on the amount of urine protein at the start of BEL or the duration of LN.

W3-5

Safety and Steroid-sparing Effect of Belimumab in the Maintenance Therapy of SLE Patients

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Conflict of interest: None

[Objective] To assess the steroid-sparing effect and safety of belimumab (BLM) in maintenance therapy for SLE. [Methods] SLE patients from our department, meeting the 1997 ACR, 2012 SLICC, or 2019 EULAR/ACR criteria, were included. Maintenance therapy was defined as low-dose glucocorticoid (GC) (<0.2 mg/kg/day, prednisone equivalent) with a SELENA-SLEDAI score <10. Since March 2018, BLM was administered to 51 patients; 28 who completed 52 week-treatment were analyzed. The primary endpoint was GC-sparing effect at 52 weeks. Adverse events were assessed using CTCAE v5.0. [Results] The mean age was 49.0±15.2 years (27 females, 1 male). Mean disease duration was 173.1±127.6 months, with 1.1±0.8 immunosuppressive agents used on average. The continuation rate at 52 weeks was 92.9%. Two patients discontinued (pregnancy and depressive symptoms). Dairy GC dose decreased from 6.9 to 5.0 mg ($p<0.0001$). The SLEDAI score improved from 3.4 to 2.8 ($p=0.0382$). However, no significant changes were observed in CH50 (33.5 to 35.7 CH50/mL, $p=0.1291$), anti-dsDNA (33.0 to 22.8 IU/mL, $p=0.1417$), or the SLICC Damage Index (0.54 to 0.50, $p=0.3262$). No patient experienced a flare (SLEDAI≧4) or CTCAE grade ≧3 adverse events. [Conclusion] BLM as maintenance therapy for SLE reduced GC dose, but did not worsen.

W3-6

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 48, and 144 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 144 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 144 weeks. SLEDAI was

2.7±1.6 at discontinuation, 2.4±1.1 at 48 weeks, 1.0±1.1 at 144 weeks, maintaining a significant reduction when comparing BEL induction and 144 weeks (p<0. 05, ANOVA). The PSL dose was 4.1±2.5 mg at discontinuation to 3.0±1.2 mg 48 weeks to 1.7±1.1 mg at 144 weeks. PSL use remained significantly lower when comparing BEL induction to 144 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 144 weeks after discontinuation of BEL.

W4-1

Do the b/tsDMARDs increase weight and muscle mass in patients with rheumatoid arthritis from multicenter prospective observational PRESENT study?

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Conflict of interest: None

[Object] We examined how the b/tsDMARDs (B/TS) affect body composition in RA patients compared to the csDMARDs (CS). [Methods] Data from weeks 0 and 52 of the prospective observational study, (PRESENT study) were analyzed. Of the 200 patients requiring enhanced therapy (100 in each group), 160 patients (80 in each group) who were available for follow-up were included. Changes in disease activity, body composition, and muscle function were compared, and multivariate analysis was performed. [Results] The median age and disease duration of all RA was 70 years and 4.4 years, DAS28ESR at week 0 was 5.07 in B/TS group, significantly higher than 4.75 in CS group (p=0.001). After 52 weeks, both groups had significantly improved DAS28ESR. The mean change in body weight was 0.87 kg in B/TS group, significantly higher than -0.54 kg in CS group (p<0.001). The median change in muscle mass in B/TS group (0.35 kg) was higher than in CS group (-0.1 kg), a significant difference (p= 0.002). B/TS treatment (OR: 3.21), DAS28ESR (OR: 0.65), and muscle mass (OR: 0.90) were identified as independent factors affecting muscle mass gain. [Conclusions] The b/tsDMARDs significantly increased body weight and muscle mass compared to the csDMARDs. Tight control with the b/tsDMARDs is useful for gain muscle mass.

W4-2

Effectiveness of certolizumab pegol in patients with rheumatoid arthritis based on RF values

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Conflict of interest: None

[Objective] To examine effectiveness of certolizumab pegol (CZP) in patients with rheumatoid arthritis (RA) based on RF values. [Methods] A retrospective study was conducted on patients with RA who underwent CZP at our hospital from 2015 to 2024. Forty-four patients were classified into quartiles based on baseline RF levels. Background of the patients and disease activities were investigated from medical records. [Results] At baseline, ACPA titer in the RF1 group was significantly lower than the other three groups. Other patient demographics and disease characteristics were similar among the four groups. DAS28-CRP in the RF1-RF3 groups significantly decreased from baseline to 1 month (1M) - 6 months (6M): RF1 [0M: 5.33±0.93, 1M: 2.91±0.97, 3M: 2.97±1.18, 6M: 2.83±1.05, p=0.02612], RF2 [0M: 4. 82±1.86, 1M: 2.88±1.73, 3M: 3.66±1.52, 6M: 2.30±1.21, p=0.0255], RF3 [0M: 4.04±1.36, 1M: 2.56±0.78, 3M: 2.21± 0.63, 6M: 1.93±0.66, p=0.00202]. However, in the RF4 group [0M: 4.71± 1.40, 1M: 3.02±1.12, 3M: 2.92±1.18, 6M: 3.07±1.69, p=0.121], DAS28-CRP decreased but was not significant different. [Conclusions] TNF inhibitor without the Fc portion has been reported to be effective in patients with high RF titer. However, this study could not demonstrate effectiveness in the highest-titer group.

W4-3

Analysis of the Therapeutic Effects of Shortening Tocilizumab Treatment Interval and Switching to Sarilumab: The ANSWER Cohort Study

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Conflict of interest: None

[Objectives] To assess the effects of shortening the dosing interval of tocilizumab (TCZ) or switching from TCZ to sarilumab (SAR) in patients with rheumatoid arthritis (RA) using data from the ANSWER cohort. [Methods] Two groups of patients were analysed. The T1W group (n=98) had their TCZ interval shortened from every two weeks to weekly. The TSS group (n=66) included patients who were switched from TCZ to SAR. The primary endpoint was the change in CDAI at 6 months and the secondary endpoint was therapeutic response according to EULAR criteria. [Results] In the T1W group, baseline CDAI was 11.0 (95% CI, 7.9-17.1), which decreased significantly to 7.5 (95% CI, 3.5-13.0) at 6 months ($p < 0.01$). Of the 58 patients with a DAS28-ESR of LDA or better at baseline, 41.4% had a good response, 19.0% had a moderate response and 39.6% had no response. In the TSS group, 60.6% (40 patients) had difficult-to-treat (D2T) RA. The baseline CDAI was 17.3 (95% CI, 10.1-26.0), which decreased to 8.7 (95% CI, 6.0-19.6) at 6 months ($p < 0.01$). Of the 40 patients with LDA or better at baseline, 24.1% had a good response, 27.6% had a moderate response and 17.2% had no response. [Conclusion] Shortening the TCZ interval and switching to SAR reduced disease activity in RA, providing options for D2T cases.

W4-4

Comparative Effectiveness of bDMARDs and JAK Inhibitors in Sustaining Remission after Discontinuation in Rheumatoid Arthritis: Insights from the ANSWER Cohort

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Conflict of interest: None

[Objectives] The comparative effectiveness of bDMARDs and JAK inhibitors (JAKi) in maintaining remission after discontinuation in rheumatoid arthritis (RA) remains unclear. This study aimed to compare their remission maintenance ability. [Methods] We enrolled RA patients achieving CDAI remission (≦2.8) at the time of bDMARD or JAKi discontinuation (b/ts-DMARDs-free remission: BTFR) from the ANSWER cohort registry. Patients who stopped treatment due to ineffectiveness were excluded. BTFR failure was defined as CDAI >2.8 or reinitiation of b/ts-DMARDs. Cox proportional hazard analysis was performed to adjust confounders. [Results] Among 355 patients (TNFi: 239, IL-6Ri: 58, CTLA4-Ig: 40, JAKi: 18), the median BTFR duration was 184 days (95% CI, 154-259) with a 1-year BTFR rate of 37.1%. TNFi (HR 0.54, 95% CI [0.31-0.95]), IL-6Ri (HR 0.41, [0.22-0.77]), and CTLA4-Ig (HR 0.51, [0.26-0.98]) showed lower BTFR failure risk than JAKi. Other factors associated with BTFR failure were as follows: disease duration (HR 1.02, [1.00-1.03]), Boolean remission (HR 0.63, [0.46-0.86]), positive rheumatoid factor (HR 1.51, [1.10-2.07]). [Conclusion] bDMARDs were favourable compared to JAKi in maintaining BTFR. Shorter disease duration, deep remission, and immunological remission were favourable predictors.

W4-5

A study on the efficacy and safety of ozoralizumab without MTX in our hospital

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Conflict of interest: None

[Objectives] Ozoralizumab (OZR), which was recently launched, has been shown to have excellent clinical efficacy in combination with MTX in the OHZORA Trial, and we present the results of a retrospective evaluation of the efficacy and safety of OZR without MTX. [Methods] In 61 patients treated with OZR at our hospital, we investigated changes in laboratory values and changes in disease activity with and without MTX. [Results] There were 17 patients (27.9%) in the MTX combination group, and the mean MTX dose was 10.0 mg, and in the MTX non-combination group 44 patients (72.1%), the change in SDAI was 23.0 and 16.8 before treatment and 5.8 and 4.0 six months later. Compared to the MTX combination group, there were many cases with higher pre-dose ACPA and RF values in the non-MTX combination group, and in particular, the higher the ACPA and high RF values in the non-MTX group, the higher the clinical efficacy and the higher the continuation rate. In addition, ADR by OZR was only one case of hepatic dysfunction for which a causal relationship could not be ruled out. [Conclusion] In this study, we investigated the efficacy and safety of OZR without MTX, but we would like to consider the possibility of increasing the efficacy by adding more cases.

W4-6

The clinical evaluation of rheumatoid arthritis patients' disease activity treated with infliximab using REMICHECK Q (REMIQ) at our hospital

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Conflict of interest: None

[Objective] We examined the relationship between the REMIQ results and RA patients' disease activity treated with IFX at our hospital. [Methods] We classified 75 RA patients (15 males and 60 females) treated with IFX between 2007 and 2023 into a REMIQ-positive group (n=60) and a REMIQ-negative group (n=15), and compared their clinical courses from 0 to 52 weeks after the introduction of IFX. [Results] There were no significant differences in age (57.5 vs 62.0 years, p=0.357), disease duration (6.0 vs 3.5 years, p=0.852), duration of IFX treatment (6.0 vs 6.0 years, p=0.476), the rate of bio-free IFX (16.7 vs 26.7%, p=0.604), or ACPA (55.8 vs 100.0 IU/mL, p=0.245). There were no significant differences in DAS28-ESR at the time of IFX introduction (4.54 vs 3.79, p=0.609) or SDAI (19.5 vs 15.0, p=0.788), but there was a significant difference in HAQ-DI (0.63 vs 0.00, p=0.002). DAS28-ESR showed significant differences at 36 weeks (2.62 vs 3.45, p=0.026) and 52 weeks (2.40 vs 3.32, p=0.0217). HAQ-DI showed significant differences at 24 weeks (0.25 vs 0.00, p=0.025) and 36 weeks (0.25 vs 0.00, p=0.005). SDAI showed no significant differences throughout the entire period. [Conclusion] REMIQ positive patients may achieve the same treatment responsiveness as those in the negative group.

W5-1

Fib-4 index is a risk factor for discontinuation of methotrexate therapy in rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] The anker drug for rheumatoid arthritis treatment about clinical and structural remission is Methotrexate (MTX). Few indicators predict MTX continuation. This study examined the association between the Fib-4 index and MTX continuation using the ROCKo cohort from Kobe University hospital rheumatoid arthritis registry. [Methods] We extracted MTX-naive patients from the ROCKo cohort. We examined effect of Fib-4 and some liver functional indicator on MTX discontinuation using logistic analysis and the Cox proportional hazards model. [Results] 443 MTX-naive patients data were extracted. AST / ALT ratio, Fib-4, and ALBI were used as liver functional indicators. These indicators have cut-off 0.87, 1.3, and 2.6. AST/ALT ratio and ALBI has no impact on MTX discontinuation through 1 year. However, Fib-4 index predicted MTX discontinuation significantly using both logistic analysis (OR=1.57, 95%CI: 1.03-2.40, p=0.03) and Cox hazard model (HR=1.49, 95%CI: 1.06-2.10, p=0.02). [Conclusion] Fib-4 may be a potential indicator for predicting the continuation rate of MTX for one year.

W5-2

Effectiveness and safety of subcutaneous methotrexate for liver dysfunction caused by oral methotrexate

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Conflict of interest: None

[Objectives] Subcutaneous methotrexate (SC MTX) is expected to have superior efficacy and safety equivalent to or higher than oral MTX (Oral MTX) in RA patients. In this study, we investigated the effect of SC

MTX on reducing liver dysfunction caused by Oral MTX. [Methods] Fifty one RA patients were started SC MTX from November 2022 to July 2024 in our hospital. Thirteen of the 51 patients who had a history of liver dysfunction by Oral MTX were enrolled. We compared the dose of MTX and folic acid, the levels of AST and ALT, and DAS28-CRP at the time of onset of liver dysfunction with Oral MTX (L) and 12 weeks after starting SC MTX (S). [Results] The MTX dose (L; 8.0 (8.0-12.0) mg/week, S; 7.5 (7.5-10.0) mg/week, p=0.342), the folic acid dose (L; 5.0 (5.0-5.0) mg/week, S; 5.0 (5.0-5.0) mg/week, p=0.149), the DAS28-CRP (L; 1.53 (1.43-1.95), S; 1.74 (1.43-1.90), p=0.239) were not significantly difference between both groups. On the other hands, the levels of AST (L; 54.0 (43.0-57.0) IU/mL, S; 24.0 (21.0-30.0) IU/mL, p<0.01) and that of ALT (L; 73.0 (42.0-82.0) IU/mL, S; 21.0 (17.0-25.0) IU/mL, p<0.01) were significantly lower in S. The continuation rate for SC MTX was 100%. [Conclusion] To switch to SC MTX is useful in cases with liver dysfunction occurs by Oral MTX.

W5-3

Methotrexate and Rheumatoid Arthritis: Efficacy and safety of subcutaneous injection versus oral-Analysis using the Kansai Multicenter ANSWER cohort-

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Conflict of interest: None

[Objectives] Oral MTX is widely used in Japan, but its bioavailability varies as dosage increases, which may affect its efficacy and side effects. In contrast, the subcutaneous injection (SC) is known to have better absorption, higher bioavailability, and fewer side effects. It has also been suggested that switching to the SC may improve therapeutic efficacy when the oral is ineffective. In this study, we analyzed cases in which patients were switched from oral to SC and evaluated their efficacy and safety. [Methods] We evaluated changes in disease activity and Fib4 index in 39 RA patients who switched to the SC. [Results] The mean age was 52.4 years, and the mean disease duration was 10.8 years. Before the change, the mean dose of the oral was 9.1 mg and the mean dose of the SC was 9.8 mg. 6 months later, the change in DAS28-ESR and CDAI were -0.9 and -4.0, respectively, and the percentage of patients with high and moderate disease activity decreased by 25% and 23%. The percentage of patients with a Fib4 index of ≧1.3, indicating liver fibrosis concern, remained similar after the change in oral and SC. [Conclusions] The change to a subcutaneous injection showed a trend toward improvement in disease activity, but no change in the effect on liver fibrosis was observed.

W5-4

Impact of Subcutaneous Methotrexate on Cumulative Medical Costs in Methotrexate-Naïve Rheumatoid Arthritis Patients

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Conflict of interest: None

[Objectives] To investigate the impact of different administration routes (subcutaneous vs. oral) of methotrexate (MTX) on cumulative medical costs until remission in treatment-naïve rheumatoid arthritis (RA) patients. [Methods] Patients diagnosed with RA who initiated MTX treatment in Phase I were divided into two groups: oral (PO) and subcutaneous (SC) administration. We retrospectively compared remission rates, time to remission, progression to Phase II, and cumulative medical costs between the two groups. [Results] A total of 177 patients received oral MTX and 65 received subcutaneous MTX. The SC group achieved significantly faster remission and higher remission rates (p=0.045). Additionally, SC patients were less likely to require additional biologic or JAK inhibitor therapies (p=0.027). Despite higher drug price, subcutaneous MTX led to lower cumulative medical costs. [Conclusion] Subcutaneous MTX administration may lead to reduced cumulative medical costs until remission compared to oral administration. This finding was likely influenced by the differences in remission rates, time to remission, and transition rates to Phase II between the two administration routes.

W5-5

Evaluation of clinical efficacy and safety of metoject in rheumatoid arthritis

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Conflict of interest: None

Purpose: Metoject is a subcutaneous injection of methotrexate and has been shown to be effective for early onset RA. The purpose of this study is to examine in detail the clinical efficacy and safety of Methoject in RA. METHODS: Patients with RA who attends our hospital and related centers as of April 2024 were selected and followed up for 6 months for the efficacy of Metoject treatment by using clinical symptoms, laboratory results, and ultrasound of joints. Results: A total of 76 patients were selected. DAS28-CRP after the start of Metoject 61.8% at 1 month, 80.1% at 3 months, and 87.1% at 6 months were in remission. S-DAI and C-DAI showed remission in 56% and 33.3% of patients after 1 month, 72.6% and 46.2% after 3 months, and 74.3% and 39.3% after 6 months. Of the patients followed by ultrasound, 55.6% improved synovitis after 1 month, 84.2% after 3 months, and 58.8% after 6 months compared to baseline. Adverse events included liver dysfunction in 3.9% of patients and renal dysfunction in 5.3% of patients during the course of the study. Stomatitis occurred in 3.9%, skin rash, gastrointestinal symptoms, and hair loss in 1.3%. Conclusion Our results suggest that Methoject has an early therapeutic effect in rheumatoid arthritis, indicating that it has a low incidence of side effects.

W5-6

Mid- to long-term outcomes of daily administration of 1 mg folic acid for dose-dependent side effects of Methotrexate

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Conflict of interest: None

[Objectives] It is well known that methotrexate (MTX) is an important drug in the treatment of rheumatoid arthritis (RA) as an anchor drug, but it is often experienced that sufficient treatment continuation becomes difficult due to MTX dose-dependent side effects. In our outpatient clinic, RA cases that show MTX dose-dependent side effects when combined with folic acid (FA) 5 mg/week are changed toFA 1 mg/day. In this study, we investigated the mid- to long-term anti-RA treatment progress with FA 1 mg/d. [Methods] Among RA patients who were receiving MTX treatment in combination with FA 5 mg/w, we investigated the clinical course of 28 cases who exhibited MTX dose-dependent side effects and switched to FA 1 mg/d. [Results] The mean duration of FA 1 mg/d was 53 months, and the MTX continuation rate was 85.7%. The mean MTX dose when changing to FA 1 mg/d was 12.3 mg/w. The mean MTX dose after changing to FA 1 mg/d was 13.9 mg/w, and 37.5% added biologics. The mean MTX dose at the final follow-up was 10.6 mg/w, and 50% achieved CDAI remission, and 75% achieved Boolean 2.0 remission. [Conclusion] In RA cases re-

ceiving MTX treatment, continuing MTX administration by changing to FA 1 mg/d is thought to contribute to maintaining good clinical outcomes in the medium to long term.

W6-1

Efficacy of Rituximab on skin Sclerosis in Systemic Sclerosis: Long-term Follow-up up to 5 years and Cases of Recurrence

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Conflict of interest: None

Objective: Rituximab (RTX) was approved for systemic sclerosis (SSc). Before this approval, our department administered RTX to patients with rapidly progressing skin sclerosis or early complications such as pulmonary hypertension (PH) or interstitial lung disease (ILD) in diffuse cutaneous SSc (dcSSc). This study retrospectively examined the course of skin sclerosis, including cases treated after RTX's expanded indication. **Methods:** The study included 17 patients diagnosed according to the ACR/EULAR criteria. The average age was 53.7±20.0 years, with a disease duration of 8.3±9.0 years and a baseline TSS of 22.6±9.2. **Results:** After 1 year, TSS decreased to 14.6±9.5 (n=17), 12.1±8.9 after 2 years (n=13), and 12.8±8.7 after 3 years (n=11). Three patients were followed for 5 years, with an average TSS of 14.3±10.8. Four cases of recurrence were observed: in one case, RTX was administered twice annually, while the other three cases were managed with biannual RTX retreatment or immunosuppressive drugs. **Conclusion:** RTX is effective for reducing skin sclerosis in SSc patients. However, recurrence risk varies depending on the timing of retreatment and the use of concomitant medications. Further case accumulation is needed to determine the optimal use of RTX.

W6-2

Mortality and causes of death in patients with systemic sclerosis (SSc)

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Conflict of interest: None

[Objectives] To investigate the prognosis of SSc patients in a single-center cohort and to elucidate changes over time by comparison with previous reports. [Methods] Of 466 SSc patients in our cohort, we enrolled 407 patients who had at least two visits with trackable outcomes. Deceased cases were classified as SSc-related or unrelated, and causes of were identified. The standardized mortality ratio (SMR) was calculated. Predictors of mortality were identified by the Cox proportional hazards model using baseline data. A systematic review was conducted to identify studies reporting SMR in SSc. [Results] Among 407 SSc patients, 344 were female and 130 had diffuse cutaneous SSc (dcSSc). Median disease duration and follow-up were 91 months and 42 months. There were 54 deaths and the SMR was 2.58. SSc-related deaths were fewer, with interstitial lung disease as the most common cause among the 14 cases. In contrast, malignancy was the leading cause of SSc-unrelated deaths. Male sex, age at diagnosis, and dcSSc were associated with mortality. Compared with 21 studies, we showed comparable SMR, but SSc-unrelated deaths were more frequent. [Conclusion] No significant improvement in SSc prognosis has been observed over the past 40 years, highlighting the persistent unmet needs in this population.

W6-3

Can the difference in grip strength between morning and evening express the morning stiffness observed in rheumatoid arthritis? An attempt to quantify the morning stiffness

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Conflict of interest: Yes

[Objectives] Morning stiffness (MS) is a major symptom of rheumatoid arthritis (RA), and should be a target for therapeutic intervention. However, there is no objective evaluation method other than patient evaluation of the degree of MS. Therefore, we explored whether MS can be quantified by measuring the difference between morning and evening handgrip strength (HG). [Methods] In accordance with the protocol for the "Multicenter study for morning stiffness in RA using low temperature warmers" (jRCTs052230138), 31 RA patients measured their HG using a glove-type dynamometer during the period without the intervention in the above study (14 days). The correlation coefficient between the MS degree recorded by the participant and the difference in HG (HG before sleeping - HG upon waking the next morning) was calculated for each participant. [Results] It was expected that "the more HG decreases upon waking, the more severe MS is felt". A strong negative correlation coefficient of over -0.6 was observed in 6, and a weak negative correlation of over -0.4 was observed in 4. In the 12 subjects, the coefficient was less than ±0.2. [Conclusion] The difference in HG between morning and evening may be an evaluation method for hands function, but it was limited to a few patients who matched MS.

W6-4

Clinical characteristics of patients with Scleroderma (SSc) associated with the physical frailty

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Conflict of interest: None

[Objective] To clarify the association between clinical characteristic of SSc and the physical frailty. [Method] SSc who visited our hospital between 2021 and 2024 and fulfilled the 2013 ACR/EULAR classification criteria were included. Physical frailty phenotypes (PFP) were recognized as frailty, pre-frailty or robust based on the definition of J-CHS. Body composition was evaluated by BMI, FFMI or Musculoskeletal Index. Clinical information was retrospectively collected and compared. [Result] Forty-nine patients were included. Mean age was 64 ± 13, 78% female, 35 (71%) were with pre-frail, 5 (10%) frail and 9 (18%) robust. When clinical information was compared among 3 groups, higher HAQ-DI ($p<0.001$), age at SSc diagnosis ($p<0.05$) and longer disease duration of SSc ($p<0.01$) were associated with PFP. As for the organ involvements, the PFP was associated with dysphagic symptom ($p<0.03$), bloating ($p<0.03$), total EAT-10 score ($p<0.01$), total F-scale score ($p<0.05$), fecal incontinence, social functioning, psychological health, constipation and total score on the UCLA GIT-2.0 ($p<0.05$, $p<0.05$, $p<0.02$, $p<0.02$, $p<0.05$, respectively), but not with body composition. [Conclusion] The PFP in SSc might be associated with disease duration and gastrointestinal involvement.

W6-5

Antinuclear antibody patterns and coexisting autoimmune diseases in patients with centromere antibody-positive limited cutaneous systemic sclerosis

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Conflict of interest: None

[Objectives] We investigated the serological characteristics and the occurrence of autoimmune diseases in patients with Anti-centromere antibody-positive limited cutaneous systemic sclerosis (ACA-positive lcSSc) [Methods] We examined the clinical symptoms and laboratory data of 130 ACA-positive lcSSc patients diagnosed and treated at our department from 2012 to 2023. [Results] There were 15 male cases and 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. The magnification of the antinuclear antibody (ANA) test were 1280x; 61.6%, 640x: 20.3%, and the staining pattern of ANA were centromere pattern only; 63.1%, centromere/speckled pattern; 12.0%, centromere/speckled/diffuse pattern: 9.7%. Autoimmune diseases were: SjS; 57.1%, PBC; 47.3%, Hashimoto's disease; 36.1%, and SLE; 21.8%. [Conclusion] ACA-positive lcSSc is frequently accompanied by SjS, Hashimoto's disease, and SLE, which are more prevalent in women, suggesting the existence of a common predisposition to the onset of the disease.

W6-6

A Case of Anti-RuvBL1/2 Antibody-Positive Systemic Sclerosis Complicated with Myositis and Interstitial Lung Disease

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Conflict of interest: None

[Case] A 77-year-old woman presented with persistent pruritus, skin induration, and muscle weakness for seven months. Laboratory findings indicated elevated muscle enzymes and positive antinuclear antibodies, suggesting inflammatory myopathy. Upon admission, she showed extensive skin hardening, biopsy results consistent with systemic sclerosis (SSc), and chest CT revealed interstitial lung disease (ILD). Anti-RuvBL1/2 antibodies were identified, and MRI confirmed myositis without Raynaud's phenomenon or skin rash. Initial treatment with high-dose glucocorticoids (GC) and mycophenolate mofetil improved skin symptoms but not ILD or myositis, leading to a switch to rituximab (RTX). Four RTX infusions were administered with ongoing GC tapering. [Clinical Significance] SSc is characterized by immune dysregulation with various disease-specific autoantibodies, including the rare anti-RuvBL1/2 antibody. Clinical features of anti-RuvBL1/2 antibody-positive cases remain largely unknown due to limited reports. This case, marked by rapidly progressive skin sclerosis, concurrent myositis and ILD, and resistance to treatment, may contribute valuable insights into the clinical profile associated with this antibody.

W7-1

Spatial Transcriptomics for Myositis: From GAPFREE4, an industry-academia-government collaborative project

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Conflict of interest: None

[Objectives] We aimed to analyze the differences in gene expression between lesional and normal areas using spatial transcriptome analysis to elucidate the pathogenesis of myositis. [Methods] Spatial transcriptome analysis was performed using Visium (10x Genomics) on muscle tissue biopsied from the left biceps brachii muscle of a 40s-year-old man with anti-EJ antibody-positive myositis. Gene expression patterns and gene functions were analyzed. [Results] Two clusters were identified in each of the inflammatory, borderline, and normal regions. In the inflammatory region, genes related to MHC class II-mediated antigen presentation and neutrophil degranulation were predominantly expressed, and genes related to chemokines, complement, and immunoregulation were characterized. In the borderline region, genes related to complement, coagulation system and some cytokines were predominantly expressed. [Conclusion] Spatial transcriptome analysis suggests that inflammation in myositis is driven by local gene expression patterns and molecular pathways. This study may provide important insights for the pathogenesis of myositis.

W7-2

Different roles of RasGRP1 and RasGPR4 in inflammatory myopathies

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Conflict of interest: None

[Objectives] Ras guanyl-releasing protein (RasGRP) has four isoforms including RasGRP1 and RasGRP4. RasGRP1 expresses mainly in lymphocytes and RasGRP4 in myeloid cells. The pathogenesis of inflammatory myopathies (IIM) involves not only autoreactive T cells but also activated macrophages. In this study, we investigated the roles of RasGRP1 and 4 in IIM. [Methods] The expression of RasGRPs were examined immunohistochemically in muscle tissues from IIM patients and C protein-induced myositis (CIM), a murine model of myositis. CD8+ cells and CD11b+ cells were isolated from lymph nodes (LNs) of CIM mice with magnetic beads. CIM was induced in *Rasgrp1* or *Rasgrp4* deficient mice. [Results] RasGRP1 expressed predominantly in CD8+ and CD68+ cells, while RasGRP4 in CD68+ cells in the muscle tissue from IIM patients as well as CIM mice. The levels of both RasGRPs were elevated sequentially in the mononuclear cells from muscle tissues after CIM induction. In the draining LN from CIM mice, higher levels of RasGRP1 and 4 than those from mice treated with CFA alone was observed in CD8+ and CD11b+ cells, respectively. The myositis was less severe both in *Rasgrp1* and *Rasgrp4* deficient mice. [Conclusion] Our results indicated the different roles of RasGRP1 and 4 in the pathogenesis of IIM.

W7-3

Stratification of anti-MDA5 antibody-positive dermatomyositis by type I/III interferons in circulation

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Conflict of interest: None

[Objectives] We aimed to stratify the mortality risk of patients with anti-MDA5$^+$ dermatomyositis (DM) using interferon (IFN) levels in circulation. [Methods] This study included patients diagnosed with anti-MDA5$^+$ DM in Nippon Medical School Hospital from August 2014 to September 2024 and Hamamatsu University Hospital from July 2014 to February 2021. Pre-treatment serum IFN-α and IFN-γ were measured by cytometric bead array, while IFN-β and IFN-λ3 were measured by enzyme immunoassay. We standardized IFN levels into *Z*-scores and subjected them to hierarchical clustering. Cumulative survival rates were compared between the clusters using the Log-rank test. [Results] We included 53 patients in total. Serum IFN-γ was elevated in none of the patients. Cluster analysis of type I/III IFN levels identified three subgroups. Cluster 1 (n=24) was characterized by mild elevations of both type I and III IFNs. Cluster 2 (n=13) demonstrated a significant increase in type III IFN alone. Cluster 3 (n=16) exhibited elevation of type I IFNs, while the elevation of type III IFN was mild to moderate. Patients in Cluster 2 tended to have a poorer prognosis than those in Clusters 1 and 3 (P=0.291, 0.090). [Conclusion] Anti-MDA5$^+$ DM patients with isolated elevation of type III IFN may have a poor prognosis.

W7-4

The relationship between radiological myositis on skeletal muscle MRI and progressive fibrotic interstitial lung disease in anti-ARS antibody-positive patients

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Conflict of interest: None

Objectives: Anti-ARS antibodies are linked to idiopathic inflammatory myopathies (IIM), often leading to interstitial lung disease (ILD). Some patients experience progressive pulmonary fibrosis despite treatment, but it's unclear which cases will progress. This study aims to explore the relationship between skeletal muscle MRI findings and lung disease progression. **Methods:** Twenty anti-ARS antibody-positive patients who had undergone skeletal muscle MRI were analyzed. Based on MRI findings, patients were grouped into three categories: Group 0 (no myositis or fasciitis), Group 1 (fasciitis without myositis), and Group 2 (myositis and fasciitis). Lung involvement was assessed by scoring ILD-related changes on CT scans. Progressive fibrosis was defined by worsening lung lesions over time. **Results:** Progressive fibrotic ILD (PF-ILD) occurred in 1 out of 4 patients in Group 0, 0 out of 4 in Group 1, and 5 out of 12 in Group 2. Lung disease scores were higher in Groups 0 and 2 compared to Group 1. **Conclusion:** Patients with fasciitis alone showed less severe lung involvement and slower progression, while those with myositis had more extensive lung disease and higher progression risk.

W7-5

The characteristics of proximal muscle MRI findings in anti-TIF1 gamma antibody-positive dermatomyositis with cancer

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Conflict of interest: None

[Objectives] This study aimed to identify the characteristics of proximal muscle MRI findings in patients with dermatomyositis (DM) positive for anti-TIF1γ antibodies complicated with cancer. [Methods] Proximal muscle MRI in the extremities was performed in 20 patients with anti-TIF1γ antibody-positive DM. The extent of high signal intensity (HSI) in the subcutaneous tissue, fascia, and muscle regions was semi-quantitatively evaluated on axial section images of STIR MRI. In the muscle, the doted HSI were also semi-quantified. The scores of each of the three regions were compared in cancer and non-cancer groups, using Mann-Whitney U-test and analyzed for association with the presence of cancer, using Fisher's exact test. [Results] The scores for dotted HSI in muscle, HSI in fascia, and HSI in subcutaneous tissue were significantly higher in cancer group than non-cancer group. The association between cancer and HSI in each region was statistically most strongly associated with HSI in the subcutaneous tissue, followed by dotted HIS in the muscle. [Conclusion] The complication rate of cancer is higher in patients with HSI in the subcutaneous tissue and dotted HSI in the muscle. Therefore, these MRI findings should raise strong suspicions of cancer complications.

W7-6

Changes in muscle strength and muscle mass over time in patients with inflammatory myopathy

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Conflict of interest: None

[Objectives] The purpose of this study is to demonstrate the usefulness of measuring skeletal muscle mass (muscle mass) using a body composition analyzer by showing the degree of recovery of muscle mass in patients with myositis. [Methods] The study included 22 first-onset cases who were followed up for more than one year. Muscle mass was measured using a body composition analyzer and muscle strength was measured using a manual dynamometer on the same day. We examined the extent to which muscle strength and muscle mass compared to the initial values one year after treatment, and the results and clinical characteristics of the cases. [Results] At the time of pre-treatment evaluation, muscle mass had decreased in 68.2% of cases, and muscle strength had decreased in 54.5% of cases. It took an average of 5.9 months for skeletal muscle mass to recover to pre-treatment levels, and 9.1% had not recovered even after one year. It took an average of 0.9 months for muscle strength to improve from pre-treatment levels, and all cases had returned to normal levels after one year. [Conclusion] In myositis patients, muscle strength recovered after treatment, but recovery of muscle mass tended to be somewhat delayed. However, after one year, 90% of patients had recovered to pre-treatment levels.

W8-1

Preventive Efficacy of Recombinant Zoster Vaccine in Rheumatoid Arthritis Patients with Janus kinase inhibitors

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) treated with Janus kinase inhibitors (JAKi) are at increased risk of herpes zoster (HZ). The aim of this study is to elucidate the efficacy of Recombinant Zoster Vaccine (RZV) in RA patients with JAKi. [Methods] We consecutively extracted 194 cases of RA patients who were newly started JAKi, from January 2020 to September 2024. These patients were divided into two groups: the RZV unvaccinated group (120 cases) and the RZV vaccinated group (74 cases). We analyzed the efficacy of RZV. [Results] The total observation period was 256.2 person-years for the RZV unvaccinated group and 124.4 person-years for the RZV vaccinated group. The incidence of HZ was 20 cases (8.7 per 100 person-years) in the RZV unvaccinated group and 6 cases (4.8 per 100 person-years) in the RZV vaccinated group. The efficacy of RZV in RA patients with JAKi was 51.4%. The incidence of HZ in the unvaccinated group by JAKi formulation was as follows: Baricitinib 9.9 per 100 person-years, Upadacitinib 6.2 per 100 person-years, and Filgotinib 1.6 per 100 person-years. [Conclusion] In RA patients with JAKi, the preventive effect of RZV on HZ incidence was confirmed. However, we should remain vigilant for the occurrence of HZ following RZV vaccination.

W8-2

Use of Recombinant Subunit Herpes Zoster Vaccine in Patients with Rheumatic Diseases

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of the recombinant subunit herpes zoster vaccine (Shingrix) in patients with rheumatic diseases. [Methods] A retrospective cohort study of adult rheumatic disease patients vaccinated at our hospital from December 2020 to October 2024. Data collected from electronic medical records included age, medical history, underlying diseases, medications, and herpes zoster occurrence. [Results] 243 patients were included (mean age 69 [61-77] years, 82.3% female). Underlying diseases: rheumatoid arthritis (67.5%), systemic lupus

erythematosus (9.5%), ANCA-associated vasculitis (5.3%), polymyalgia rheumatica (5.3%). Comorbidities: diabetes (5.3%), malignancy (7.4%). Treatments: steroids (29.2%), MTX (35.8%), bDMARDs (37.9%), JAK inhibitors (20.6%). 90.1% completed both vaccine doses. Mean follow-up: 829 [581-1095] days. Herpes zoster occurred in 6 patients (2.5%, 0.03/1000 person-years). Mild adverse events in 15 patients (6.2%). No serious adverse events reported. [Conclusion] Shingrix is effective and safe for immunosuppressed patients with rheumatic diseases.

W8-3

Low-dose atovaquone for prophylaxis of pneumocystis jirovecii pneumonia in rheumatic diseases patients treated with glucocorticoids: A single-arm, phase II trial

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Conflict of interest: None

[Objectives] *Pneumocystis jirovecii* pneumonia (PCP) is an opportunistic infection that occurred in patients with rheumatic diseases under glucocorticoids treatments. Continuing atovaquone 1500 mg/day, one of the standard prophylactic options of PCP, is often difficult due to its side effects or cost. This trial aimed to assess the efficacy and safety of low-dose atovaquone (750 mg/day) for prophylaxis of PCP in patients with rheumatic diseases who were started glucocorticoids. [Methods] In this single-arm, phase 2 trial, subjects were patients with rheumatic diseases who had started or scheduled to start 0.5 mg/kg/day or more of prednisolone or an equivalent dose of glucocorticoids. All patients received low-dose atovaquone for 24 weeks. The primary end point was the incidence of PCP at 24 weeks. [Results] Fifty patients were assigned to receive low-dose atovaquone, and 45 were included in the primary analysis. None developed PCP during the trial period. Although there were two serious adverse events, both events were not related to low-dose atovaquone. [Conclusion] Low-dose atovaquone may have sufficient efficacy for the prophylaxis of PCP and a good safety profile in patients with rheumatic diseases treated with glucocorticoids.

W8-4

A case of Pneumocystis pneumonia developing during atovaquone prophylaxis in a patient with TAFRO syndrome

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Conflict of interest: None

[Case] A 64-year-old male presented with fatigue and fever. Hospitalization revealed fluid retention, thrombocytopenia, fever, elevated inflammatory markers, renal impairment, and lymphadenopathy. TAFRO syndrome was diagnosed based on Masaki criteria. Treatment included rituximab and methylprednisolone pulse therapy, followed by prednisolone tapering. The patient underwent hemodialysis and received blood transfusions. Atovaquone was chosen over trimethoprim-sulfamethoxazole (TMP-SMX) for Pneumocystis jirovecii pneumonia (PCP) prophylaxis to avoid worsening renal function and cytopenia. On day 76, the patient developed fever and hypoxemia. CT showed diffuse ground-glass opacities. Elevated β-D-glucan and positive Pneumocystis PCR from BAL confirmed PCP. TMP-SMX was initiated despite mild renal dysfunction. Intravenous prednisolone was added. After 3 weeks of treatment with TMP-SMX, the patient improved and was discharged on day 108. [Discussion] Several cases of PCP breakthrough during atovaquone prophylaxis have been reported internationally, but this is the first such case in Japan. International studies have linked cytochrome *b* mutations to atovaquone resistance. In this case, drug resistance due to genetic mutation was suspected.

W8-5

A case of refractory anti-MDA5 antibody-positive dermatomyositis with muscle abscess due to disseminated aspergillosis under the combination of cyclophosphamide, glucocorticoids, tacrolimus, and tofacitinib

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Conflict of interest: None

[Case] A 49-year-old man with anti-MDA-5 antibody-positive dermatomyositis (MDA5+ DM)-associated interstitial lung disease and mediastinal emphysema presented with a 10-day history of fever and muscle pain. 50 days before admission, tofacitinib was added for interstitial pneumonia resistant to cyclophosphamide, glucocorticoids, and tacrolimus. A contrast-enhanced CT and blood culture made a tentative diagnosis of pyomyositis with *Methicillin-resistant Staphylococcus* aureus. He was treated with vancomycin, but the muscle abscess was formed. *Aspergillus fumigatus* was isolated by the punctum. Retrospective, from 61 days before admission, a nodular shadow suggestive of pulmonary aspergillosis had appeared, increased, and cavitated in the left lower lobe of the lung. Still, it was not identified on the back of interstitial shadows and mediastinal emphysema. He was diagnosed with muscle aspergillosis disseminated from pulmonary aspergillosis and treated with voriconazole and muscle debridement. However, he developed multiple organ failure and died 151 days after admission. [Clinical Significance] When adding JAK inhibitor to refractory MDA5+ DM, we should note pulmonary nodules mixed in with interstitial pneumonia and mediastinal emphysema.

W8-6

The Impact of SGLT2 Inhibitors on the Risk of Urinary Tract Infections in Rheumatoid Arthritis Patients with Diabetes

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Conflict of interest: None

Objective: To evaluate the effect of SGLT2 inhibitors (SGLT2i) on the risk of urinary tract infection (UTI) in rheumatoid arthritis (RA) patients with diabetes. **Methods:** We used data from the Medical Data Vision Co. database to identify RA patients aged 18 and older with type 2 diabetes between April 2015 and April 2023. RA was defined by disease name registration and prescription of antirheumatic drugs or glucocorticoids (GCs), and diabetes by disease name registration and prescription of oral hypoglycemic agents (OHAs). The observation started with the initiation of new SGLT2i or other OHAs prescription. The primary outcome was the development of UTI within one year, identified by disease name registration and antibiotic prescription. A Poisson mixed-effects model adjusted for time-dependent confounders (OHAs and GCs) was used to assess the effect of SGLT2i on UTI risk. **Results:** The study included 9,672 patients with a mean age of 71 years; 59% were female. SGLT2 inhibitors were newly initiated in 19%, GC use was 59%, and UTIs developed in 14%. The analysis showed that both SGLT2i and other OHAs initiation reduced the risk of UTI (SGLT2i: adjusted HR 0.58, 95% CI 0.45-0.75; non-SGLT2i: HR 0.708, 95% CI 0.63-0.80). **Conclusions:** OHAs, including SGLT2i, may reduce the risk of UTI.

W9-1

Comparative analysis of CD8 T cells in rheumatoid arthritis and osteoarthritis

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Conflict of interest: None

[Objectives] In recent years, the importance of CD8T cells in the pathology of rheumatoid arthritis (RA) has attracted attention. However, it remains unclear whether these findings are specific to RA, as comparative analyses with osteoarthritis (OA) and healthy controls (HC) have not been fully conducted. [Methods] Single-cell gene expression data of RA, OA, and HC synovial CD8T cells from public databases were integrated and analyzed using the Seurat package in R. Synovial samples from RA and OA patients were analyzed by flow cytometry (FCM) for CD8T cell surface antigens and cytokine expression. OA synovial cells were cultured with IL-15 or IL-15+IL-12, and CD8T cell phenotype and function were compared before culture. [Results] Single-cell analysis showed an increase in CD8T cell clusters co-expressing GzmK and GzmB in RA compared to OA and HC. This was consistent with our FCM analysis. RA CD8T cells also showed more terminally differentiated Temra cells. IL-15 stimulation of OA synovial CD8T cells increased Temra cells and GzmB, and adding IL-12 further upregulated CD69, GzmB, GzmK, and IFN-γ. [Conclusion] The study clarified the characteristics of CD8T cell subsets that increase in RA synovium and suggested the involvement of IL-15 and IL-12 in their formation.

W9-2

Analysis of cellular senescence in rheumatoid arthritis-associated interstitial lung disease using a mouse model

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Conflict of interest: None

[Objectives] The etiology of rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is unknown. We analyzed the involvement of cellular senescence (CSen) in the pathogenesis of RA-ILD using SKG/Jcl mice. [Methods] We induced ILD in SKG/Jcl mice (SKG-ILD) by administration of zymosan. Immunohistochemistry (IHC) was performed to detect CSen markers including $p21^{WAF1/CIP1}$ (p21). Immunofluorescence (IF) and flow cytometric analysis (FCM) was performed to identified the senescent cells. Single cell RNA sequencing (scRNA-seq) was performed to analyze detailed profile and function of senescent cells. [Results] CSen marker-positive cells were found in SKG-ILD by IHC, and $p21^+$ cells increased along with fibrosis progression. IF and FCM showed the majority of the $p21^+$ cells were $CD45^+$ immune cells. scRNA-seq analysis revealed that *Cdkn1a* (cording p21) was significantly upregulated in the clusters of macrophages and neutrophils, moreover, the analysis of the correlated genes with *Cdkn1a* showed the gene sets related Cen including senescence-associated secretory phenotype (SASP) and p53 pathway and gene sets for inflammation including TNF and signaling were enriched. [Conclusions] In SKG-ILD, CSen of macrophages and neutrophils may be involved in pathogenesis of ILD through SASP.

W9-3

Inflammatory changes in the olfactory bulb related to food intake in a mouse model of arthritis correlate with changes in steroid-related factors in the hypothalamus

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Conflict of interest: None

[Objectives] Control of symptoms that reduce the QOL in rheumatoid arthritis (RA) is important in the treatment of D2TRA. Recently, we reported that decreased food intake (symptoms) in a mouse model of RA is associated with inflammatory changes in the olfactory bulb (OB). HPA axis is known to be involved in the pathogenesis of RA, and the regulation of food intake. In this study, we analyzed the relationship between the expression of steroid-related factors in the hypothalamus (HT) of RA model mice and inflammatory changes in the OB. [Methods] A collagen-induced arthritis model was created, and brains were removed at each stage of arthritis. Total mRNA was extracted from the OB and HT, and the expression of inflammatory cytokines, glial cell markers, and steroid-related factors were analyzed by RT-PCR. [Results] In the HT, there were increase in expression of microglial markers (ITGAM) and Steroid-related factors such as CRH and DDIT4. The expression of ITGAM in the OB correlated with that of CRH and DDIT4 in the HT. [Conclusion] Elevations of CRH and DDIT4 during the acute phase of arthritis suggested a transient increase in the HPA axis. These elevations correlated with inflammatory changes in the OB, suggesting that they may be involved in the pathogenesis of reduced food intake.

W9-4

Identification of characteristic vascular endothelial cell population by a web-based integrative transcriptome analysis of CD146mid/high cells derived from pannus in RA mouse model

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Conflict of interest: None

[Objectives] We investigated how pannus formation contribute to the develop of rheumatoid arthritis in the D1BC mouse, more chronic inflammatory arthritis model. We focus relatively minor population, the characterization of vascular endothelial cells. [Methods] D1BC mice were immunized low-dose bovine type II collagen. Pannus was biopsied, isolated cells were sorted by FACS, and $CD146^{mid/high}$ cells were analyzed by RNA-seq. In addition, transcriptome analysis of scRNAseq from the same population partially purified by positive selection was performed. A web-based integrative transcriptome analysis comparing our data, rheumatoid arthritis, lung, and lung cancer data was performed. [Results] FACS analysis revealed that the isolated synovial cells were composed of macrophages and fibroblasts, but immature CD146 cells were also identified. RNAseq analysis resulted in $CD146^{mid}$ cells differentiated into osteochondrogenic lineage close to osteocytes via hyperchondrocyte, leading to bony ankylosis. $CD146^{high}$ cells, on the other hand, exhibits characteristics of vascular endothelial cells that form new blood vessels in the pannus. [Conclusion] It is suggesting that $CD146^{high}$ cells may be comparable to vascular endothelial cells present in rheumatoid arthritis, lung, and lung cancer.

W9-5

Establishment of infrastructure for large-scale T-cell receptor analysis to elucidate the pathogenesis of autoimmune diseases

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Conflict of interest: None

[Objectives] Antigen-specific responses are thought to be involved in the pathogenesis of many autoimmune diseases, including rheumatoid arthritis. Nevertheless, the disease-specific sequence patterns of T-cell receptors, which are the direct mediators of antigen-specific responses, remain unknown. Bridging the gap between disease development and HLA polymorphisms, major risk factor for disease development, by disease-specific T-cell receptor sequences would lead to elucidating the pathogenesis of autoimmune diseases and discovery of novel biomarkers. The aim of this study was establishing the infrastructure for large-scale T-cell receptor analysis. [Methods] We developed T-cell receptor analysis system based on multiplex PCR from DNA samples. To benchmark the performance of our system, we prepared a blood sample from the same donor. An aliquot of the sample was analyzed in Adaptive, sliver standard of T-cell receptor analysis. [Results] Adaptive reported 29434 clonotypes, while our system detected 39533 clonotypes. Our system detected about 90% of clonotypes with clone size greater than 4, and 100% of clonotypes with clone size greater than 20. [Conclusion] This result showed validity of our system. Also, we successfully established the infrastructure for analysis on population-scale.

W9-6

Effect of CDK6 deficiency on synovial hyperplasia in collagen-induced arthritis mice

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Conflict of interest: None

[Objectives] In our research focusing on the proliferation of rheumatoid arthritis synovial fibroblasts (RASFs), we have reported that SPACIA1 controls the progression of the G1 phase of the cell cycle and that the target gene of SPACIA1 in vitro is CDK6, not CDK4. In this study, we aimed to clarify the role of the CDK6 gene in synovial hyperplasia in mice and G1 phase progression in RASFs. [Methods] Global Cdk6-deficient mice (KO) backcrossed to DBA/1J mice were immunized with bovine type II collagen (Col) and analyzed for arthritis incidence, score, knee joint histological evaluation, and serum anti-Col antibodies. TNFα-stimulated RASFs were treated with CDK4 or CDK6 siRNA and measured viable cells using a CCK8. G1-phase-associated factor mRNA levels were quantified by qPCR. RB phosphorylation levels were evaluated by Western blotting. [Results] KO mice showed significantly delayed onset of arthritis, lower scores, and no knee synovial hyperplasia in all cases compared to controls; anti-Col level were significantly decreased in KO mice. TNFα-induced Cell viability and RB phosphorylation levels were significantly suppressed only by CDK6 siRNA. [Conclusion] Targeting CDK6 expression, but not CDK4, may be an effective therapeutic strategy for rheumatoid arthritis synovial hyperplasia.

W10-1

Efficacy of Risankizumab Across Distinct PsA Phenotypes Identified With Machine Learning Analytics Using Data From Biologic DMARD-Naive Patients in Two Phase 3 Clinical Trials (Encore)

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Conflict of interest: Yes

[Objectives] This cluster (CL) analysis classified patients (pts) into PsA phenotype CLs using baseline (BL) characteristics and the probability of response to Risankizumab (RZB) was assessed by CL. [Methods] This post hoc analysis of KEEPsAKE 1 and 2 evaluated data from bDMARD-naive pts with PsA. Using descriptive statistics, BL clinical and demographic characteristics were described for each CL, as was efficacy by CL at weeks 24, 52, and 100 for pts who received continuous RZB. [Results] Out of 1196 pts, 1119 (93.6%) were analyzed after excluding missing data. Five distinct phenotypic CLs were identified: pts that was (1) moderate disease activity (n [%] = 451 [40.3]), (2) hand (154 [13.8]), (3) high disease activity (157 [14.0]), (4) dactylitis and feet (124 [11.1]), and (5) enthesitis and large joints (233 [20.8]). The achievement of remission/low disease appeared higher in the more moderate disease activity CL, with 32.2%-57.0% of pts achieving MDA at week 100; however, rates of response appeared similar in all CLs, indicating consistent efficacy of RZB across the spectrum of PsA pts. [Conclusion] RZB demonstrated efficacy across all 5 CLs with highest achievement of remission/low disease in CLs 1 and 4. These findings help to identify PsA phenotypes that may respond well to RZB.

W10-2

Analysis of achievement of minimal disease activity (MDA) by molecular targeted drug for psoriatic arthritis

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Conflict of interest: Yes

[Objectives] Inhibition of joint destruction will be expected by T2T strategy for psoriatic arthritis (PsA). Achievement of minimal disease activity (MDA) is a target for PsA. Components of MDA include tender joint count, swollen joint count, PASI, pain VAS, global VAS, HAQ, and tenderness on enthesis. MDA achievement is defined as achievement of 5 or more components. We assessed MDA achievement and each component by molecular targeted drug for PsA. [Methods] In PsA patients treated with molecular targeted drug, achievement of MDA and each component at 1 year were assessed. [Results] In 23 PsA patients, 25 molecular targeted drugs (IL-17 inhibitor 15, TNF inhibitor 4, JAK inhibitor 3, and IL-23 inhibitor 3) were used. Among 25 drugs, MDA was achieved in 15 (60%), and very low disease activity (VLDA) was achieved in 7 (28%). Drugs used in MDA achieved group were IL-17 inhibitor 11, JAK inhibitor 2, and TNF inhibitor 2. Achievement of tender joint count, swollen joint count, pain VAS, and global VAS was statistically different between MDA achieved and non-MDA achieved groups. [Conclusion] MDA was achieved in 60% of PsA patients treated with molecular targeted drug. Achievement rate was different by component, suggesting that each MDA component needs to be noted for T2T strategy for PsA.

W10-3

Evaluation Methods for Psoriatic Arthritis in Real-World Clinical Practice

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Conflict of interest: None

Objectives: Recent studies have examined the effectiveness of simplified 3 VAS (PhGA, Pt. GA, Pt. skinVAS) and 4 VAS (PhGA, Pt. Pain, Pt. GA, Pt. skinVAS) scales developed by OMERACT under GRAPPA for assessing psoriatic arthritis (PsA). However, no data exists on their application in Japanese clinical settings. **Methods:** This study assessed the correlation and treatment response of composite PsA tools (PASDAS, DAPSA, sCPDAI) with 3VAS and 4VAS at 0M, 3M and 6M in PsA patients, all of whom continued b/tDMARDs for at least six months. **Results:** Participants were 226 PsA patients (age 58, 57% male, disease duration 8 yrs). After treatment, minimal disease activity rates were 55% (3M) and 59% (6M). Both 3VAS and 4VAS demonstrated higher effect sizes and standardized response means than existing tools. Their correlation with composite scores was slightly lower than PASDAS and DAPSA but nearly matched sCPDAI. Component correlation was lower, and while 3VAS correlated slightly with PASI, no significant correlation was found between 4VAS and PASI. **Conclusion:** The 3VAS and 4VAS scales are effective for assessing PsA activity in Japanese patients undergoing b/tDMARDs in real-world practice. However, their limited correlation with PASI highlights a need for further studies on skin-related symptoms.

W10-4

Investigation of difficult-to-treat PsA in real-world clinical practice

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Conflict of interest: Yes

[Objectives] Psoriatic arthritis (PsA) has become an indication for numerous b/tDMARDs, but there are many cases of difficult-to-treat (D2T) PsA. In this study, we use the D2TPsA proposed by the European College of Rheumatology in 2021 and validate it in real-world clinical practice. [Methods] We selected a group defined as D2TPsA from 224 PsA patients in our department's spondyloarthritis registry (TOSPAR) who had received b/tDMARDs and 145 patients who had started b/tDMARDs at our hospital, and analyzed the characteristics of these patients. [Results] D2TPsA was 78 patients (35%), with significantly more patients in the D2TPsA group having a longer history of psoriasis and starting with TNF inhibitors as 1st b/tDMARDs. Among the PsA who started 1st b/tDMARDs at our hospital, 34 (23%) were D2TPsA. In addition to the above characteristics, there was a high number of nail lesions, a significantly higher mSASSS in the thoracic spine, and a significantly lower response to treatment after 6 months of 1st b/tDMARDs, especially residual skin lesions. [Conclusion] D2TPsA was not uncommon, and therapeutic intervention targeting Il-17/23axis inhibition is desirable early on to avoid D2TPsA. Although the definition of D2TPsA is controversial, there are many challenges to achieving remission.

W10-5

Epidemiological Feature of the patients with Pustulotic arthro-osteitis in Japan through a nationwide survey

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Conflict of interest: None

[Objectives] To investigate the epidemiological features of patients with Pustulotic arthro-osteitis (PAO) in Japan. [Methods] The secondary survey was conducted on 2,386 patients with confirmed PAO cases (January 1, 2020, to December 31, 2022) in the nationwide survey in 2023. We analyzed the demographics/clinical symptoms. [Results] The response rate was 43.4% and 346 patients with female dominance (84%) were included. Although 85% of cases met the classical criteria, 15% were diagnosed with newly established guidance in 2022. The median age at the survey, onset, and confirmed diagnoses were 57.8/57.2 years, 51.3/51.3 years, and 55.1/54.5 years, respectively. The most common clinical symptoms were swelling/ tenderness in the anterior chest (73.6%/82.5%), followed by spinal pain (41.3%/40.8%). Among cases with normal X-rays in the anterior chest, 73.9% showed abnormalities in MRI. Approximately 29% of cases were classified as severe, defined by refractory bone ankylosis or destructed joints. Approximately 60% had palmoplantar pustulosis, which was not associated with the severity of PAO. [Conclusion] Modified guidance could be helpful for the additional diagnosis of PAO. Since there were a substantial number of severe cases with PAO, it is essential to provide appropriate medical care.

W10-6

A case of SAPHO syndrome with bone destruction lesion in the cervical spine

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Conflict of interest: None

[Case] A 73-year-old woman. One month before her visit, she had experienced particularly provocative pain in the neck and the left upper arm. A plain X-ray of the cervical spine revealed bone destruction in the C5/6 intervertebral disc and the upper and lower vertebral bodies. At the same time, blisters were observed on the soles of both feet, and the patient was diagnosed with palmoplantar pustulosis by a dermatologist. The cervical bone destruction lesion was diagnosed as SAPHO syndrome. Oral administration of NSAIDs was started on the first visit. Oral administration of alendronate was started two weeks later. Cervical kyphosis due to the destruction of the C5/6 cervical vertebral bodies had progressed. C2-7 cervical posterior fixation was performed 8 weeks later. Golimumab administration was started 2 weeks after the surgery. Three months after the surgery, bone formation and bone union were achieved in the C5/6 vertebral destruction site. [Clinical Significance] SAPHO syndrome is often difficult to diagnose, but in this case, palmoplantar pustulosis was also present, making an early diagnosis possible. By promptly starting NSAIDs, bisphosphonates, and biological agents after diagnosis, vertebral destruction due to spondyloarthritis could be minimized.

W11-1

Elucidating the Molecular Mechanisms of Tissue Remodeling in Giant Cell Arteritis: Integration of Single-Cell Analysis and In Situ Gene Expression Data

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Conflict of interest: Yes

[Objective] This study aims to elucidate the characteristics of cell populations responsible for tissue remodeling in giant cell arteritis (GCA) through integrating single-cell gene expression analysis and in situ hybridization. [Methods] Single-cell RNA sequencing was performed on GCA temporal artery biopsy samples to obtain gene expression profiles. In situ hybridization was used to analyze the distribution of gene expression within the tissue. These datasets were integrated to identify disease-related cell clusters involving GCA pathogenesis. [Results] Single-cell analysis revealed the presence of macrophages expressing disease-specific genes that were predominantly localized in GCA lesions. Multiple subtypes of multinucleated giant cells (MNGC) and macrophages were identified within the GCA vasculature. Notably, clusters containing MNGC exhibited high expression of genes involved in tissue remodeling. These cells displayed gene expression profiles similar to osteoclasts, indicating their involvement in vascular destruction and tissue reconstruction. [Conclusion] MNGC and macrophages identified in GCA exhibit diverse subtypes, each contributing to tissue remodeling, including processes such as tissue destruction and fibrosis, which play a crucial role in the pathogenesis of GCA.

W11-2

Efficacy and Safety of Upadacitinib in Patients With Giant Cell Arteritis (SELECT-GCA): A Double-Blind, Randomized Controlled Phase 3 Trial: Overall Results and Sub-Analysis of Japanese Subjects

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Conflict of interest: Yes

Objective: To assess efficacy and safety of upadacitinib (UPA) with glucocorticoid (GC) taper in patients (pts) with GCA. Methods: Pts received UPA 7.5 or 15 mg (UPA7.5 or UPA15) +26-week (wk) GC taper or placebo (PBO) +52-wk GC taper. The primary endpoint was sustained remission at wk 52. Treatment-emergent adverse events were documented over 52 wks. **Results:** 428 pts (20 from Japan) were randomized and dosed PBO, UPA7.5, UPA15 (overall N=112, 107, 209; Japan N=5, 5, 10). Primary endpoint was achieved with UPA15 (46%) vs PBO (29%, P=.0019). UPA15 had reduced risk of flares and lower cumulative GC exposure. UPA7.5 had numerically better efficacy vs PBO but this difference was not statistically significant. Safety outcomes were similar among UPA and PBO including rates of VTE. Numerically higher rates of serious infections were observed in PBO. No MACE events were reported in UPA. Rates of herpes zoster, lymphopenia, anemia, NMSC were numerically higher in UPA15 than PBO. There were 4 treatment-emergent deaths: 2 in PBO, 2 in UPA15. Despite the small sample size requiring caution, efficacy and safety in the Japanese population were generally consistent with those in the overall. **Conclusion:** UPA15+26-wk GC taper demonstrated superior efficacy vs PBO+52-wk GC taper with no new safety signals.

W11-3

Efficacy of Upadacitinib in Patients With Giant Cell Arteritis: Subgroup Analysis of the SELECT-GCA Phase 3 Trial (encore presentation)

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Conflict of interest: Yes

Objectives: Upadacitinib 15 mg (UPA15) efficacy was analyzed in SELECT-GCA subgroups of patients (pts) categorized by baseline (BL) characteristics. **Methods:** SELECT-GCA is a double-blind, placebo (PBO)-controlled Ph3 trial where pts received UPA15 or UPA7.5+26-week (wk) glucocorticoid (GC) taper or PBO+52-wk GC taper. This subgroup analysis presents UPA15 or PBO data. Achievement of the primary endpoint (sustained remission at wk 52) and the secondary endpoint of sustained complete remission from wk 12 to 52 was descriptively evaluated. Data were analyzed by nonresponder imputation with multiple imputation. **Results:** 321 pts received UPA15 or PBO (N=209, 112). BL characteristics were balanced between the two groups. Across nearly all subgroups analyzed, rates of sustained remission and sustained complete remission favored UPA15 over PBO, including subgroups based on age, sex, new-onset vs relapsing GCA, history of polymyalgia rheumatica. Response rates in some subgroups showed high variability, potentially due to limited sample sizes. **Conclusion:** In nearly all evaluated subgroups, UPA15 showed generally similar rates of sustained remission and sustained complete remission as observed in the overall population. These results support UPA15 efficacy across the population of pts with GCA.

W11-4

Risk factors of serious infections in patients with giant cell arteritis

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Conflict of interest: None

[Objectives] To investigate the medications associated with serious infections (SI) in patients with giant cell arteritis (GCA). [Methods] Using claims data provided by Medical Data Vision Co., Ltd, we defined individuals as GCA cases if they were diagnosed with GCA between August 2017 and July 2022, prescribed oral corticosteroids (GC) or immunosuppressants for 14 days or more, and were 50 years of age or older at the time of the first prescription (T_0). SI was defined using both ICD10 codes corresponding to infections and implementation of related tests after T_0. Using sex, age, and the time from T_0 to the date of hospitalization, we matched up to five controls for each case. We calculated the odds ratio (OR [95% CI]) using conditional logistic regression analysis for GC, tocilizumab (TCZ), and other immunosuppressants prescribed in the 90 days prior to the date of hospitalization. [Results] Of the 2,171 patients with GCA (63.4% female, mean age 75.5 years), 149 cases and 745 controls were analyzed. The prescription of GC was significantly associated with SI (OR: 2.4 [1.4-4.1]), but that of TCZ was not (OR: 0.9 [0.5-1.5]). [Conclusion] The prescription of GC was significantly associated with SI in patients with GCA.

W11-5

Characteristics of vascular ultrasound findings and transitions to the temporal artery in giant cell arteritis

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Conflict of interest: None

[Objectives] In recent years, US has been recommended as the first choice of imaging examination for giant cell arteritis (GCA), to determine its characteristics and trends. [Methods] Forty-eight patients diagnosed with GCA and undergoing US were included in the study, and US findings were compared with symptoms and imaging findings. The evolution of US findings in patients was also assessed at 1, 3, 6, 12 months after treatment using a four point scale for the halo sign. [Results] US findings correlated with visual impairment in 88.9% cranial (13/3), LV (3/9) and mixed (3/17), number of symptoms (2.18/1.67) and days of diagnosis (166/148), temporal pain (78.1/21.4), jaw claudication (57.6/21/4), visual impairment (36.4/16.3) and CTA (58.6/20), PETCT (50/9.1). The halo sign rating was 116/467 for a diagnostic period (days) of 6/2 points, the number of symptoms 3.0/3.7 and the mean score was 4.42/2.84/1.30/0.46/0.40 at 0/1/3/6/12 months. [Conclusion] US findings were suggested to be associated with visual impairment, temporal pain, jaw claudication, and head CTA and PETCT findings. The halo sign may be stronger the shorter the duration of diagnosis, and the findings disappear six months after the start of treatment.

W11-6

Examination of factors with poor long-term life prognosis in Takayasu arteritis

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Conflict of interest: None

[Objectives] There are few reports of long-term observation of multiple cases for more than 10 years, and we report on a total of 71 cases with a long-term follow-up period of 18.7 years on average. [Methods] We retrospectively analyzed the clinical data of patients with Takayasu's arteritis (N=71) at our hospital. [Results] There were 27 relapses in 14 cases that met Kerr's criteria, and 7 cases had new vascular stenosis that required reconstructive surgery and was negative for CRP and ESR. Although the prognosis for life is good, with a 10-year survival rate of 96% and a 20-year survival rate of 85.2%, 9 patients died an average of 25.4 years after diagnosis, and the majority of deaths were due to infections and vascular complications. In addition, coronary artery lesions unrelated to vasculitis frequently appeared, and in multivariate analysis, cases with cerebral infarction, coronary artery lesions, or severe AR had poor survival prognosis (p=0.00003 Log rank). [Conclusion] While Takayasu's arteritis can cause vascular stenosis and aneurysm even if CRP is negative, MACE is the leading cause of death, and GC-induced arteriosclerosis must be noted. It is necessary to reduce the dose of steroids using biological agents in cases with poor prognostic factors.

W12-1

Treatment responsiveness and prognostic predictors in idiopathic multicentric Castleman's disease and TAFRO Syndrome

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Conflict of interest: None

Background: Idiopathic multicentric Castleman's disease (iMCD) is a rare inflammatory disorder and its precise pathogenesis remains elusive yet. This study aimed to investigate treatment responses in iMCD, as well as TAFRO syndrome. Methods: We collected cases of iMCD-NOS, iMCD-IPL, 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 (20%), iMCD-IPL (43%), iMCD-TAFRO (25%), suspected iMCD (1.9%), UCD (1.4%), and TAFRO syndrome (8.9%). Compared to patients with a CHAP score of less than 2 points, those with a CHAP score of 2 points or higher at 24 months post-PSL initiation had a significantly longer time from PSL administration to TCZ administration ($p<0.001$) and a significantly higher IgG level at diagnosis ($p=0.036$). Conclusion: Early suppression of IL-6 were considered important for improving the prognosis of Castleman's disease. The results also suggest that IgG levels at the time of diagnosis may be a useful prognostic factor.

W12-2

Treatment Course of TAFRO Syndrome and Considerations in ProlongedThrombocytopenia: A Case Series of 7 Patients

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Conflict of interest: None

Objective: To investigate the clinical course of cases of TAFRO syndrome. Methods: We reviewed 7 cases diagnosed with TAFRO syndrome and their treatment from January 2009 to May 2024. Data on history, physical findings, histopathology and treatment were collected. Improvement of each parameter was defined as follows: CRP normalization to negative, renal function improvement to sustained decrease in creatinine levels, platelet recovery to sustained levels above 50,000/μL, and resolution of pleural or abdominal effusion to sustained decrease in body weight or abdominal circumference. Results: The median age of the 7 cases was 61 years (IQR: 51-64.5), with 4 males. Histopathological findings were consistent with iMCD-TAFRO in 6 cases. All cases received glucocorticoids, and immunosuppressive agents were used in combination. The time to improvement for each parameter was as follows: renal function improvement (median: 7.0 days [5.8-9.0]), CRP normalization (23.5 days [16.0-31.3]), resolution of generalized edema (28.5 days [17.8-41.3]) and platelet recovery (48.0 days [43.5-60.0]). Conclusion: Treatment of TAFRO syndrome shows that even with a favorable clinical course, improvement in platelet count may take considerable time.

W12-3

Clinical features and long-term treatment course of TAFRO syndrome

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Conflict of interest: None

[Objective] To clarify the longitudinal clinical course of patients with TAFRO syndrome. [Method] Patients with TAFRO syndrome who visited our hospital between April 2016 and September 2024 were involved. The diagnosis of TAFRO is based on the 2015 criteria from Japanese Ministry of Health, Labour and Welfare. Complete remission (CR) was defined as patients without inflammation and pleurisy/ascites, normal renal function and the platelet count. [Results] Six cases were involved. Median age and follow-up were 53.3 years and 23.3 months, respectively. All were initially treated with glucocorticoid (GC). Of these, 2 were treated with GC alone, 3 were added Tocilizumab (TCZ) alone, the one with TCZ+cyclosporine (CyA). Tacrolimus (Tac), CyA or Rituximab (RTX) were further added to 3 cases. Five were in CR and the time to CR was 7.4 months. Five were survived and 2 had relapse. All survivors needed the continuation of the maintenance for CR. Of the relapsed cases, the one relapsed after treatment discontinuation. And the other partially responded to GC+TCZ+CyA but relapsed and deceased despite of RTX and cyclophosphamide introduction. [Conclusion] Initial response and the continuation of the maintenance may be a determinant for the better long-term outcome of patients with TAFRO.

W12-4

An Observational Study of the Onset of Response to Combination Therapy with Prednisolone and Cyclosporine in TAFRO Syndrome and the Number of Days to Platelet and Serum CRP Normalization

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Conflict of interest: None

[Objectives] Treatment with prednisolone (PSL) and cyclosporine A

(CYA) is said to be effective in TAFRO syndrome, but it often takes time for the effect to develop. The purpose of this study is to determine the number of days until the onset and normalization of the therapeutic effect on platelets and serum CRP after the start of each drug. [Methods] Of the 8 patients diagnosed with TAFRO syndrome in our department from December 2015 to September 2024, in 7 patients treated with PSL and CYA, the number of days from the start date of each drug to the improvement of serum CRP and platelet count and other parameters in the medical record Investigation. [Results] CYA was initiated at a mean of 9 days after the start of PSL treatment; platelet count showed an upward trend at a mean of 40 days after the start of PSL treatment and rose to the reference range (≧ 145,000/μL) at a mean of 66 days. As for serum CRP, there was a decreasing trend at a mean of 7 days after the start of PSL treatment, and it improved to <1 mg/dL at a mean of 31 days. [Conclusion] In TAFRO syndrome, normalization of platelet counts and reduction of serum CRP to <1 mg/dL take an average of 66 days and 31 days, respectively, after initiation of PSL therapy, even when PSL and CYA are combined.

W12-5

Long-term efficacy and safety of tocilizumab in patients with idiopathic multicentric Castleman disease: a single-center cohort study

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Conflict of interest: None

[Objectives] The efficacy of tocilizumab (TCZ) for the treatment of idiopathic multicentric Castleman disease (iMCD) has been demonstrated in recent years. The aim of this study is to assess the optimal dosage and long-term safety of TCZ in iMCD treatment, along with possible alternatives for patients who are unable to continue TCZ treatment. [Methods] This study is a retrospective analysis of iMCD patients, excluding TAFRO syndrome, treated with TCZ at our institution between January 2010 and June 2024. [Results] 17 iMCD patients satisfied the above criteria. The average age at the time of onset was 46.2±17.5 years, and 5 (29.4%) were women. The average administration period of TCZ was 1731±1246 days, and the dosing interval of intravenous TCZ was less than 2 weeks in 1 case (5.9%), 2-3 weeks in 9 cases (52.9%), and 4-5 weeks in 5 cases (29.4%). 2 cases (11.8%) received weekly subcutaneous TCZ administration. The average CHAP score was 0.1 at the time of final TCZ administration. The incidence of infection requiring hospitalization was 4.4% per person-year. TCZ treatment was discontinued in 3 cases, of which 2 were switched to Janus kinase inhibitors and 1 to rituximab. [Conclusion] Intravenous or subcutaneous TCZ was highly effective in iMCD, with a good long-term safety profile.

W12-6

Successful Treatment of Two Cases of Idiopathic Multicentric Castleman Disease Complicated by IgA Vasculitis with Tocilizumab

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Conflict of interest: None

[Background] Idiopathic multicentric Castleman disease (iMCD) complicated IgA vasculitis is rare. We present two cases of IgA vasculitis associated with iMCD, both successfully treated with tocilizumab (TCZ). [Results] Case 1: A 41-year-old male presented with hypergammaglobulinemia. He exhibited multiple enlarged lymph nodes confirmed iMCD of plasma cell type. He developed petechial purpura on his lower legs, abdominal pain, tarry stools, and renal biopsy confirmed IgA vasculitis. After initial treatment with mPSL pulse therapy and azathioprine, TCZ was introduced at 8 mg/kg/month, successfully maintaining remission. Case 2: A 32-year-old male presented with fever, enlarged cervical lymph nodes, elevated CRP, and hyper IgG. He was diagnosed with iMCD via cervical lymph node biopsy and referred to our hospital. One month prior, he exhibited low-grade fever and petechial purpura. Renal biopsy showed cellular crescentic glomerulonephritis and tubulointerstitial nephritis with IgA deposition, confirming IgA vasculitis. Treatment with mPSL pulse therapy, and TCZ at 8 mg/kg/month improved renal manifestations. [Conclusion] IL-6 plays a major role in the pathogenesis of IgA vasculitis associated with iMCD and TCZ may represent a viable therapeutic option for affected patients.

W13-1

Comparative Analysis of Ozoralizumab and Certolizumab Pegol in Patients with Rheumatoid Arthritis: Insights from the ANSWER Cohort

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Conflict of interest: None

Objectives: Ozoralizumab (OZR) and certolizumab pegol (CZP) are distinctive TNF inhibitors characterized by the absence of an Fc region, setting them apart from conventional anti-TNF agents. This study aimed to evaluate the comparative real-world effectiveness and retention rates of OZR and CZP in patients with rheumatoid arthritis (RA). Methods: Patients with RA in the ANSWER cohort, enrolled between 2002 and December 2023 and treated with either OZR or CZP, were included. Propensity score matching (PSM) accounted for age, prior use of biologics and methotrexate, and CDAI at treatment initiation. Six-month retention rates were examined by the Log-rank test, and changes in CDAI, SDAI, DAS28-CRP, and DAS28-ESR were evaluated. Additionally, a stratified analysis by rheumatoid factor (RF) titer was conducted. Results: Among 478 patients receiving OZR or CZP, 76 (OZR: 38; CZP: 38) were identified by PSM. No significant difference was observed in 6-month retention rates (P=0.407). Changes across all disease activity indices were comparable (all P>0.05). Stratified analysis by RF titer yielded similar results. Conclusion: In real-world settings, OZR demonstrates efficacy comparable to CZP.

W13-2

Tocilizumab injection spacing in patients with rheumatoid arthritis in daily clinical practice

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Conflict of interest: None

[Objectives] To investigate the extended interval of tocilizumab (TCZ) for patients with rheumatoid arthritis in clinical practice. [Methods] Treatments with tocilizumab for RA patients were entered in this study from RA clinical database of our hospital (SUNSET registry). Administration at intervals 1.5 times or more longer than the usual interval was considered intentional extensions in this study. [Results] Four hundred twenty-five treatments with TCZ in RA patients which started between 2008 and 2020 were examined. Three hundred and thirty -six (79.1%) patients were female, the average age at the start of treatment was 60.2 years, and the average disease duration was 10.3 years. In 112 treatments (26.3%), injection interval was tried to extend with shared decision making. The longest extension period was 8 weeks for intravenous infusion of TCZ and

4 weeks for subcutaneous injection. Of the 253 treatments that were continued for one year, 84 treatments (33.2%) were extended. [Conclusion] TCZ suppresses C-reactive protein production in liver and those blood concentration can be estimated relatively easily. In the RA patients who have achieved and sustained clinical remission, extending the administration interval is considered useful.

W13-3

Efficacy in patients with rheumatoid arthritis treated ozoralizumab in daily clinical practice (Second Report)

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Conflict of interest: None

[Objectives] We investigate the real-world efficacy of ozoralizumab (OZR) in clinical practice. [Methods] We conducted a retrospective survey of 19 RA patients receiving OZR, and examined the patient demographics, disease activity, retention rates, and safety at the baseline, 4, 12, 24, 52 weeks. [Results] Among the 19 patients (18 females), the mean age was 71±2 years, with an average disease duration of 11±2 years. 74% received methotrexate at a dose of 7.1±0.8 mg/week. Included 14 naïve cases and 3 cases with prior treatment with three or more b/tsDMARDs. Baseline disease activity scores were as follows: DAS28 4.2±0.4, SDAI 17±2, mHAQ 0.5±0.1, and RF 170±61 U/mL. The average treatment duration was 19±3 months. Proportion of patients achieving low disease activity or less, based on SDAI, was 25%, 53%, 79%, 70%, and 100% at weeks 0, 4, 12, 24, and 52, respectively. Patients with higher baseline RF levels (≧163 U/mL) showed initially elevated SDAI scores, though differences between high and low RF groups were no longer apparent from week 4 onwards. The 24-week retention rate was 72%, with three cases of inefficacy, and two adverse events (herpes zoster and urinary tract infection). [Conclusion] OZR demonstrates effectiveness even in patients with high RF levels.

W13-4

Effect of ozoralizumab in elderly patients with Rheumatoid arthritis

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Conflict of interest: None

[Purpose] We examined the efficacy and safety of osoralizumab in patients with rheumatoid arthritis. [Methods] 51 patients who treated with ozoralizmab were included. We examined the duration of illness, concomitant medications, presence or absence of prior treatment, complications, and reasons for discontinuation of ozoralizumab about 34 patients in the continuation group (Group A) and 17 patients in the discontinuation group (Group B). We also examined the retention rate for people under 65 years of age (Group 1), 65 to 80 years old (Group 2), and 80 years old and older (Group 3). [Results] The mean age was 75.6±11.9 years in Group A, 73.3±10.2 years in Group B, duration of illness was 100.7±99.5 days, 145.4±169.3 days, CRP at baseline: 1.96±2.79 mg/dl, 2.71±4.6 mg/ dl and SDAI: 19.7±10.9, 25.2±12.1 and JHAQ was 1.75±0.9 and 1.54±1.2. By age, the number of continuing cases was 5/8 (62.5%) in Group 1, 14/24 (58.3%) in Group2, and 15/19 (78.9%) in Group 3. The concomitant rate with MTX and PSL, and the incidence of severe adverse events were not different among the Group 1-3. [Conclusion] In the elderly patients, the continuing rate of treatment with ozoralizumab was higher than young patients. It seemed to be considered as one of the treatment options for the elderly patients.

W13-5

Comparison of the effects of sarilumab and JAK inhibitors on PRO in patients with rheumatoid arthritis: 1-year evaluation using RAPID3

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Conflict of interest: Yes

[Objectives] To compare the effects of sarilumab (SAR) and JAK inhibitors (JAKi) on patient-reported outcome (PRO) in rheumatoid arthritis (RA) patients treated at our hospital. [Methods] We compared the effects of (SAR) (68 cases) and JAKi (96 cases [baricitinib: 33 cases, upadacitinib: 33 cases, filgotinib: 30 cases]) on PRO in RA patients at our hospital. we evaluated PRO using RAPID3 at baseline, 2 weeks, 1, 2, 3, 6 months and 1 year, and compared ΔRAPID3 and the proportion of patients with meaningful improvement. [Results] The mean ΔRAPID3 values for SAR/JAKi were -2.69/-2.56 at 2 weeks, -4.07/-3.86 at 1 month (M), -6.37/-4.62 at 3M, -7.14/-4.86 at 6M, -6.55/-5.11 at 1 year, and in both groups, there was a significant decrease at each evaluation point after 2 weeks ($P<0.001$ for respective points after 2 weeks). There was no significant difference between the SAR and JAKi groups at any point. The percentage of patients with meaningful improvement in the SAR/JAKi groups was 29/27 at 2 weeks, 44/37 at 1M, 54/46 at 3M, 59/49 at 6M, and 56/49 at 1 year, and the percentage of improvement increased over time in both groups, with similar rates in both groups. [Conclusion] SAR is expected to have the same effect as JAKi in improving PRO quickly and maintaining that improvement.

W13-6

A study on the selection of b/tsDMARDs for rheumatoid arthritis patients in our hospital

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Conflict of interest: None

Objective: We investigated the efficacy and safety of b/tsDMARDs in patients who selected b/tsDMARDs in Phase 2 and thereafter, although in actual clinical practice, treatment is conducted in accordance with various Recommendations and guidelines. Methods: From July 2013, when JAK inhibitors became available, to March 2024, we investigated 712 patients who started b/tsDMARDs at our hospital and were followed up for at least 6 months. Results: 1) IL-6 receptor inhibitors and JAK inhibitors showed higher CDAI remission rates at 6 months and continuation rates at 1 year, and 24.3% of patients were shifted to the second drug due to insufficient response. 2) 72.3% of patients were switched to a drug with a different mechanism of action in the second drug. 3) The transition rate for D2TRA patients (inadequate response to 2 drugs) was TNF inhibitor > ABT > IL-6 receptor inhibitor > JAK inhibitor, and the efficacy of the third drug was higher for IL-6 receptor inhibitors and JAK inhibitors. Conclusion: The efficacy and persistence rates of IL-6 receptor inhibitors and JAK inhibitors in the first-line treatment were high, and it is important to select from IL-6 receptor inhibitors and JAK inhibitors to reduce the transition to D2TRA patients.

W14-1

Efficacy of Azathioprine as Maintenance Therapy for IgG4-Related Disease

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Conflict of interest: None

[Objectives] Appropriate maintenance therapies to be used alongside steroids for IgG4-related disease (IgG4-RD) have not been clearly established. We evaluated the efficacy of azathioprine (AZP) in this context. [Methods] A retrospective analysis was performed on cases of IgG4-RD diagnosed at our institution, where AZP was used alongside prednisolone (PSL). We compared two groups: a continuation group (group C: who were able to continue AZP) and a discontinuation group (group D: who stopped AZP due to adverse events). We evaluated relapse during the fol-

low-up period, whether PSL could be discontinued and the dose at the last visit. [Results] A total of 25 cases (M: F=21:4, median age 65 years) were analyzed, with 16 in the group C and 9 in the group D. In the group D, 5 cases switched to other drugs (RTX in 1 case, MTX in 3, and MMF in 1). No relapses occurred in the group C, while 3 relapses were observed in the group D. At the final evaluation, 11 patients in the group C were able to discontinue PSL, compared to 3 in the group D, with median doses of 0 mg and 3 mg, respectively (p=0.0525). [Conclusion] The continuation group experienced no relapses and showed a trend toward greater steroid reduction or discontinuation. AZP may be an effective maintenance therapy for IgG4-RD.

W14-2

Hypocomplementemia in IgG4-related kidney disease (IgG4-RKD) is associated with rapid improved renal function after glucocorticoid induction therapy

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Conflict of interest: None

[Objectives] To compare the response to glucocorticoid (GC) induction therapy in IgG4-related kidney disease (IgG4-RKD), with and without hypocomplementemia. [Methods] We retrospectively examined the degree of improvement of estimated glomerular filtration rate (eGFR; ml/min/1.73 m2) during the initial 1 month of GC induction therapy in 54 patients with IgG4-RKD, collected from the institutions associated with IgG4-RKD working group between April 2012 and May 2019, with reference to the presence of hypocomplementemia. [Results] Among 54 patients with IgG4-RKD treated with GC, hypocomplementemia was evident in 72%. Although the estimated glomerular filtration rate (eGFR; ml/min/1.73 m2) before GC therapy and the initial dose of GC did not differ significantly between the groups, the degree of improvement of eGFR during the initial 1 month of GC therapy (eGFR at 1 month after GC therapy minus the pretreatment eGFR) was significantly higher in the HC group (6.1 vs. 0.9, p=0.01). Levels of CH50 and C4 were inversely correlated with the degree of improvement of eGFR during the initial 1 month of GC therapy (p=0.03). [Conclusion] Hypocomplementemia in IgG4-RKD was associated with rapid improved renal function after GC induction therapy.

W14-3

Factors associated with relapse in 45 patients with IgG4-related disease in our department

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Conflict of interest: None

[Objectives] We longitudinally assessed Responder index (RI) in patients with IgG4-related disease (IgG4-RD) in our department and investigated factors associated with relapse. [Methods] We enrolled patients between 1 April 2021 and 30 September 2024, and assessed RI at diagnosis, month 1, 3, 6, 12, 24 and 36. [Results] We enrolled 45 patients (47% female) with median age of 65 (54-71) years. Twenty-three patients received prednisolone (PSL) 0.6 mg/kg/day (group A). During 24 (6-36) months, RI decreased (p=0.009) and 4 patients (17%) relapsed. Four patients received PSL 0.2-0.3 mg/kg/day (group B). During 36 (36-36) months, RI did not decrease (p=0.152) and 3 (75%) relapsed. Eighteen patients were followed without PSL (group C). During 18 (2-33) months, RI did not decrease (p=0.787), 8 (44%) relapsed and 6 (33%) required PSL. Relapse rate was higher in group B and C than in group A (p=0.046, p=0.044). In group A, relapse rate tended to be lower in patients with normal serum IgG4 level at month 6 (p=0.084). In group C, serum IgG4 level at diagnosis was associated with relapse (p=0.042) and serum IgG4 level was longitudinally elevated in relapsed patients (p<0.001). [Conclusion] Serum IgG4 level at diagnosis, along with its longitudinal assessment, may be useful in predicting relapse.

W14-4

Clinical course of six cases of IgG4-related disease treated with rituximab

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Conflict of interest: None

[Objective] IgG4-related disease (IgG4RD) is a chronic systemic fibro-inflammatory disease. Treatment of IgG4RD includes various immunosuppressants for glucocorticoid (GC) sparing and organ lesion. Although rituximab (RTX) has been reported effective, RTX for IgG4RD is not approved and few cases have been reported in Japan. We herein report all IgG4RD cases treated with RTX at our department. [Methods] We reviewed the medical records of all IgG4RD cases treated with RTX at our department from Apr 2015 to Sep 2024. IgG4RD responder index (RI), serum IgG4 and daily GC dose were compared before and 1, 3, 6, 9, 12 mo after RTX. RTX use was authorized by relevant boards in our hospital. [Results] Six cases (all males, age at diagnosis: 66 yrs old, duration at first RTX: 1.5 yrs, serum IgG4: 864 mg/dl, RI: 18.2 (mean)) were extracted. After RTX initiation, 5 followed good course and 1 relapsed. At 12 mo, RI was 3.8, serum IgG4 was 108 mg/dl, and daily GC dose was 6.8 mg PSL/day (mean). No hospitalization due to adverse events were observed within 1 yr. [Conclusion] We report up to 1-year follow-up of 6 IgG4RD cases treated with RTX. 5 followed good course with improving RI and serum IgG4.

W14-5

Clinical characteristics and outcomes of IgG4-related disease without therapeutic intervention

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Conflict of interest: None

[Objectives] To clarify the clinical features and outcomes of IgG4-related disease (IgG4-RD) patients without therapeutic intervention. [Methods] IgG4-RD patients at our institution were included. Clinical indicators, laboratory findings and IgG4-RD Responder Index (IgG4-RD RI) were retrospectively collected. Among the cases who were followed up without therapeutic intervention, we analyzed the clinical features of those who subsequently required treatment. [Results] Of the 80 patients, 54 were immediately treated and 26 were followed up without treatment. Patients who were followed up were younger and had significantly lower CRP and IgG levels, sIL-2R levels, and IgG4-RD RI. Most follow-up cases had only glandular and lymph node involvement. 7 required therapeutic intervention after follow-up, and there was no significant difference in clinical features at diagnosis compared with the 19 that could be followed up. 5 cases had new organ lesions at the time of therapeutic intervention. The mean time to the start of treatment was 30±25 months, and IgG4 levels were elevated at the time of treatment in 5 cases compared to when diagnosed. [Conclusion] The clinical indicators of cases that required treatment after follow-up were not unique. Monitoring of organ lesions is important in all cases.

W14-6

Evaluation of the Safety, Efficacy, and Mechanism of Action of Obexelimab for the Treatment of Patients with IgG4-Related Disease: An Open-Label, Single-Arm, Single-Centre, Phase 2 Pilot Trial (Encore presentation)

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Conflict of interest: Yes

[Objectives] Obexelimab (OBX) is a bifunctional, non-cytolytic, humanised monoclonal antibody that binds CD19 and FcγRIIb inhibiting B cells, plasmablasts and CD19-expressing plasma cells. Phase 2 NCT 02725476 trial evaluated efficacy and safety of OBX in active IgG4RD. We evaluated the efficacy, safety and pharmacodynamic effects of OBX in active IgG4RD. [Methods] A single-centre, open-label, single-arm Ph2 trial was conducted at Massachusetts General Hospital. 15 patients aged 18-80 years with IgG4RD responder index (RI) ≧3 received OBX (5 mg/kg IV every 2 weeks for 24 weeks). Pts on glucocorticoids (GCs) discontinued them within 2 months. Primary endpoint was a decrease of ≧2 in IgG4-RD RI at day 169. [Results] 12 (80%) pts met the primary endpoint, 14 (93%) were responders. 8 (53%) achieved complete remission (IgG4-RD RI score of 0). B-cell and plasmablast reductions were observed but rebounded post-treatment. No apoptosis was seen in B or T cells, though B-cell receptor signaling was impaired. 13 pts (87%) reported adverse events, one leading to discontinuation. [Conclusion] OBX was well tolerated and demonstrated clinical response in most patients with rapid rebound of B cells with treatment discontinuation. Findings support further development of OBX in ongoing Ph3 trial.

W15-1

The efficacy and glucocorticoid dose-reduction effect of anifrolumab in patients with systemic lupus erythematosus

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Conflict of interest: None

[Purpose] To evaluate the efficacy and glucocorticoid (GC) dose-reduction effect of anifrolumab (ANI) in patients with systemic lupus erythematosus (SLE) in our institute. [Methods] Medical records of 46 SLE patients who had received ANI and had been observed for at least 1 year were retrospectively analyzed. [Results] The average age was 45.9 ± 14.2 years. Clinical features at baseline were as follows; skin rash in 12 cases, proteinuria in 10 cases, arthritis in 9 cases, fatigue in 8 cases, neuropsychiatric lesions in 1 cases. Average anti-ds-DNA antibody titer was 123.6 ± 58.9 U/ml, and average SLEDAI-2K was 5.6 ± 3.4. ALL patients received prednisolone (PSL) and the average dose of PSL was 10.8 ± 13.3 mg/day. After 12 months from the commencement of ANI administration, SLEDAI-2K decreased significantly to 1.1 ± 1.8 and anti-ds-DNA antibody titer decreased significantly to 15.0 ± 25.9 U/ml. In addition, the average dose of PSL could be lowered to 4.5 ± 3.1 mg/day significantly. The continuation rate of ANI was 71%. Thirteen cases discontinued ANI; ineffectiveness in 10 cases, infection in 2 cases, and remission in 4 cases. No serious adverse events were seen during the observation period. [Conclusion] ANI could improve SLE disease activity and reduce the dose of GC.

W15-2

Clinical Characters in Patients with Systemic Lupus Erythematosus treated with Anifrolumab

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Conflict of interest: None

[Objectives] To evaluate the clinical characteristics, efficacy and tolerability in SLE patients treated with anifrolumab (ANF). [Methods] We retrospectively evaluated 1) their baseline characteristics, 2) the relative changes in dose of PSL and laboratory data, and 3) the tolerability and the adverse events in cases of SLE treated with ANF in University of Tsukuba Hospital. [Results] 1) We identified 4 male and 16 female cases. Mean age and disease duration were 44.0±12.8 years old, and 154.6±130.5 months. ANF was started for remission induction in 4 cases., HCQ and immunosuppressive drugs were concomitantly used in 15 and 14 cases, respectively. 2) The mean dose of PSL was 10±10.1 mg/day at baseline, and significantly reduced at 3, 6 and 9 months after starting ANF. Titer of anti-dsDNA antibody was also decreased at 3 and 6 months compared with baseline. 3) Mean treatment duration of ANF was 11.9 months, and the continuation rate at 1 year was 75%. Adverse events were fever in 1 case, infections in 6 cases and lymphoma in 1 case. ANF was terminated in cases with fever and lymphoma. [Conclusion] Our observations suggested that ANF is effective in cases with SLE in daily clinical practice, while prompted us to pay attention to adverse effects during the treatment with ANF.

W15-3

Effectiveness of Glucocorticoid-Sparing Effect of Anifrolumab (ANF) in Maintenance Therapy in Systemic Lupus Erythematosus (SLE) Patients

Kodai Ueno[1], Shigeru Iwata[1], Ryo Matsumiya[1], Takashi Kato[1], Yuta Shimomura[1], Takeru Sonoda[1,2], Taro Nishikawa[1], Takao Fujii[1]
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Conflict of interest: None

Objective: To evaluate the efficacy and safety of ANF in remission maintenance therapy for SLE. Methods: This retrospective observational study involved patients with SLE on maintenance therapy, defined as a SELENA-SLEDAI score <10 and low-dose glucocorticoids (GC) (≦0.2 mg/kg/day). 28 patients received ANF as maintenance therapy, with 17 patients observed over 52 weeks. The primary outcome was GC dose at 52 weeks, and adverse events were evaluated using the CTCAE. Results: Patients' mean age was 41.1±13.6 years, with a disease duration of 71.3 ±53.9 months. GC dosage decreased significantly from 6.4±2.0 to 2.6±2.6 mg/day (p=0.0007) at 52 weeks. SELENA-SLEDAI scores improved from 4.5±2.0 to 2.1±2.3 (p<0.001), and no flares were observed. No CTCAE grade 3 or higher adverse events occurred. Importantly, no disease flares (SELENA-SLEDAI score >4) or severe adverse events (grade 3 or higher) were observed during the study. Conclusion: ANF in remission maintenance therapy for SLE reduced GC requirements and improved disease activity, showing potential benefits even for patients unresponsive to belimumab.

W15-4

Switching from belimumab to anifrolumab in patients with systemic lupus erythematosus: real world use and efficacy

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Conflict of interest: None

[Objectives] We aimed to examine the characteristics and outcomes

among patients with systemic lupus erythematosus (SLE) who experienced switching from belimumab (BEL) to anifrolumab (ANI). [Methods] Participants in this study were patients with SLE who received belimumab between 2018 and 2023 (n=32). Patients treated with continued BEL, discontinued BEL, and swictching from BEL to ANI were assigned to BEL group (n=12), discontinuation group (n=8), and ANI group (n=8), respectively. Patients who treated BEL within 3 months were excluded (n=4). We compared the clinical parameters among these groups. [Results] Patients in ANI group were younger than those in other groups. Higher rates of skin, articular, and neuropsychiatric manifestations and higher scores of SLEDAI-2K were observed in ANI group than in other groups. Patients with kidney involvement and positive results for anti-DNA antibodies were frequently observed in BEL group. Improvement of SLEDAI, glucocorticoid reduction, and achievement of LLDAS were observed in most of the patients in ANI group. [Conclusion] ANI can show the efficacy for the patients who exhibited no response to belimumab.

W15-5

Investigation of clinical predictors at the start of anifrolumab treatment associated with fatigue at 24 weeks after treatment for SLE

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Conflict of interest: None

[Objective] We investigated the clinical characteristics at the start of Ani administration that correlate with fatigue at 24 weeks after administration in SLE patients. [Methods] We investigated the relationship between blood/urine tests, SLEDAI, PRO indicators before the start of Ani, and Fatigue VAS at 24 weeks for 23 out of 29 cases treating Ani for SLE in our department. [Results] In univariate analysis, Fatigue VAS at 24 weeks after the start of Ani was significantly correlated with C4 (r=0.435, p=0.043), urinary WBC count (r=0.436, p=0.038), urinary RBC count (r=0.534, p=0.009), PGA (r=0.55, p=0.010), and Fatigue VAS (r=0.715, p=0.001) at the start of treatment. Further multivariate regression analysis identified baseline Fatigue VAS as the only significant predictor of fatigue at 24 weeks (r=0.57, SE=0.14, t=4.09, p=0.0009). [Conclusion] When using Ani for SLE, baseline fatigue level was identified as the primary predictor of fatigue at 24 weeks, while other clinical factors, including various blood and urine markers and disease activity indices like SLEDAI, were less effective in predicting fatigue levels at this point. The findings suggest that the stronger the baseline fatigue, the more likely it is to persist at 24 weeks.

W15-6

Current status of anifrolumab treatment for systemic lupus erythematosus at our hospital

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Conflict of interest: None

[Objectives] The purpose of this study is to determine the efficacy and safety of anifrolumab (ANI) in systemic lupus erythematosus (SLE) patients in clinical practice. [Methods] SLE patients who were observed for 24 weeks after induction of ANI at our hospital were included, and disease activity (SLEDAI-2K, LLDAS achievement rate, dsDNA antibody titer, serum complement titer), glucocorticoid (GC) dose per day (prednisolone equivalent), and adverse events were retrospectively analysis was performed. [Results] Eighteen patients were included; 16 were female, age 43.2±11.1 years, disease duration 12.3±7.6 years, SLEDAI at induction 7.4±5.4. The concomitant medications were GC alone 11.1%, GC+hydroxychloroquine (HCQ) 11.1%, GC+immunosuppressant (IS) 22.2%, HCQ+IS 5.6%, GC+HCQ+IS 50.0%, and GC dose was 6.6±7.3 mg/day. At 24 weeks, SLEDAI 2.11±2.13, significantly decreased ($p<0.01$), GC dose per day tended to decrease to 3.8±2.8 mg/day (p=0.32), and 11 patients achieved LLDAS. Adverse events were observed in 9 patients: COVID-19 in 5 patients, herpes zoster in 3 patients, and influenza in 2 patients. [Conclusion] ANI was effective in improving disease activity and reducing GC. Viral infections should be noted. We report the results, including the association with changes in interferon signatures.

W16-1

The change of treatment and effectiveness of Gold Sodium Thiomalate (GST) over 20 years: considerations for supply instability

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Conflict of interest: None

Objective: Gold Sodium Thiomalate (GST) is an antirheumatic drug approved for manufacture in 1970. Despite the advent of b/tsDMARDs, GST remains beneficial for some patients. However, concerning about its unstable supply, this study aimed to investigate the usefulness of GST over 21 years. **Methods:** We performed a retrospective analysis of RA patients registered in NinJa database at Sagamihara hospital from 2002 to 2022. We compared backgrounds and outcomes between GST and non-GST groups. **Results:** GST usage (GST users / total registrations) declined from 13.5% (184/1364 cases) in 2002 to 1.0% (22/2151 cases) in 2022. Initially, GST was used in the patients with better disease activity, physical function, and stage compared to non-users, but this reversed over time. Age, RF, and CCP antibody levels were similar between groups. GST users had longer RA disease durations but lower hospitalization rates, especially for infections. Some patients with serious histories used only GST for safety, while others improved on resuming GST after worsening with other DMARDs. **Discussion:** GST is often continued in patients at high infection risk or those stable on monotherapy, highlighting its clinical and economic value. **Conclusion:** GST has shown unique clinical utility over time.

W16-2

Evaluation of Neutrophil-to-Lymphocyte Ratio as a Predictor of Efficacy for Biologic Agents and JAK Inhibitors in Patients with Rheumatoid Arthritis: The ANSWER Cohort

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Conflict of interest: None

[Objectives] In the treatment of rheumatoid arthritis (RA), the neutrophil-to-lymphocyte ratio (NLR) has been reported as an indicator of disease activity. This study aimed to compare the drug retention rates based on initial NLR values in patients starting b/ts DMARDs. [Methods] We extracted data from the ANSWER Cohort, targeting 776 RA patients with moderate or higher disease activity (CDAI >10) who started treatment with b/ts DMARDs after 2013. Patients were categorized into high and low NLR groups at baseline, and the study analyzed the progression of CDAI and 2-year retention rates for each drug type: TNFi, IL-6R inhibitors, CTLA4-Ig, and JAKi. [Results] The high NLR group showed signifi-

cantly higher CDAI scores than those in the low NLR group (P=0.004), and the rate of concomitant GCs use was also higher (p<0.001). A multivariate Cox proportional hazards model adjusting for background factors showed that, compared to TNFi, IL-6R and JAKi demonstrated significantly higher retention rates sue to ineffectiveness in the high NLR group (HR=0.52, HR=0.35), though there was no significant difference with CTLA4-Ig (HR=0.79). [Conclusion] In RA patients with high NLR at the start of b/ts DMARDs, IL-6R inhibitors and JAK inhibitors demonstrated higher retention rates.

W16-3

Investigation of backgrounds of rheumatoid patients initiated on Tacrolimus in our hospital

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Conflict of interest: None

[Objectives] This study aimed to investigate patients newly introduced to TAC at our hospital and to evaluate the background and clinical effectiveness of TAC in real-world settings. [Methods] Patients who were newly started on TAC from April 2021 to April 2024 were included in this study. The main outcome measure was CDAI at weeks 0, 4, 12, and 24 following TAC initiation. We also examined reasons for TAC selection and for adverse event-related discontinuation, analyzing the patients based on MTX co-administration and by treatment phase. [Results] A total of 94 cases were reviewed. The primary reason for TAC selection was limitations in MTX use, accounting for 79.8% of cases. Among these cases, respiratory disorders were noted in 25.5%, liver disorders in 24.5%, followed by gastrointestinal and lymphoproliferative disorders. [Conclusion] TAC demonstrated a certain degree of efficacy in both the MTX combination and non-combination groups. These findings suggest that TAC could be a viable treatment option when MTX is contraindicated due to respiratory infections. Additionally, TAC showed consistent utility across all phases, indicating its potential as an alternative treatment option when biological agents cannot be used.

W16-4

Challenges of Hospital-Clinic Cooperation at Our Hospital Based on a Post-Hoc Analysis of Glucocorticoid Use in Rheumatoid Arthritis Treatment

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Conflict of interest: None

[Objectives] To explore the challenges of hospital-clinic cooperation in RA treatment through a post-hoc analysis of glucocorticoid (GC) administration results. [Methods] The study included 446 RA patients who visited the hospital between January and March 2020 (P1) and continued until January to March 2023 (P2). The relationship between GC administration results and referral status was analyzed. [Results] In P1, 122 patients received GC treatment. In P2, this number decreased to 67 (54.7%), with the dosage reducing from 4.4±3.3 mg to 2.3±2.7 mg. DAS28 scores were similar in both periods (2.3±0.92 in P1 and 2.01±0.84 in P2). In P1, 20 referred patients (16.3%) had higher GC dosages, older RA onset age, and higher DAS28 scores compared to non-referred patients. Their disease duration was shorter. Methotrexate was given to 8 patients (40%) at a lower dosage compared to non-referred patients, with no biological agents or JAK inhibitors administered. In P2, 13 out of 67 patients taking GC were referred patients (19.4%). [Conclusion] The number of patients taking GC decreased by about half in P2, but reducing the number of referred patients was challenging. Improving regional RA treatment requires promoting the RA treatment algorithm and strengthening cooperation efforts.

W16-5

The efficacy and safety of switching from oral MTX to subcutaneous injection in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of switching from oral MTX to subcutaneous injection in RA patients in real world clinical practice. [Method] The study included 42 RA patients who had been treated with Metoject in our department for 6 months after its approval in September 2022. [Results] The primary endpoint, retention rate after 6 months was 83.3%. 32/44 patients switched from oral to subcutaneous injection. After switching from oral MTX 11.2 mg/week, the maximum dose of Metoject was 12.3 mg/week. Adverse effects improved in 5/32 cases, and side effects newly appeared in 13/42 cases. In cases with improvement, gastrointestinal symptoms were alleviated, as well as alopecia, liver damage, and dysgeusia. In cases with newly appeared side effects, MTX dosage were increased after the change (10/13 cases). Adverse events commonly seen with MTX, which quickly improved with a reduction in dosage. In 16/32 cases where the drug was changed from oral to subcutaneous injection without changes other than MTX, DAS28-ESR, CDAI, and SDAI improved at 6 months. [Conclusion] By switching from high-dose oral MTX to subcutaneous injection, further efficacy and reduction in side effects are expected. However appropriate reduction in dose is necessary if adverse events occur.

W16-6

Investigation of Initial Treatment Strategies in MTX-Ineligible Patients in the ANSWER Cohort

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Conflict of interest: None

Objective: This study evaluates the effectiveness of conventional synthetic DMARDs (csDMARDs) other than methotrexate (MTX) in RA patients unable to use MTX, comparing outcomes between those needing biological DMARDs (bDMARDs) or JAK inhibitors (tsDMARDs) and those managed without them. **Methods:** 426 patients from the ANSWER registry, diagnosed within 2 years, were analyzed. All began csDMARDs without MTX and maintained treatment for 12 months. The main outcome was the initiation of b/tsDMARDs within 12 months, comparing patients who added csDMARDs within 3 months to those who did not. Propensity score matching and Log-rank testing were used for analysis. **Results:** Patients adding csDMARDs within 3 months had a higher b/tsDMARDs initiation rate and higher DAS28 scores, indicating greater disease activity. **Conclusion:** For patients unable to use MTX, early addition of b/ts DMARDs within 3-6 months often proves necessary for effective RA control, underscoring the need for timely treatment escalation.

W17-1

Analysis of factors associated with Upadacitinib-effective patients with Japanese rheumatoid arthritis: A Multi-Center Observational Study in Niigata Prefecture (SELECT-NIIGATA study)

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Conflict of interest: None

[Objectives] This study examined factors related to upadacitinib (UPA) efficacy in Japanese rheumatoid arthritis (RA) patients through a multi-center observational study in Niigata Prefecture. [Methods] Data from 112 RA patients (23 males, 89 females) who began UPA between November 2020 and June 2023 were analyzed for patient background, treatment response at 52 weeks, continuation rates, and adverse events. [Results] The average patient age was 65.7±9.5 years, with a disease duration of 13.6±7.9 years. Rheumatoid factor positivity was 62.5%, and anti-CCP antibody positivity was 72.3%. Of the patients, 40 used prednisolone (PSL), 58 used methotrexate (MTX), 37 were naïve to biologics/JAK inhibitors, and 40 had prior exposure to two or more agents. Anti-CCP antibody-positive patients had higher continuation rates (91.4% vs. 78.4%, p=0.036). Continuation was also higher in patients using MTX at ≧8 mg (100% vs. 81.6%, p < 0.01). The good EULAR response group had higher initial platelet counts. Logistic regression confirmed this association (OR 1.12, p=0.0163) after adjusting for age, sex, anti-CCP antibodies, and MTX dose. [Conclusion] UPA with MTX may enhance continuation rates, and higher platelet counts are potential markers of treatment response in RA.

W17-2

Analysis of efficacy, safety and related factors in 450 cases of rheumatoid arthritis treated with JAK inhibitors -Study in the rheumatoid arthritis cohort FIT-RA-

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Conflict of interest: None

[Objectives] To clarify the efficacy and safety of JAKi for RA. [Method] We investigated the background, treatment response, and adverse events of 450 RA cases using JAKi registered in the FIT-RA. Factors related to low disease activity and remission at 6, 12, and 24 months were explored using multivariate logistic regression analysis. The number of each adverse event was compiled and associated factors were explored using COX regression analysis. [Results] The mean age was 65, 82% were female, the mean disease duration was 182 months, and the use rates of MTX and PSL were 51% and 50%, and D2TRA was 46.9%. Logistic regression analysis showed that for SDAI at 6 and 12 months, only high SDAI at 0 month were associated with low disease activity and remission (OR 0.93 and 0.93), but for SDAI at 24 months, high SDAI at 0 month and D2TRA were associated factors (OR 0.93 and 0.46). The number of adverse events [EAIR] was 17 severe infections [1.8], 52 herpes zoster [6.0], 20 malignant tumors [2.1], 11 MACE [1.2], and 1 DVT/PE [0.11]. Age was associated with a lower risk of severe infection and herpes zoster (HR 1.05, 1.04), and female was associated with a lower risk of malignant tumors (HR 0.37). [Conclusion] These results suggest the possibility of a reduced effect of JAKi in D2TRA patients.

W17-3

Treatment response in patients with rheumatoid arthritis treated with certolizumab pegol based on rheumatoid factor levels

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Conflict of interest: None

[Objectives] We investigated the certolizumab pegol (CZP) treatment response in 132 patients with rheumatoid arthritis who were enrolled in the Tsurumai Biologics Communication Registry and had initiated the CZP treatment in 2023. [Methods] Our primary endpoints were rheumatoid factor (RF) levels. We focused on 96 patients treated with CZP for > 52 weeks whose DAS28-ESR could be evaluated before and after the treatment. On the basis of the initial RF levels, we divided the patients into the low-RF group (L) (RF < 55; n=42), middle-RF group (M) (55 ≦ RF < 160; n=25), and high-RF group (H) (160 ≦ RF; n=29). We then assessed the CZP treatment response based on the DAS28-ESR results. [Results] The mean changes in DAS28-ESR were the reductions of the scores from 4.49±1.25 to 3.26±1.53 for the L group; from 5.39±1.20 to 3.31±1.33 for the M group, and from 5.28±1.15 to 3.29±1.30 for the H group. All groups exhibited significant improvements at 52 weeks (p<0.05). The magnitude of improvement in ΔDAS28-ESR from the initial values was L group < H group (p=0.04). We observed a significant improvement to a higher extent in patients with high RF levels. [Conclusion] CZP significantly improved DAS28-ESR in patients with high RF levels in a proportional manner.

W17-4

Development of Artificial Intelligence (AI) for Predicting Treatment Outcomes of RA with Molecular Targeted Therapy: The ANSWER Cohort Study

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Conflict of interest: Yes

[Objectives] To develop an AI model for predicting RA treatment outcomes using a large-scale cohort. [Methods] We analyzed 5,309 RA cases treated with molecular-targeted therapies from 2000 to 2024 (TNF inhibitors 54.0%, IL-6 inhibitors 19.0%, CTLA4-Ig 13.4%, JAK inhibitors

13.6%, Bio/JAK naïve 48.9%; age 60.0 years; 82.0% female; disease duration 10.5 years). Patient background served as explanatory variables, and treatment outcomes at 6 months (ineffectiveness, adverse event discontinuation, continuation) were target variables. We used random forest with five-fold cross-validation, splitting data 4:1 for training and testing. Accuracy, sensitivity, and specificity were assessed, and SHAP (SHapley Additive exPlanations) evaluated each variable's contribution. [Results] The model's accuracy was 0.64. Sensitivity/specificity for ineffectiveness, adverse events, and continuation were 0.67/0.43, 0.43/0.75, and 0.38/0.92, respectively. SHAP analysis showed that multiple drug changes and non-use of IL-6 inhibitors predicted ineffectiveness, while age and low body weight were linked to adverse events, and fewer drug changes and lower glucocorticoid doses to continuation. [Conclusion] This AI model's predictions align with clinical reports, supporting its clinical utility.

W17-5

Affects of Janus kinase inhibitor (JAKi) and Abatacept (ABT) on lung involvements in rheumatoid arthritis (RA)

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Conflict of interest: None

Objective: To clarify affects of JAKi and ABT on lung involvements in RA. **Methods:** 78 RA patients for whom JAKi or ABT were introduced between Aug 2013 and Aug 2024, and who were examined by chest CT before and after administration, were enrolled. We retrospectively evaluated, 1) clinical backgrounds, 2) CT findings before administration, 3) change of CT findings after administration, 4) comparison between improvement or no change cases and worsening or new lesion cases in each drug. **Results:** 1) In JAKi group (N=14), CRP at baseline was significantly lower, and frequency and numbers of previous biologics were significantly higher than in ABT group (N=64). 2) The most common lung involvement before administration was ILD (50%) in JAKi group, while ILD (26.6%) and ILD with airway disease (26.6%) in ABT group. However, frequency of each kind of lung involvement was similar between groups. 3) Change of CT findings was no change 78.6% and worsening or new lesion 21.4% in JAKi group, while improvement 6.3%, no change 75.0%, and worsening or new lesion 18.7% in ABT group. 4) Only in ABT group, disease duration was significantly longer in worsening or new lesion cases than in other cases. **Conclusion:** In both JAKi and ABT groups, lung involvements were stable in most cases after administration.

W17-6

Immunogenicity of an Adjuvant Recombinant Zoster Vaccine in Patients With Rheumatoid Arthritis Treated With Upadacitinib: 60-Week Results From a Randomized Substudy

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Conflict of interest: Yes

[Objective] To assess the long-term 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 trial received two RZV doses (at the baseline and wk12). The humoral response and cell-mediated immunogenicity to RZV were evaluated at wk4,16 and 60. [Results] Of the 95 pts who received ≧ 1 RZV dose, 93 (98%) received both RZV doses (mean age (sd): 62.4 (7.5), median exposure (range) to UPA: 3.9 (2.9-5.8) years). At baseline, most patients (91/93) were on MTX and half were taking oral CSs. Five pt discontinued UPA. Satisfactory humoral responses to RZV occurred in 64% [95% CI: 55-74] of pts at wk4, 88% [81-95] at wk16, and 71% [62-81] at wk60. Age and concomitant CS use at baseline did not affect humoral responses at wk60. Over 60% of pts achieved a cell-mediated immune response to RZV at all timepoints. Within 30 days after either RZV dose no serious AEs were reported. Through wk60, 1 event of HZ occurred 4 months after the second RZV dose. [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 wk4, 16 and 60. RZV was well tolerated with no serious AEs reported within 30 days post-RZV vaccination.

W18-1

The impact of pulmonary non-tuberculous mycobacteria on RA treatment

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Conflict of interest: Yes

[Objectives] To clarify the impact of pulmonary non-tuberculous mycobacteria (NTM) disease on RA treatment. [Methods] We retrospectively analysed the treatment outcomes of RA patients who visited our hospital from 2019 to 2024 and were diagnosed with NTM, comparing them with those without NTM, using medical record data. [Results] Of the 1451 cases of RA, 14 were diagnosed with NTM diasese by bacteriological criteria. In RA without NTM, biological DMARDs (bDMARDs) or JAK inhibitors were administrated in 632 cases (43.5%) while RA with NTM patients were treated with bDMARDs in 4 cases (28.6%) with higher disease activity. In bDMARDs treatment group of RA with NTM, all cases were treated with chemotherapy for NTM effectively, allowing the continuation of bDMARDs. All cases in the bDMARDs group had non-cavitary, nodular, or bronchiectatic disease caused by *M. avium* or *M. intracellulare*, while bDMARDs were not administered in cases of cavitary lesions or *M. abscessus* disease. [Conclusion] The administration rate of bDMARDs was lower and the disease activity was higher in RA patients with NTM than in those without NTM, but in RA patients with non-cavitary nodular or bronchiectatic MAC disease, it was possible to treat them with bDMARDs under chemotherapy for NTM disease.

W18-2

Rheumatoid arthritis as an independent adverse prognostic factor in pulmonary nontuberculous mycobacterial disease: a single-center retrospective study

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Conflict of interest: None

Objective: Patients with rheumatoid arthritis (RA) demonstrate an increased prevalence of pulmonary non-tuberculous mycobacterial disease (NTM-PD). Therefore, we examined whether RA alters the prognosis of NTM-PD. Methods: From 2012 to 2021, we conducted a retrospective analysis of the clinical trajectories of 1,116 patients newly diagnosed with NTM-PD at our institution, examining factors such as age, sex, duration of NTM-PD, RA status, NTM-PD classification, presence of pre-existing pulmonary lesions, treatment history for NTM-PD, and clinical outcomes. Prognostic factors associated with NTM-PD were identified through multivariate analysis, and the backgrounds of the RA-NTM and non-RA-NTM groups were adjusted for these variables using propensity score matching. Results: Among the 1,116 patients, 44 (3.9%) were diagnosed with RA-associated NTM. The five- and ten-year survival rates were 91.0% and 83.0 % for the non-RA NTM cohort, respectively, in contrast to 68.1% at both time points for the RA-NTM group, which exhibited a markedly poorer prognosis (p=0.0011). After adjusting for adverse prognostic indicators for NTM-PD, the RA-NTM cohort continued to show a significantly worse prognosis (p=0.0319). Conclusion: RA represents an independent adverse

prognostic factor for NTM-PD.

W18-3

A reconfirmation of the 20-year trend in standardized incidence rates (SIRs) of tuberculosis (TB) in rheumatoid arthritis (RA) patients based on National Database of Rheumatic Diseases in Japan (NinJa) and the analysis of the clinical characteristics of 84 newly developed TB cases

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Conflict of interest: None

[Objectives] In 2021, Japan's TB incidence rate was 9.2 per 100,000 population, making it the long-awaited low-TB incidence country. Is the incidence of TB decreasing in RA patients ? [Methods] We have now re-examined the "20-year trend in SIR of TB in RA patients" from the ***NinJa*** from 2003 to 2022. [Results] Of 221,600 RA patients registered with ***NinJa*** from 2003 to 22, 84 developed TB. The SIR for TB in RA patients was 1.48 for men, 2.06 for women, and 1.51 (95%CI: 1.19-1.83) for all patients. Looking at the two-year trends, it peaked at 3.56 in 2007-08 and decreased to 0.81 in 2021-22. When comparing the SIR for TB in the first decade (2003-12) with the second decade (2013-22), it was 2.72 (1.98-3.46) >1.05 (0.69-1.42). Comparing 84 cases who developed TB (26 men and 58 women) over the first decade with the last decade, the mean age was 66<73 ys, the rate of MTX use was 32.7>28.1%, the rate of biological agent use was 13.5<28.1%, and the incidence of extrapulmonary TB was 21.2<25.0%. [Conclusion] The incidence of TB in Japan is decreasing, and a 20-year prospective study reconfirmed that the SIR of TB in RA patients is also on a downward trend. However, in elderly RA patients using biologics, attention to TB, especially extrapulmonary TB, is still required.

W18-4

Efficacy of abatacept for rheumatoid arthritis complicated with nontuberoculous mycobacterium

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Conflict of interest: None

[Objectives] This study assessed the effectiveness and safety of abatacept (ABT) in rheumatoid arthritis (RA) patients with coexisting pulmonary mycobacterium avium complex (MAC) disease. [Methods] We conducted a retrospective analysis of RA patients with and without pulmonary MAC disease who received ABT as their first biologic treatment. Patient data were collected and reviewed to assess disease activity changes, steroid usage, and treatment continuation. [Results] Thirteen RA patients with pulmonary MAC disease and 203 RA patients without pulmonary MAC disease received ABT. Disease activity score 28-CRP (DAS28-CRP) reduction was comparable between the two groups, with no significant differences in disease activity change or steroid dose reduction. However, ABT continuation rates were lower for patients with pulmonary MAC disease. No significant differences in overall survival after starting ABT were observed between the groups, though case numbers were limited. [Conclusion] Abatacept was effective in reducing disease activity and steroid use in RA patients with pulmonary MAC disease, comparable to RA patients without MAC disease. Further research with more cases is needed.

W18-5

Nontuberculous mycobacterial arthritis as an extrapulmonary lesion in a patient with rheumatoid arthritis

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Conflict of interest: None

[Case] An 64-year-old female patient was diagnosed with rheumatoid arthritis (RA) and maintained long-term remission with methotrexate. At the age of 84, the right wrist arthritis was developed. Magnetic resonance imaging revealed synovitis and tenosynovitis, suggesting an RA flare, leading to the initiation of abatacept (ABT), with subsequent rapid improvement of wrist arthritis. At the age of 85, the arthritis recurred, and intra-articular triamcinolone injections were ineffective. A rapidly enlarging mass subsequently appeared in the right wrist, and radiographs showed bone destruction of the carpal bones. Aspiration yielded yellowish fluid; bacterial cultures were negative, and cytology showed no malignancy. Synovectomy was performed, and cultures identified *Mycobacterium intracellulare*. No other lesions suggestive of nontuberculous mycobacterium (NTM) infection were found, supporting a diagnosis of extrapulmonary NTM infection. ABT was discontinued, and combination antimicrobial therapy was initiated, resulting in clinical improvement. [Clinical Significance] In cases where arthritis worsens or remains refractory despite effective treatment strategies in RA, NTM arthritis should be considered. Prompt diagnosis and treatment are essential to prevent further joint damage.

W18-6

Comparison of glucocorticoid (GC) therapy and JAK inhibitor therapy in patients with PMR (PolyMyalgia Rheumatica)

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Conflict of interest: Yes

[Objective] To compare the treatment outcomes, occurrence of adverse events (AEs), and drug-free rates of patients treated with JAK inhibitors (JAKi) for PMR with those treated with standard GC therapy. [Subjects] Patients with PMR registered at our hospital from January 2013 to September 2024 [Methods] Patients with PMR using JAKi were classified as the J group (Jg), and patients using GC were classified as the GC group (GCg). AEs were defined as proximal femoral vertebral fractures, infections, and other events requiring hospitalization. The time-dependent PMR-AS and GC discontinuation rates in the Jg, as well as the incidence of AEs and drug-free (DF) rates in both groups were compared using chi-square tests. [Results] The Jg, 21 patients (14 men), with a mean age of 76.0 years. PMR-AS decreased significantly after JAKi. All 21 patients were able to discontinue GC after JAKi. The GCg, 91 patients (40 men), with an average age of 77.6 years. The incidence of AEs during 2 years was significantly higher in the GCg (p=0.0389). The DF rate was 39.4% and 29.2%, respectively. [Conclusion] The results of this study suggest that it is easy to switch to JAKi before GC adrenal insufficiency in PMR patients, and that although there is no difference in the DF rate, the toxicity of GC may be avoided.

W19-1

Analysis of chest HRCT findings defined by progressive pulmonary fibrosis in idiopathic inflammatory myopathy-related interstitial lung disease

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Conflict of interest: Yes

[Objectives] The chest high-resolution computed tomography (HRCT) findings in progressive pulmonary fibrosis (PPF) associated with idiopathic inflammatory myopathy-related interstitial lung disease (IIM-ILD) remain unclear. This study evaluated HRCT findings in IIM-ILD patients with PPF and compared these across autoantibody profiles. [Methods] We retrospectively reviewed IIM-ILD patients who met the PPF criteria after

treatment. Two radiologists assessed HRCT findings by consensus. [Results] Of 85 IIM-ILD patients (17 anti-MDA5-positive, 68 antibody-negative), 5 anti-MDA5-positive and 9 antibody-negative (7 anti-ARS-positive) cases met the PPF criteria. All anti-MDA5-positive patients developed PPF within 6 months. No significant differences in fibrotic shadows were found between the groups, but traction bronchiectasis, bronchiolectasis, and ground-glass opacities appeared earlier in the anti-MDA5-positive group (*P*=0.016 and 0.023, respectively). Fine reticulations and reticular coarseness also appeared earlier. [Conclusion] While fibrotic shadows did not differ between groups, fibrotic changes occurred earlier in anti-MDA5-positive patients.

W19-2

Predictors of good Long-Term Prognosis in Patients with ILD-associated anti-MDA-5 antibody-positive dermatomyositis

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Conflict of interest: None

[Objectives] We analyzed the predictive factors for good long-term prognosis in ILD-associated anti-MDA-5 antibody-positive dermatomyositis retrospectively. [Methods] Patients diagnosed with the disease between April 2014 and September 2021 and who completed the 3-year observation period were included. Poor prognosis (PP) was defined as death during the observation period, ILD relapse, difficulty in reducing GC, or HOT, and the other patients were defined as good prognosis (GP). [Results] 49 patients were analyzed, 32 in the GP group and 17 in the PP group (death 9, relapse 3, difficulty in reducing GC 3, HOT 2). Patients in the GP group tended to have fewer systemic symptoms, a lower age, a higher percentage of negative ANA (<40x), and fewer severe illness scores. Multivariate analysis using these factors as explanatory variables revealed that the following factors were predictive of good prognosis: less than one serious illness score (OR=18.9, 95% CI [1.8, 105.4]) and negative ANA (OR=7.4, 95% CI [1.1, 51.7]). A trend test showed that an increase the number of the factors increased the proportion of cases with a good prognosis (p=0.0003). [Conclusion] Negative ANA may be useful as a predictor of good long-term prognosis in this disease.

W19-3

The characteristics and outcome of anti-MDA5 antibody-positive dermatomyositis cases during 7 years in our single center

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Conflict of interest: None

[Objective] To investigate the clinical characteristics and outcomes of patients with anti-MDA5-positive dermatomyositis at our institution. [Methods] We analyzed sex, age, BMI, anti-MDA5 antibody, serum KL-6, ferritin levels, treatment regimen, therapy start days, observation period, and prognosis in patients diagnosed with MDA5-DM from May 2017 to October 2024. [Results] Among 5 MDA5-DM patients (4 males, 1 female), the mean age was 51.4 years, BMI was 24.5 kg/m^2, and mean anti-MDA5, KL-6, and ferritin titers were 2630/2643, 1046/1805 U/mL, and 532.3/1452.1 ng/mL at initial/peak diagnosis, respectively. All patients received steroid and cyclophosphamide pulse therapies with a calcineurin inhibitor, and a fourth immunosuppressive agent (tofacitinib in 4, etanercept in 1) was added. Plasma exchange was also performed in one case. After a 1053-day mean follow-up, the survival rate was 100%, steroid discontinuation was achieved in 40% (2 patients), and anti-MDA5 titer significantly decreased to 95.6 (p=0.04). Femoral head osteonecrosis occurred in 40% (2 patients) after a mean of 174 days post-treatment. [Conclusion] The survival rate for MDA5-DM at our center was 100%. Early initiation of a fourth agent, including biologics or JAK inhibitors, may support successful outcomes.

W19-4

Validation of the MCK model for predicting outcomes in inflammatory myopathy associated interstitial lung disease: A multicentre MYKO cohort study

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Conflict of interest: None

[Objectives] The MCK model, a prognostic tool for interstitial lung disease (ILD) related to idiopathic inflammatory myopathy (IIM), stratifies risk based on anti-MDA5 antibodies, CRP, and KL-6. This study externally validated the model using the MYKO cohort. [Methods] Patients with ILD associated with IIM were categorised into three groups: anti-MDA5 antibody-positive IIM (MDA5-positive-IIM), anti-MDA5 antibody-negative IIM (MDA5-negative-IIM), and anti-synthetase syndrome (ASSD). The MCK score was defined by criteria of CRP≧0.8 mg/dl and KL-6≧1000 U/ml for MDA5-positive cases and CRP≧1.1 mg/dl and KL-6≧1000 U/ml for MDA5-negative cases. Event-free survival for all-cause mortality, flare, and infection requiring hospitalisation were analysed using Kaplan-Meier and Cox proportional hazards models. [Results] In MDA5-negative-IIM, patients with an MCK score of 2 had significantly higher risks for all-cause mortality (HR: 6.94, 95%CI: 1.54-31.2), flare (HR: 3.11, 95%CI: 1.45-6.70), and infection requiring hospitalisation (HR: 7.20, 95%CI: 2.40-21.6). A similar trend was observed in ASSD, but not in MDA5-positive-IIM. [Conclusion] The MCK model effectively predicts outcomes in MDA5-negative-IIM and ASSD within the MYKO cohort but may have limited applicability in MDA5-positive-IIM.

W19-5

Potential for a novel disease classification in myositis-associated interstitial lung disease: Analysis in the JAMI-2R cohort

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Conflict of interest: None

[Objectives] To validate the current criteria for idiopathic inflammatory myopathies (IIM) in a multicenter cohort of myositis-associated interstitial lung disease (ILD) (JAMI) and explore a novel disease classification. [Methods] This study included patients aged >18 years at onset registered in the JAMI-2R database. We stratified the entire cohort and

three subgroups of anti-ARS-positive, anti-MDA5-positive, and anti-ARS/MDA5-negative into those who met the EULAR/ACR criteria or the Ministry of Health, Labour, Welfare (MHLW) criteria and those who did not. We compared cumulative survival rates between the two groups using Log-rank test. [Results] Among 1145 patients, 695, 254, and 132 were anti-ARS-positive, anti-MDA5-positive, and anti-ARS/MDA5-negative. Of these, 314 (45.2%), 184 (72.4%), and 89 (67.4%) met the EULAR/ACR criteria, while 404 (58.1%), 236 (92.9%), and 101 (76.5%) met the MHLW criteria. Anti-ARS-positive patients who did not meet the EULAR/ACR and MHLW criteria had a worse prognosis than those who met the criteria (*P*=0.008 and 0.020), while there was no inter-group difference among the entire cohort and other subgroups. [Conclusion] Anti-ARS-positive patients who did not meet the IIM criteria had a poor prognosis, highlighting the need for a novel classification.

W19-6

Predictive Factors for the Efficacy of High-Dose Intravenous Immunoglobulin Therapy: A Retrospective Analysis of Dermatomyositis with Rapidly Progressive Interstitial Lung Disease

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Conflict of interest: None

[Objective] To identify factors influencing the efficacy of high-dose intravenous immunoglobulin (IVIg) therapy in dermatomyositis (DM) patients with rapidly progressive interstitial lung disease (RP-ILD) resistant to multiple combination therapies. [Methods] Fifteen DM patients with RP-ILD (median age 61 years [46-69]; 7 females) refractory to combination therapies (corticosteroids, calcineurin inhibitors, cyclophosphamide, mycophenolate mofetil) who underwent IVIg were studied. CRP, KL-6, S/F ratio, ferritin, and CT score changes from initial treatment to before IVIg were compared between survivors (n=8) and non-survivors (n=7) using mixed-effects models. Optimal cutoff values were determined via ROC analysis; survival analyzed with Kaplan-Meier and Cox models. [Results] Patients with CRP > 3.65 mg/dL had significantly lower survival rates (log-rank test p=0.0019; hazard ratio 20.7, p=0.0278). While KL-6, ferritin, and S/F ratio showed no significant differences, CT score changes differed significantly between survivors and non-survivors (p<0.05). [Conclusion] CRP is an important biomarker for predicting IVIg response in DM patients with RP-ILD. Changes in CT scores after initial treatment may also predict effectiveness. These findings could aid in selecting treatment strategies.

W20-1

Risk Factors for Mortality in patients with ANCA-associated Vasculitis

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Conflict of interest: None

[Objectives] The aim of our study was to investigate risk factors for mortality in patients with AAV. [Methods] This study was retrospective study and analyzed patients with AAV treated at our hospital. Mortality risk factors and related factors were investigated with patient background prior to initiation of AAV treatment by Cox regression analysis [Results] A total of 40 patients, male 16 and female 24 were enrolled in this study. The median onset age was 71 years old (interquartile range [IQR] 64.25-78.50). During the observation period of 24 months, seven of the patients (17.5%) died. The causes of death were primary disease in 2 cases, malignancy in 2 cases, and infection in 3 cases. Median period from start of treatment for AAV to death was 10.5 months (6.0-18.0). Our analysis resulted that onset age (HR: 1.164: 95%CI 1.01-1.34) was independently and significantly associated with risk of death for AAV. [Conclusion] The 24-month survival rate of AAV in our hospital was 82.5%. The aging of the population has resulted in an aging population of AAV patients. Therefore, the study found that an older age of onset of AAV had an impact on survival.

W20-2

Predictive factors for home discharge in microscopic polyangiitis: A multicenter REVEAL cohort study

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Conflict of interest: None

[Objective] This study aimed to investigate the clinical predictive factors for home discharge in microscopic polyangiitis (MPA) patients. [Methods] Data from the multicenter REVEAL cohort enrolled through June 2024 were analyzed. 287 MPA patients were extracted, excluding those with unknown outcomes or who died. [Results] 258 patients were able to be discharged to home, but 29 were not. The home discharge impossible group was older, had lower serum albumin levels, higher Five Factor Score (FFS), higher initial dose of prednisolone, higher rate of nursing care insurance application before hospitalization, and higher rate of rehabilitation during hospitalization (*P*=0.004, 0.003, 0.003, 0.019, 0.014, 0.001). In multivariate analysis, age was significantly associated with home discharge (HR 1.08, 95%CI 1.02-1.14, P=0.014) ROC analysis identified a age cutoff of 73.5 years (AUC 0.665, sensitivity 82.8%, specificity 48.1%). In the group aged 75 years or older, serum Alb levels were significantly associated with home discharge (P=0.025), with a cutoff of 2.5 g/dl. The more predictor factors (age 75 years or older and serum Alb level less than 2.5 g/dl), the lower the home discharge rate (P=0.001) [Conclusion] Age and serum albumin levels may be useful in predicting home discharge.

W20-3

A study of the relapse and prognosis in granulomatosis with polyangiitis (GPA) - The REVEAL cohort study-

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Conflict of interest: None

[Objectives] To clarify the predictors of relapse and the prognosis of relapsed cases in patients with GPA. [Methods] We studied 81 patients with GPA who were enrolled in the REVEAL cohort between 2001 and May 2024. Diagnosis used the Chapel Hill classification. We retrospectively compared relapsed and non-relapsed group. [Results] The median age of the 81 GPA patients was 68 years, 53.1% were female, the WBC was 7,652/μL, CRP was 4.1 mg/dL. MPO-ANCA was 36.4%, and PR3-ANCA was 58.2% positive. The average follow-up period was about 5 years, and 38 patients (46.9%) relapsed after treatment. The median time to relapse was 321 days. When we compared the 38 relapsed and the 43 non-relapsed group, the BVAS before treatment was lower in the relapsed

group. There was no difference in the initial dose of GC or immunosuppressants between the two groups, but the relapse group had higher CRP levels at 6 and 9 months and higher GC doses. In addition, there were more cases of hospitalisation for infection, infection-related deaths and all-cause deaths after treatment. [Conclusion] Relapse cases had higher CRP levels and higher GC intake at 6 and 9 months after treatment. Relapse cases also had significantly higher rates of hospitalisation for infection and infection-related deaths.

W20-4

Risk factors for severe respiratory distress in patients with AAV complicated by diffuse alveolar hemorrhage: the REVEAL cohort study

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Conflict of interest: Yes

[Objectives] This study aimed to identify risk factors for severe respiratory distress (SRD) in patients with antineutrophil cytoplasmic antibody-associated vasculitis (AAV) complicated by diffuse alveolar hemorrhage (DAH). [Methods] Data from the multicenter REVEAL cohort in the Kansai region (2005-2024), were analyzed. Among 556 AAV cases, 50 patients (34 with MPA, 6 with GPA, and 10 with EGPA) who had DAH and underwent remission induction therapy were included. SRD was defined as the need for mechanical ventilation/ICU admission or a PaO2/FiO2 ratio ≦200. [Results] SRD occurred in 14 patients, with a median onset of 1.5 days (IQR: 1-12) after treatment. Four patients died from alveolar hemorrhage. The SRD group showed higher leukocyte counts, neutrophil counts, CRP levels, and corticosteroid pulse therapy use (P=0.023, 0.001, 0.015, and 0.01). Cox analysis revealed elevated neutrophil counts were associated with SRD (HR 4.04, 95% CI 1.512-11.991, P=0.008). ROC analysis identified a neutrophil cutoff of 8,782/μL (AUC 0.8, sensitivity 78.6%, specificity 77.1%). Neutrophil counts ≧8,800/μL were linked to higher SRD incidence within one month (P=0.002, log-rank test). [Conclusion] Elevated neutrophil counts are a risk factor for SRD in AAV patients with DAH during remission induction.

W20-5

Clinical characteristics and prognostic factors in patients with ANCA-associated vasculitis with diffuse alveolar hemorrhage

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Conflict of interest: None

[Objectives] We aimed to study the clinical characteristics and prognostic factors in patients with ANCA-associated vasculitis (AAV) with diffuse alveolar hemorrhage (DAH). [Methods] We investigated 186 microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA) enrolled in the KVAS cohort between 2012 and 2024. We compared clinical manifestations between 13 AAV patients with DAH and 173 without DAH. In AAV patients with DAH, we also compared clinical manifestations between surviving and deceased patients. [Results] Renal manifestations more common in AAV patients with DAH than those without DAH. More patients died within the first year in AAV patients with DAH than those without DAH, and the main cause of death was DAH. Among 13 AAV patients with DAH, 6 patients died, and they were older than the surviving patients. Most deceased patients with DAH had interstitial lung disease (ILD) with the usual interstitial pneumonia (UIP) pattern, and all patients with UIP died. All deceased patients were positive for MPO-ANCA and had renal manifestations. [Conclusion] In AAV with DAH, more patients had renal manifestations and died within the first year. Age, MPO-ANCA positivity, ILD with UIP, and renal manifestations were associated with the prognosis of AAV with DAH.

W20-6

Comparative Study of ANCA-Associated Vasculitis in Patients With and Without Rheumatoid Arthritis: Analysis of Clinical Manifestations and Renal Outcomes

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Conflict of interest: None

[Objectives] Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) can co-occur with rheumatoid arthritis (RA). No reports focused on renal pathology in AAV with RA (RA+) versus without RA (RA-), so we investigated this. [Methods] We reviewed 125 AAV patients who had renal biopsy: 13 RA+ and 112 RA-. The primary endpoint was the 10-year dialysis initiation rate; secondary endpoints were renal pathology, 3-month renal function, and proteinuria. [Results] The RA+ group was all female. No significant differences were found in age, creatinine (Cre), eGFR, proteinuria, or CRP. The RA+ group had lower Cre, less proteinuria, fewer global glomerulosclerosis, and more crescents (32.0% vs 20.1%, $p<0.05$). No significant differences were found in interstitial inflammation, fibrosis, or tubular atrophy. The RA+ group had a significantly higher rate of 30% eGFR improvement (53.8% vs 22.9%, $p<0.05$) but showed less proteinuria reduction. No significant difference was found in the 10-year dialysis initiation rate, though RA+ showed better trends (21.2% vs 41.6%, Log-rank test, p=0.088). [Conclusion] The RA+ group had more crescents but better renal prognosis and treatment response. This suggests RA+ AAV may be a distinct subgroup in renal pathology and outcomes compared to RA- AAV.

W21-1

Elevated expression of a BAFF receptor, BR3, in peripheral monocytes and serum level of soluble BR3 are correlated with clinical features of Sjögren's syndrome

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Conflict of interest: None

[Objectives] We reported that the elevated expression of BAFF receptor, BR3, in peripheral monocytes was correlated with the clinical parameters of patients with Sjögren's syndrome (SS). BR3 is shed from the cells

to form soluble BR3 (sBR3) when BR3 binds soluble BAFF. However, the function of sBR3 and role of sBR3 in the development of SS remain unclear. The purpose of this study is to investigate the relationship between the expression of BR3 as well as sBR3 in SS monocytes and the clinical features of SS. [Methods] The serum level of sBR3 of SS patients (n=79) and healthy controls (HC, n=25) was measured by electrochemiluminescence ELISA. The expression level of BR3 in peripheral monocytes (BR3/CD14 ratio) was analyzed by FACS. The correlation between the values measured as above and clinical parameters of the patients were analyzed by Spearman correlation coefficient. [Results] The serum level of sBR3 in SS patients was significantly higher than that of HC ($p<0.001$) and showed positive and significant correlation not only with the BR3/CD14 ratio, but also with the serum IgG level and ESSDAI scores of the patients. [Conclusion] Our results suggest that the elevated expression of BR3 in monocytes are involved in the development of SS through elevation of sBR3 and IgG.

W21-2

The involvement of TLR4 signaling pathways in the elevation of BAFF receptor, BR3, expression in peripheral monocytes of patients with Sjögren's syndrome

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Conflict of interest: None

[Objectives] We reported that the expression level of BAFF receptor, BR3, was elevated in peripheral monocytes of patients with Sjögren's syndrome (SS). We also found that BR3 expression was positively correlated with TLR4 expression in SS monocytes. The purpose of this study is to elucidate a possible involvement of TLR4-signaling pathways in the expression of BR3 in SS monocytes as well as the development of SS. [Methods] Peripheral monocytes of SS patients and healthy individuals were stimulated with LPS for 15 min in the presence or absence of a TLR4 inhibitor, TAK242, and phosphorylation of TLR4-associated signaling molecules was analyzed by Western blotting. PBMC were cultured for 3 days in the presence of TLR4 ligands, such as LPS and S100A9, with or without TAK242, and the expression of BR3 in CD14+ cells was analyzed by FACS. [Results] Western blotting showed that TLR4-associated molecules, i.e., IKKa/b, TAK1 and NF-kB p65 were phosphorylated in SS monocytes upon stimulation with LPS, and TAK242 suppressed the phosphorylation of these molecules. FACS revealed that TLR4 ligands induced the BR3 expression on CD14+ cells, which was inhibited by TAK242. [Conclusion] Our results suggest that the TLR4 signaling pathways are involved in the elevated expression of BR3 in SS monocytes.

W21-3

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 via 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 populations of peripheral $CD8^+$ and $CD4^+$Treg were compared by FCM between pSS and age gender-matched HC (each N=20). 2) In pSS, association between $CD8^+$ and $CD4^+$Treg population and clinical features was analyzed. 3) Effects of CDK8/19 inhibitor (CDKi) on $CD8^+Foxp3^+$T cells differentiation from HC and pSS derived peripheral memory $CD8^+$T cells by IL-2 and TGFb. 4) The expression of functional molecules, suppressive ability for proliferation of responder T cells, IL-10 production, and cytotoxic activity 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 than in HC, while that of $CD4^+$Treg was comparable. 2) Only $CD8^+$Treg population had significant positive correlation with age and negative correlation with dryness of ESSPRI. 3) The induction of $CD8^+Foxp3^+$T cells were enhanced by CDKi in HC and pSS. 4) The expression of CD25, GITR, CTLA4, and suppressive ability for proliferation were significantly enhanced, and IL-10 production tended to increase, and cytotoxic activity was downregulated. [Conclusion] CDKi might regulate pathogenesis via converting memory $CD8^+$T cells into decreased $CD8^+$Treg in pSS.

W21-4

Analysis of intestinal flora in patients with Sjögren's syndrome

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Conflict of interest: Yes

Objective: There are increasing reports of Sjögren's syndrome (SS), so we investigated the intestinal flora in Japanese SS patients. Methods: The subjects were 67 Japanese women aged 20 years or older who were diagnosed with SS according to the 2016 ACR/EU classification criteria, and a control group (C) was a group of subjects previously collected by SSI that was age-matched to the SS group. 16S rRNA gene sequences were decoded and analyzed using a next-generation sequencer. Results: Comparison of relative abundance between the two groups revealed that the genera Lactobacillus, Streptococcus, Merdimonas, Bifidobacterium, Eggerthella, Enterocloster, Erysipelatoclostridium, Flavonifractor, and Anaerobutyricum were significantly increased in the SS group. Conclusion: The Eggerthella genus has been reported to be associated with increased INF-γ and IL-17, but also contains a large amount of equol (Eq)-producing bacteria. Eq exhibits weak estrogen (E) activity, but at high E concentrations, it significantly attenuates the estrogen activity. It has been believed that SS develops after menopause due to a decrease in E and a weakening of the protective effect on the salivary and lacrimal glands, but these results suggest that the Eggerella genus may be involved in the development of SS.

W21-5

Central sensitivity syndrome in patients with Sjögren syndrome

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Conflict of interest: None

[Objectives] Patients with Sjögren's syndrome (SS) often experience subjective symptoms, including non-inflammatory joint pain and fatigue, in addition to sicca symptoms. Central sensitization may contribute to these symptoms, though no reports have addressed this issue. We aimed to assess central sensitization symptoms in SS patients using the Central Sensitization Inventory (CSI) and examine the frequency and clinical characteristics. [Methods] We administered the CSI to SS outpatients to assess the frequency and severity of central sensitivity syndrome (CSS). We also evaluated disease activity (ESSPRI, ESSDAI, RF, IgG, WBC), depression/anxiety (HADS), and health-related quality of life (SF-36). Multivariate analysis was performed to assess relationships between CSS, disease activity, subjective symptoms, and quality of life. [Results] Among 40 patients (mean age 54.0 ± 11.7), the mean CSI score was 31.1 ± 16.5. CSS (CSI ≧40) was observed in 25% of patients. CSS was significantly associated with ESSPRI ($p = 0.08$, OR: 3.65), depression ($p = 0.011$, OR: 2.20), pain ($p = 0.032$, OR: 1.92), and negatively with SF-36 physical health component ($p = 0.041$, $\beta = -0.366$). [Conclusion] Central sensitization is common in SS, associated with pain, depression, and reduced quality of life.

W21-6

A case of tubulointerstitial nephritis and Fanconi syndrome in a patient with primary Sjögren's syndrome accompanied by anti-mitochondrial antibodies

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Conflict of interest: None

A 60-year-old woman with primary biliary cholangitis presented to our rheumatology clinic with glycosuria and high urinaryβ2MG and NAG. Laboratory tests showed SCr 1.25 mg/dL, anti-SS-A antibody >240 U/mL, anti-SS-B antibody 75 U/mL, pH 7.35, HCO3- 21.4 mmol/L, base excess -3.7 mmoL/L. Urinalysis showed urine pH 7.0, urinary protein 670 mg/gCr, urinary β2MG 22000μg/L, urinary generalized aminoaciduria, and glycosuria. A lip biopsy specimen revealed lymphocytic infiltration around the ducts. Histological findings of kidney biopsy specimen revealed inflammatory cell infiltration in the interstitium. Based on above findings, she was diagnosed as having Sjögren's syndrome complicated with tubulointerstitial nephritis and Fanconi syndrome. Initial treatment was started with 20 mg/day prednisolone, and subsequently, her symptoms improved. Recently, some cases of Sjögren's syndrome with tubulointerstitial nephritis positive for antimitochondrial antibodies that present with Fanconi syndrome have been reported. Clinicians should pay attention that antimitochondrial antibodies may be related to the pathophysiology of Fanconi syndrome.

W22-1

Evaluation of the Efficacy and Safety of Dose-Adjusted versus Non-Dose-Adjusted JAK Inhibitors Based on Renal Function: the ANSWER cohort study

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of JAK inhibitor dose adjustments based on renal function. [Methods] We analyzed 437 patients from the ANSWER cohort who received JAK inhibitors, dividing them into four groups: (A) dose-reduced due to renal impairment, (B) standard dose without impairment, (C) dose-reduced without impairment, and (D) renal-independent dose-reduced inhibitors (UPA, PEF). Using IPTW to adjust for background factors, we compared one-year treatment continuation rates due to efficacy or adverse events. [Results] Mean age was 66.5 years, with 86% female and mean Baseline CDAI was 15.1, with prior b/tsDMARDs usage averaging 3.0 agents. Cox proportional hazards analysis for factors affecting treatment discontinuation due to inefficacy over one year yielded an HR of 2.11 (95% CI: 0.81-5.52, p = 0.126) for Group B, an HR of 0.32 (95% CI: 0.10-1.03, p = 0.057) for Group C, and an HR of 0.58 (95% CI: 0.20-1.74, p = 0.332) for Group D, with no statistically significant differences observed. Adverse event-related discontinuations followed similar trends. [Conclusion] Dose adjustments for renal impairment in JAK inhibitors did not significantly affect treatment continuation rates due to inefficacy or adverse events compared to non-adjusted cases.

W22-2

Evaluation of Whether Biologic Agents and JAK Inhibitors Suppress Renal Function Decline in Rheumatoid Arthritis Patients (Single-Center Retrospective Observational Study)

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Conflict of interest: None

Purpose: To determine which biologic agent (Bio) or JAK inhibitor (JAK) best suppresses renal function decline in rheumatoid arthritis (RA) patients. **Methods:** This study included RA patients who visited our hospital from November 2009 to September 2024 and used Bio/JAK for over one year. Patients with eGFR <30 mL/min/1.73 m^2 were excluded. ΔeGFR/year was compared using propensity score matching (PS) to adjust for confounders: age, sex, BMI, disease duration, observation period, smoking, RF, ACPA, comorbidities (hypertension, diabetes, dyslipidemia), eGFR, HbA1c, LDL-C, baseline medications, Hb, ESR, CRP, and RA activity. **Results:** Patients using TNF inhibitors (TNF), IL-6 inhibitors (IL-6), abatacept (ABT), and JAK inhibitors were 512, 441, 214, and 250, respectively. ΔeGFR/year was -2.5/-2.8/-2.7/-4.4 mL/min/1.73 m^2. PS-matched pairs showed: TNF/IL-6 (292 each), ΔeGFR/year -2.4/-2.7 (p=0.60); TNF/ABT (157 each), -2.2/-2.8 (p=0.37); TNF/JAK (170 each), -2.3/-4.4 (p=0.001); IL-6/ABT (174 each), -2.8/-3.1 (p=0.57); IL-6/JAK (178 each), -3.1/-4.5 (p=0.03); and ABT/JAK (135 each), -2.6/-4.4 (p=0.01). **Conclusion:** No differences in renal function decline were seen among Bio agents. However, JAK inhibitors showed a significantly greater decline than any Bio agent.

W22-3

Investigation of the effects and safety of JAK inhibitors in rheumatoid arthritis with interstitial lung disease

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the efficacy and safety of JAK inhibitors (JAKi) in rheumatoid arthritis (RA) patients (pts) with interstitial lung disease (ILD) using data from the FIT RA (Fukui Ishikawa Toyama Database of Rheumatoid Arthritis) cohort. [Methods] We divided the 396 pts who received JAKi into two groups: one with ILD (ILD group, 33 pts) and one without ILD (non-ILD group, 363 pts) and examined the effects and continuation rates. We also compared the ILD group with patients with RA and ILD who received abatacept (ABT group, 31 pts). [Results] The mean age of the ILD and non-ILD groups was 72.3 and 63.7 years, respectively, and the ILD group was significantly older (p<0.001). There was no significant difference in DAS28-CRP before and 6 months after treatment or in the 2-year retention rate between the ILD and non-ILD groups, which were 44.1% and 53.3%, respectively. The JAK and ABT groups had similar ages, disease activity, and change in DAS at 6 and 12 months. The 2-year retention rates for the JAK and ABT groups

were similar. There were 5 and 6 discontinuations due to adverse events in the JAK and ABT groups, respectively, but only 1 case of ILD worsening in each group. [Conclusion] The results suggest that JAKi may be an option for RA with ILD.

W22-4

Complications of interstitial pneumonia and progression of tofacitinib in 46 patients treated with tofacitinib for 5 years at our hospital

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Conflict of interest: None

[Objectives] In particular, medication for elderly patients with interstitial pneumonia (ILD) is a trump card in terms of both safety and efficacy. Recently there are more and more reports showing the safety of JAK inhibitors in RA patients with existing ILD. In this study, we investigated ILD complications and progression of RA in 46 patients treated with tofacitinib (TOF) for 5 years at our hospital. [Methods] The mean age of the patients was 67.0 years, and the mean disease duration was 15.0 years. We compared the results of chest CT readings by imaging physicians regarding interstitial pneumonia, progression over 5 years, RF, ACPA and KL-6 changes, and so on. [Results] The mean RF, ACPA, and KL-6 of patients with ILD (group A) at the start of TOF treatment was 26.1%, and the mean RF, ACPA, and KL-6 of group A was higher than that of patients without ILD (group B) at the start of TOF treatment, but the mean RF, ACPA, and KL-6 of group A showed a downward trend over 5 years. [Conclusion] The existing ILD progression rate after long-term continuous treatment with TOF is lower than that of 568 ILD progression rates by age group in our hospital, and TOF seems to be promising in terms of both efficacy and safety for RA patients with mild complications of ILD.

W22-5

Efficacy and safety of filgotinib in patients with rheumatoid arthritis focusing on pulmonary lesions

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Conflict of interest: None

The purpose of this study was to clarify the efficacy and safety of FIL on lung lesions in RA patients. The study included 43 patients who received FIL between August 2021 and September 2024, and who underwent chest CT and respiratory function tests at the time of administration and 52 weeks later. The mean age at the start of FIL was 75.6 years, 26 were female, 18 were past and 4 were current smokers. A total of 30 patients had pulmonary lesions at the start of treatment: IP in 10, bronchiectasis in 3, emphysema in 3, NTM infection in 1, frosted glass shadows in 4, emphysematous changes in 7, and rheumatoid nodules in 2. Disease activity improved from DAS28-CRP 3.47 and CDAI 15.8 at the time of treatment to DAS28-CRP 2.13 and CDAI 6.4 at 52 weeks of FIL treatment. Chest CT showed improvement in 11.6%, stable in 72.0%, and worsened in 16.3%, while FVC and DLco were 98.3% and 91.5% at treatment, and 98.1% and 93.5% at 52 weeks of FIL treatment, respectively. Pneumonia requiring hospitalization was observed in 2 patients, and the treatment was discontinued. In conclusion, FIL can be used relatively safely in RA patients with lung lesions and is effective in controlling disease activity, although the development of infection must be taken into consideration.

W22-6

Influence of Prior b/tsDMARD Use on JAK Inhibitor Discontinuation in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To examine how prior b/tsDMARD use affects JAK inhibitor discontinuation in rheumatoid arthritis (RA) patients. [Methods] We analyzed data from 723 RA patients who began JAK inhibitors from September 2017 to August 2024. Four Cox proportional hazards models were created: Model 1 included b/tsDMARD history; Model 2, the number of prior b/tsDMARDs; Model 3, the mode of action (MOA) of the latest b/tsDMARD; and Model 4, the reason for discontinuing the previous b/tsDMARD. [Results] Of participants, 457 (63%) had prior b/tsDMARD use: 25% used one, 17% two, and 22% three or more. The last b/tsDMARD MOA comprised TNF inhibitors (22%), IL-6 inhibitors (13%), CTLA4-Ig (7%), and JAK inhibitors (22%), with discontinuation reasons of insufficient efficacy (45%), adverse events (7%), and others (11%). Multivariable analysis found prior b/tsDMARD use independently predicted JAK inhibitor discontinuation due to insufficient efficacy (HR 2.20, 95% CI: 1.38-3.52). Models 2, 3, and 4 confirmed similar findings. Prior b/tsDMARD use was not a predictor of discontinuation due to adverse events. [Conclusion] RA patients discontinuing b/tsDMARDs for insufficient efficacy are more likely to discontinue subsequent JAK inhibitors for the same reason.

W23-1

Efficacy and Safety of Rituximab in Rheumatoid Arthritis Patients with Comorbid Lymphoproliferative Disorders or ANCA-Associated Vasculitis

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Conflict of interest: None

[Objectives] Rituximab (RTX) is approved as a standard therapy for rheumatoid arthritis (RA) in Western countries, but it remains unapproved in Japan. However, RTX is sometimes administered to RA patients with a history of OIIA-LPD or with concomitant ANCA-associated vasculitis (AAV). This study aimed to examine the effectiveness and safety of RTX in these specific RA patients. [Methods] We retrospectively reviewed medical records to identify RA patients who initiated RTX therapy between January 2014 and July 2024. We analyzed patient demographics, disease activity (DAS28-CRP, CDAI), adverse events, and RTX continuation rates. [Results] Of the 219 patients who received RTX at our hospital, 29 had RA. They included 15 with a history of OIIA-LPD (LPD group) and 9 with AAV (AAV group). The mean age was 73.2 years, and 75.9% were female. Changes in DAS28-CRP at baseline, 12, 24, and 36 months were: LPD group: 3.88, 2.45, 2.22, 1.93; AAV group: 4.04, 1.98, 1.88, 2.90. CDAI

scores in the LPD group decreased similarly. Adverse events occurred in 9 patients (31%), including 5 in the LPD group. RTX continuation rates were 74.4%, 65.9%, and 51.8% at 12, 24, and 36 months, respectively. [Conclusion] RTX showed long-term efficacy in RA patients with a history of OIIA-LPD or with concomitant AAV.

W23-2

Serious infections during abatacept treatment for rheumatoid arthritis

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Conflict of interest: None

[Objective] To investigate serious infections during abatacept (ABT) treatment for rheumatoid arthritis (RA). [Methods] Clinical information from RA patients treated with ABT since 2011 was retrospectively collected. The clinical feature of RA and serious infection was analyzed. [Results] 187 cases were enrolled; female 68%, median age 71 y/o, RA duration 5.1 years, RF positive 83%, ACPA positive 88%, MTX combination 28%, PSL combination 65%, b/ts-DMARD naïve 78%, and pulmonary complication 62% at ABT initiation. Serious infection occurred in 26 patients (lung 13, GI 7, urinary 5, joint 2, skin 1). In the serious infection group (N=26), RA duration was significantly longer (7.3 vs 4.8 years, P=0.03), PSL dose was significantly higher (10.0 vs 5.0 mg/day, P<0.01), and b/ts-DMARD naïve was significantly higher (96.2% vs 75.2%) than no serious infection group (N=161). ROC analysis revealed that a cutoff value of PSL dose > 5 mg/day at ABT initiation predicted serious infection with a sensitivity of 61.5% and a specificity of 68.3%. No significant difference was shown in the incidence of serious infections based on age or pulmonary complications. [Conclusion] Patients receiving PSL > 5 mg/day or a long duration of RA were at risk of serious infections after the initiation of ABT.

W23-3

Efficacy of ozoralizumab in rheumatoid arthritis patients with high rheumatoid factor titers

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Conflict of interest: None

[Objectives] It has been reported that in rheumatoid arthritis (RA) patients with high rheumatoid factor (RF) titer, the therapeutic effect of TNF inhibitors (TNFi) with the Fc region is attenuated, while that of TNFi without the Fc region is maintained. We statistically investigated whether the titer of RF is related to therapeutic efficacy with ozolalizumab (OZR), one of the TNFi without Fc region. [Methods] The patients enrolled in FIT-RA, a multicenter study in three prefectures in Hokuriku, who received at least one dose of OZR or TNFi with Fc region (Fc+TNFi), were included in this study. The change in DAS28CRP was compared between the OZR and Fc+TNFi in each group. [Results] Fifteen patients treated with OZR and 191 patients treated with Fc+TNFi were included. These 206 patients were classified into 4 groups according to the quartiles of RF titer at the beginning of treatment. The change in DAS28CRP between the OZR and Fc+TNFi groups was not significantly different; in the Fc+TNFi group, the change tended to decrease as RF titer increased, but this was not the case in the OZR group. [Conclusion] In RA patients with high RF titers, the advantage of OZR over Fc+TNFi could not be demonstrated statistically, but there was a trend toward preservation of therapeutic efficacy.

W23-4

Report on our experience with ozoralizumab at our hospital

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Conflict of interest: None

[Objective] To evaluate the efficacy, persistence rate, and side effects of ozolalizumab (OZP) in our hospital. [Methods] 33 rheumatoid arthritis patients who started OZP at our hospital from March 2023 to July 2024 were included in this study. The mean age was 64.9 years, the mean duration of disease was 12.3 years, 20 patients were treated with MTX, and 18 patients had a history of biologic agents or JAK inhibitors. [Results] 20 of 33 patients were able to continue OZP. The continuation rate in the MTX group was 75%, which was significantly higher than that in the MTX-naive group (38%). The continuation rate in the group of patients who had never used biologic agents or JAK inhibitors was 87%, which was significantly higher than that in the group of patients who had used biologic agents or JAK inhibitors in the past (39%). The continuation rate in the group of patients over 75 years old was 71%, which was higher than that in the group of patients under 75 years old (58%). [Conclusion] Ozoralizumab started in combination with MTX or as 1st BIO has a high continuation rate, and is expected to be effective with a high continuation rate in late-stage elderly patients as well.

W23-5

Rheumatoid Factor in rheumatoid arthritis patients Using Tocilizumab (TCZ) does not affect disease activity

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Conflict of interest: None

[Objectives] To examine the association between RF levels and disease activity in RA patients using TCZ. [Methods] This study enrolled RA patients treated with TCZ in our department, with continuous administration of over one year. Based on RF (positive; >15 IU/mL) at the start of TCZ administration / at the final follow-up, patients were classified into four groups: Group G1 (negative/negative), G2 (negative/positive), G3 (positive/decreased), and G4 (positive/increased). The association between these groups and disease activity was examined. [Results] There were 137 cases (19 males, 118 females). The mean TCZ administration period at the final follow-up was 7.2±5.0 years, and cases were distributed as follows: G1 (24), G2 (9), G3 (55), and G4 (49). RF at baseline/final follow-up were: G1 (3.9±3.8/3.5±4.5), G2 (11.4±3.2/46.1±27.8), G3 (264 ±323/112±164), and G4 (101±124/316±494). DASCRP28 was as follows: G1 (3.7±0.9/1.5±0.4), G2 (3.6±1.2/1.5±0.37), G3 (3.4±0.9/1.4±0.5), and G4 (3.5±0.7/1.4±0.5). CDAI were G1 (17±8.0/3.6±2.5), G2 (18.2±7.1/3.9 ±3.4), G3 (13.0±6.5/3.1±3.6), and G4 (13.1±6.0/2.9±3.2). [Conclusion] DASCRP28 and CDAI remained in the low disease activity across all groups, suggesting that an increase in RF does not affect disease activity in RA patients using TCZ.

W23-6

Comparison of clinical treatment outcomes of tocilizumab and sarilumab in rheumatoid arthritis taking into account historical background

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Conflict of interest: Yes

[Objective] We compared the clinical treatment outcomes of TCZ and SAR for RA taking into account the current historical background. [Method] We used 29 TCZ cases [T group] and 46 SAR cases [S group] who started treatment after July 2019. To match the comparative conditions, we divided the cases into 1st biologic cases (14 TCZ cases vs. 19 SAR cases) and 2nd or subsequent biologic cases (15 TCZ cases vs. 27 SAR cases) for comparison. [Results] Patient background [T group/S group]: Age 73.1/64.7 years, RA disease duration 10.7/11.2 years. ΔSDAI [1/3/6 months] was [-8.5/-12.2/-15.2] for 1st case, S group [-7.5/-13.1/-14.5] for 2nd case and later, T group [-7.4/-8.4/-10.7], S group [-7.5/-8.8/-8.4] for 2nd case and later, no significant difference was observed between groups at any time point. There was also no statistically significant difference between the T and S groups in the change in MMP-3 and mHAQ. The administration continuation rate (%) [180 days/365 days] was 85.7/71.4 in the T group and 84.2/73.0 in the S group in the 1st case, and 80.0/64.7 in the T group and 92.5/73.7 in the SAR group in the 2nd and subsequent cases, with no significant difference between the groups in either comparison. [Conclusion] TCZ and SAR showed comparable efficacy and treatment continuity.

W24-1

Could the Okomarigoto sheet become a new RA PROs?

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Conflict of interest: Yes

[Objectives] The Okomarigoto Sheet (OS) was devised to enhance the communication barriers between patients and physicians, and is anticipated to serve as a novel approach for assessing patient-reported outcomes (PROs) in rheumatoid arthritis (RA). This study aimed to validate the correlation between OS, RA disease activity, and established PROs. [Methods] The study enrolled 333 RA patients who visited the hospital between June and August 2024. The OS comprised five items each for morning stiffness, pain, and fatigue, with a scoring system of 2 for severe symptoms, 1 for moderate symptoms, and 0 for no symptoms. Correlations with RA disease activity (CDAI, SDAI) and PROs (HAQ-DI, mHAQ, MDHAQ, RAPID3) were assessed. [Results] The OS demonstrated a significant correlation with CDAI (r=0.58) and SDAI (r=0.56) ($p<0.001$). CDAI showed significant correlations with established PROs (HAQ-DI; r=0.53, mHAQ; r=0.47, MDHAQ; r=0.50, RAPID3; r=0.83). Furthermore, OS was strongly correlated with HAQ-DI (r=0.65), mHAQ (r=0.61), MDHAQ (r=0.63), and RAPID3 (r=0.68) ($p<0.001$). [Conclusion] The OS exhibited a strong correlation not only with established RA disease activity assessments but also with existing PRO evaluations.

W24-2

The Relationship Between Difficult-to-Treat Rheumatoid Arthritis and Sarcopenia: A Multicenter Observational Study -T-FLAG study-

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Conflict of interest: None

[Objectives] Sarcopenia is often observed in Difficult-to-Treat Rheumatoid Arthritis (D2T-RA). This study aimed to explore the factors associated with sarcopenia and D2T-RA in RA patients. [Methods] Sarcopenia was diagnosed using the SARC-F. D2T-RA was defined as moderate/high disease activity despite using ≧2 b/ts DMARDs. Of 666 RA patients in 2023, 180 were excluded for using fewer than two b/ts DMARDs but with moderate/high disease activity. The remaining 486 patients were analyzed, with 101 classified as sarcopenia (SARC-F ≧4) and 385 as non-sarcopenia (SARC-F <4). Logistic regression identified factors linked to sarcopenia. Patients were also divided into D2T-RA and non-D2T-RA groups for comparison. [Results] Sarcopenia was significantly associated with age (OR: 1.04, $p<0.01$), BMI (OR: 1.19, $p<0.01$), D2T-RA (OR: 2.88, $p<0.01$), and HAQ-DI (OR: 26.80, $p<0.001$). Sarcopenia prevalence was significantly higher in the D2T-RA group than in the non-D2T-RA group (60.5% vs. 17.4%, $p<0.01$). D2T-RA patients also showed lower MTX use (34.2% vs. 64.1%, $p<0.01$). Most D2T-RA patients used two or more b/ts DMARDs (68.4% on two, 21.1% on three, 7.9% on four or more). [Conclusion] Overcoming D2T-RA is critical for improving sarcopenia, and tight control by treatment enhancement may be effective.

W24-3

A study on the reversibility of social frailty in patients with rheumatoid arthritis from a multicenter observational study (T-FLAG study)

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Conflict of interest: None

[Objectives] This study aims to investigate the reversibility of social frailty in RA patients. [Methods] We conducted a frailty survey among 605 RA patients. Social frailty was evaluated using Makizako's social frailty index. Patients were categorized into two groups based on laughter frequency: "daily, 1-5 times per week" and "1-3 times per month, almost never". Among the 216 patients identified as socially frail, 87 patients improved, while 129 remained socially frail after one year. [Results] The baseline characteristics of the 216 RA patients were as follows: mean age of 70 years, disease duration of 14 years, 70% female, SDAI score of 8.3. There were no significant differences in age, gender, disease duration, or SDAI between the improved and non-improved groups. In terms of laughter, more patients in the improved group reported a higher frequency of laughter compared to the non-improved group. Multivariate analysis revealed that laughter frequency was an independent factor associated with improvement in social frailty. [Conclusion] In RA patients, social frailty is associated with laughter, and regardless of disease activity, patients who laugh more frequently may have a higher likelihood of overcoming social frailty.

W24-4

The Impact of Grip Strength Imbalance on Frailty Diagnosis in Patients with RheumatoidArthritis: A multicenter observational study: -T-FLAG-

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Conflict of interest: None

Objective: Rheumatoid arthritis (RA) patients often show grip strength asymmetry, which may underestimate frailty since diagnosis uses the stronger hand's grip. This study examines the impact of grip asymmetry on frailty diagnosis. Methods: In 2024, bilateral grip strength was measured in 680 RA patients. Frailty was diagnosed by the Japanese-Cardiovascular Health Study (J-CHS) criteria: Robust (0 points), Pre-frailty (1-2 points), and Frailty (≧3 points). Patients with grip strength asymmetry ≧20% were classified as the asymmetry group (n=258), and those with <20% as the non-asymmetry group (n=422). J-CHS changes based on the weaker hand's grip and factors related to worsening J-CHS scores were examined. Results: Using the weaker hand's grip, more patients in the asymmetry group showed worsening J-CHS scores (30.2% vs. 10.9%). Of those initially classified as Robust, 31.3% progressed to Pre-frailty, while 68.7% remained Robust. Among Pre-frailty patients, 7.9% advanced to Frailty, and 92.1% stayed in the same category. No changes were seen in the Frailty group. Factors associated with worsening J-CHS were disease duration (OR: 0.96), DAS28-ESR (OR: 0.79), and grip asymmetry ≧20% (OR: 4.60). Conclusion: Grip strength asymmetry in RA patients may lead to underestimating frailty.

W24-5

Is Increased Red Cell Distribution Width Associated with Frailty in Rheumatoid Arthritis Patients? A Multicenter Observational Study: -T-FLAG Study-

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Conflict of interest: None

[Objective] Red cell distribution width (RDW) increases due to anemia, chronic inflammation, and malnutrition and is often elevated in active rheumatoid arthritis (RA). This study examines whether elevated RDW is associated with frailty in RA patients. [Methods] 687 RA patients with RDW data from 2024 were included. Patients were divided into a high RDW group (RDW ≧ 14.5, n = 167) and a normal RDW group (RDW < 14.5, n = 520). Frailty was assessed by the Kihon Checklist (KCL). Factors related to high RDW were analyzed using logistic regression. [Results] Compared to the normal RDW group, the high RDW group was older (70.8 years vs. 68.4 years), had higher DAS28-ESR (3.01 vs. 2.70) and HAQ-DI scores (0.69 vs. 0.43), and had higher usage rates of methotrexate (MTX) (66.5% vs. 57.5%) and steroids (41.9% vs. 20.8%), as well as lower serum albumin levels (3.9 vs. 4.1). The KCL total score was also higher in the high RDW group (56.8% vs. 40.3%). Factors associated with high RDW included serum Alb levels (OR: 0.43), steroid use (OR: 2.23), MTX use (OR: 2.23), and KCL score (OR: 1.05). [Conclusion] RDW is linked to frailty in RA patients. However, steroid and MTX use was associated with high RDW. Future studies are needed to explore these results.

W24-6

Validation of the drug treatment algorithm from the 2024 update of the Japan College of Rheumatology clinical practice guidelines for late-onset rheumatoid arthritis

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Conflict of interest: Yes

[Object] To validate the drug treatment algorithm from the 2024 update of the Japan College of Rheumatology clinical practice guidelines for the management of late-onset rheumatoid arthritis (LORA). [Methods] Achievement of remission/low disease activity (LDA) and discontinuation of glucocorticoids (GC) were evaluated in the Late-onset Rheumatoid Arthritis Registry Study (LORIS), a multicenter prospective cohort study. [Results] 141 patients started MTX (MTX group) and 69 patients started csDMARDs other than MTX (csDMARDs group). Compared to the cs DMARDS group, the MTX group was younger and had higher SDAI and less use of GC (34.0% vs. 50.7%). Reasons for not selecting MTX were patient preference (18.8%), renal dysfunction (14.5%), malignancy (11.6%), age (7.2%), and dementia (13.7%). The prevalence of GC use at 6 months was significantly lower in the MTX group (22.8% vs 43.5%, p=0.003), and the achievement rate of GC-free SDAI LDA after 6 months was 56.0% in the MTX group and 44.0% in the csDMARDs group (p= 0.057), and the achievement rate of GC-free remission was similar. The incidence of serious adverse events was significantly higher in the csDMARDs group. [Conclusion] The current practice of patients who do not select MTX in the treatment algorithm for LORA was clarified.

W25-1

Contraception-related issues among female patients with rheumatic diseases in Japan: A questionnaire survey at 14 facilities (first report)

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Conflict of interest: Yes

[Objectives] Rheumatic disease patients need to plan their pregnancies. However, only half of pregnancies among patients are planned (Mod Rheumatol, 2019). The survey to clarify the issues on contraception and reproduction was conducted. [Methods] Two types of questionnaire surveys were conducted at 14 facilities: one targeting female patients aged 18-45 and one targeting their doctors. They were anonymous, but the both were linked by the number on the sheet. [Results] The 157 patients returned them (avg. age; 35.3, avg. age at disease onset; 26.3). 55 hoped pregnancy in the future, 72 did not. Regarding the necessity of contraception; no 65, yes 61, 21 do not know but use it, and 9 do not know but do not use it. Only 16 used a highly reliable method of contraception, and 49 used a less reliable one. Six had undergone induced abortion after the disease onset, but only 3 had consulted their doctors. 60 had not heard about contraception from medical staffs, 61 had done 1-2 times, and 34 had done 3 or more. 11 had received explanations on contraception methods, and 78 had only been informed the necessity. 86 wanted active explanations from staffs, and 65 only wanted it when asked. [Conclusion] The contraception, a part of pregnancy planning for patients, is not always sufficient.

W25-2

Evaluation of Mental Development in Children Born to Mothers with Systemic Lupus Erythematosus (Interim Report)

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Conflict of interest: None

[Objectives] This study aims to evaluate the mental development of SLE offspring. [Methods] The study included offspring who reached the corrected age of 24 months and were born to women registered in the PLEASURE-J cohort study between December 2017 and September 2022. The CBCL, Denver II, and the Japanese version of the M-CHAT were mailed to the parents for completion. Specialists in developmental-behavioral pediatrics and certified psychologists comprehensively evaluated the results. [Results] As of September 2024, consent was obtained from the parents of 19 (73%) of the 26 offspring who had reached the corrected age of 24 months, and 17 eligible cases were analyzed. Four cases (23.5%) were born before 37 weeks of gestation, and 10 cases (58.8%) had a birth weight of less than 2500 g. Offspring who exceeded the cut-off values on the tests included 4 cases (23.5%) for the CBCL, 7 cases (36.8%) for the Denver II, and 5 cases (26.3%) for the M-CHAT. Ten offspring (58.8%) exceeded the cut-off values in at least one of the three screening tests. [Conclusion] Based on the screening test results, a mental developmental evaluation of SLE offspring was conducted. Long-term developmental follow-up is necessary.

W25-3

Hydroxychloroquine and low-dose aspirin in lupus pregnancy outcomes

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Conflict of interest: None

[Objective] The aim of this study was to evaluate the efficacy of HCQ and ASA on pregnancy outcomes. [Methods] We studied lupus pregnancies from three hospitals (April 2010-January 2024), analyzing first-trimester HCQ and ASA use and their impact on pregnancy outcomes. [Results] A total of 191 pregnancies were analyzed, with a miscarriage rate of 7.9%, an induced abortion rate of 6.8%, and a live birth rate of 85.3%. HCQ was used in 35.1% of pregnancies, ASA in 30.9%, with 18.8% using both. Preeclampsia occurred in 10.5% and PROMISSE adverse pregnancy outcomes (APO) in 25.1%. Among the 169 live births, 21.3% were small for gestational age (SGA). Inverse probability weighting analysis showed that the odds ratio (OR) for preeclampsia was 0.60 (95% CI: 0.21-1.76) with HCQ use, 0.64 (95% CI: 0.19-2.17) with ASA use, and 0.78 (95% CI: 0.18-3.38) for combined use. For SGA, the OR was 0.52 (95% CI: 0.21-1.24) with HCQ, 0.31 (95% CI: 0.11-0.86) with ASA, and 0.18 (95% CI: 0.04-0.86) for combined use. For PROMISSE APO, the OR was 0.55 (95% CI: 0.25-1.19) with HCQ, 0.64 (95% CI: 0.29-1.42) with ASA, and 0.37 (95% CI: 0.12-1.14) for combined use. [Conclusion] Combined HCQ and ASA significantly reduced SGA rates in lupus pregnancies and suggested lower preeclampsia and PROMISSE APO rates.

W25-4

Usefulness of anti-Ro52 antibody in pregnancy complicated with anti-SS-A antibody positive patients

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Conflict of interest: None

[Purpose] We clarify the relationship between anti-Ro52 antibody and pregnancy outcomes in anti-SS-A antibody-positive pregnancy cases in our institution. [Methods] We used the data of anti-SS-A antibody-positive cases from the registry in our institution. The relationship between the titer of anti-RO52 antibody and anti-SS-A antibody was examined and we retrospectively analyzed whether the presence or absence of anti-RO52 antibody is a risk factor for pregnancy outcomes. [Results] The subjects were 103 cases. Of the 52 cases in which anti-Ro52 antibody could be measured, 28 cases were positive, and significant correlation was observed between the titer of anti-R052 antibody and anti-SS-A antibody. The titers of anti-SS-A antibody were significantly higher in anti-Ro52 antibody positive cases, and the cut-off value of anti-SS-A antibody which were positive for anti-Ro52 antibody was 1648.0 IU/ml. Congenital heart block was observed in two cases, both of which had high titers of anti-SS-A and anti-Ro52 antibodies. Anti-Ro52 antibody or the titers were not risk factors for pregnancy outcomes. [Conclusion] In patients with positive for anti-SS-A antibody, risk assessment and management, including the presence or absence of anti-Ro52 antibody, are important.

W25-5

Efforts to improve preconception care for patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] We decided to create educational materials to help provide preconception care for patients with underlying diseases. We conducted a survey of academic societies to identify issues, and we will report on the results in the field of rheumatology. [Methods] An online questionnaire was conducted for doctors. The survey items included information on the respondents' backgrounds, the situation of explaining pregnancy and childbirth in daily medical practice, and the constraints on providing information on preconception care. [Results] A total of 5025 people were surveyed, and 185 (3.6%) responded. 91.8% of doctors said they explained to their patients the impact of underlying diseases on pregnancy and childbirth, but 41.1% explained about appropriate contraceptive methods during times when pregnancy is not desirable from a medical perspective. The main constraints on providing information were (1) time (90.3%) and (2) the knowledge of healthcare professionals (65.4%). [Conclusion] Many of the doctors who responded explained about diseases and pregnancy and childbirth, but did not provide a sufficient explanation. Issues such as the limited time for outpatient consultations and the lack of opportunities to gain knowledge were cited.

W26-1

Validation of the International Myositis Assessment and Clinical Studies Group guideline on idiopathic inflammatory myopathy-associated cancer risk stratification: a single-center retrospective cohort study

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Conflict of interest: None

[Objectives] To validate the International Myositis Assessment and Clinical Studies Group (IMACS) guideline on idiopathic inflammatory myopathy (IIM) -associated cancer risk stratification in a myositis referral center in Japan. [Methods] We retrospectively assessed consecutive patients diagnosed with IIM from August 2014 to May 2024 who had no cancer within three years before IIM diagnosis. We stratified patients into high-, moderate-, or standard-risk of cancer according to the IMACS guideline and investigated cancer events within three years after IIM diagnosis in each risk group. [Results] Our study included 183 patients in total (median age at IIM onset 61 years; 66.7% female). The median follow-up period was 34 months. The IMACS model classified 75 (41.0%), 100 (54.6%), and 8 (4.4%) patients into high-, moderate-, and standard-risk. We identified 15 (20.0%), 8 (8.0%), and 0 cancer events in each risk group. Given all patients with cancer events were over 50 years at IIM onset, we modified the age cutoff for high-risk from 40 to 50 years, resulting in 15/65 (23.1%), 8/94 (8.5%), and 0/24 cancer events in each group. [Conclusion] Our results upheld the IMACS cancer risk stratification model. There might be a room for optimization in the age cutoff for cancer high-risk in Japan.

W26-2

Clinical features of malignancy-associated anti-TIF1-gamma antibody-positive dermatomyositis

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Conflict of interest: None

[Objectives] To compare the clinical presentation of malignancy-associated and non-associated cases of anti-TIF1-γ antibody-positive dermatomyositis (DM). [Methods] We compared the clinical features of anti-TIF1-antibody-positive dermatomyositis (DM) diagnosed after 2016 in cases complicated with malignancy (Ca+ group) and in uncomplicated cases (Ca- group). [Results] Ca+ group 11 patients (7 males), Ca- group 10 patients (3 males). Malignancies included 4 gastrointestinal cancers and 3 breast cancers. Comparison of the two groups (Ca+ vs. Ca-) showed a mean age of 71.3 vs. 65.8 years. No differences were observed in skin, muscle, joint symptoms. Laboratory findings showed that CK, CRP, and anti-TIF1-γ antibody were higher in the Ca+ group. Scoring the sum of 5 items (1 point each): age >=60 years, anti-TIF1-γ antibody >=100 Index, CK >=1000 U/L, CRP >=1.0 mg/dl, and positive antinuclear antibody, the Ca+ group showed a median of 3 (2-5) and the Ca- group a median of 1 (0-3) (P = 0.0003). [Conclusion] There were differences in laboratory findings between cases with and without malignancy in anti-TIF1-γ antibody-positive DM.

W26-3

Clinical Characteristics of Patients with Relapsed Anti-MDA5-Positive Dermatomyositis: A Case Series Report

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Conflict of interest: None

[Objectives] To investigate the clinical characteristics of patients with relapsed anti-MDA5-positive dermatomyositis (DM). [Methods] The clinical data of patients with anti-MDA5-positive DM-associated ILD initially treated with glucocorticoids (GC) were retrospectively reviewed. Cases in which the GC dose was increased again after the dose was reduced to prednisolone (PSL)-equivalent ≦7.5 mg/day were defined as relapse cases. [Results] 5 patients relapsed among the 29 hospitalized and survived patients with anti-MDA5-positive DM associated with ILD. All patients received GC alone or in combination with tacrolimus or cyclosporine. 2 patients were initially treated in other hospitals, and anti-MDA5 antibody positivity had not been recognized in 2 cases. At the time of relapse, patients were treated with 2-6 mg/day of PSL-equivalent GC and tacrolimus or cyclosporine concomitantly. The serum anti-MDA5 antibodies were positive, and the serum ferritin levels were elevated (92-4938 ng/mL). The GC dose was increased, and the patients received triple-combination therapy, including tacrolimus/cyclosporine and cyclophosphamide. All patients were ameliorated. [Conclusion] In patients with anti-MDA5-positive DM, anti-MDA5 antibody positivity and hyperferritinemia were observed upon relapse.

W26-4

Anti-Synthetase Syndrome (ASS): A Comparative Analysis of Clinical Features and Cutaneous Manifestations Between Japanese and European Patients

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Conflict of interest: None

[Objectives] Anti-synthetase syndrome (ASS) is an idiopathic inflammatory myopathy characterized by the presence of anti-ARS antibody. Reports on the skin lesions of ASS are scarce, and racial differences have not been adequately investigated. This study aimed to investigate the clinical features of ASS in our cohort and compare them with previous reports. [Methods] We retrospectively analyzed the clinical features of 48 ASS patients who visited our department from January 2010 to July 2024. [Results] The mean age at onset was 56.5 years, with a male-to-female ratio of 13:35. Interstitial lung disease was observed in 97% of patients, and myositis in 52%. The most frequent skin lesions were Gottron's papules (73%), followed by mechanic's hands (65%), and periungual erythema (40%). Thirty-six patients (75%) fulfilled the Japanese diagnostic criteria for DM. A comparison with a report by Hamaguchi et al. showed a similar tendency to our cohort. However, comparison with the MYONET registry revealed that heliotrope rash, Raynaud's phenomenon, and myositis was more frequent in the European population while mechanic's hands and shawl sign were more common in our cohort. [Conclusion] Our study demonstrates that the clinical features of ASS may be different by race.

W26-5

Clinical review of polymyositis and dermatomyositis experienced at our hospital

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Conflict of interest: None

[Objectives] Polymyositis (PM)/ dermatomyositis (DM) is a type of autoimmune disease that causes muscle disorders and is known to be associated with interstitial pneumoniae (IP) and malignant tumors. In addition, there are many autoantibodies and it is known each antibody has different clinical characteristics. The purpose of this study was to clarify the characteristics of each of these antibodies. [Methods] 105 patients with first-episode myositis admitted to our department were selected. The clinical history, symptoms, examination findings, treatment details, and course of the patients were investigated retrospectively from the medical records. [Results] Age 18-87 (mean 61) years. There were 76 female patients: 50 with DM, 55 with PM, and 53 with IP complications. DM was most common with anti-MDA5 antibody (9 cases, 100%), and PM was most common with anti-SRP antibody (7 cases, 87%). IP was most common with anti-MDA5 antibody (8 cases, 89%), followed by anti-ARS antibody (27 cases, 79%). Malignancies were most common with anti-TIF1-γ antibodies (3 cases) and anti-ARS antibodies (3 cases). [Conclusion] All deaths due to myositis were caused by IP with anti-MDA5 antibody (+) patients, but it is important to know that deaths were also found in severeal anti-ARS antibody (+) patients.

W26-6

A retrospective study of dysphagia in dermatomyositis/polymyositis (PM/DM)

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Conflict of interest: None

[Objective] We report the characteristics and outcome of dysphagia in patients with dermatomyositis/polymyositis (PM/DM). [Methods] Sixty-six patients (mean age: 58.8±15.3 years) diagnosed with PM/DM between January 2015 and September 2024 were subjected the study. PM/DM patients who had dysphagia were retrospectively analyzed. [Results] Thirty-four patients (twenty-one females, mean age 61.0±15.0 years, antibodies: anti-TIF1γ eight cases, anti-SRP four, anti-MDA5 four, anti-ARS two, anti-Ro52/SS-A four, anti-PM-Scl two, scleroderma seven, autoantibody-negative three) had dysphagia. Eight patients presented with severe dysphagia and required gastrostomy or tube feeding. Videofluoroscopic swallowing study showed decreased pharyngeal contractility and failure of opening of the esophageal entrance. Patients with tumors tended to be refractory to the treatment. In addition to immunosuppressive therapy, intermittent oro-esophageal tube feeding significantly improved symptoms in two patients. [Conclusion] PM/DM with dysphagia attributes to abnormalities in the pharyngeal stage. Patients with severe dysphagia have a poor prognosis, but there are cases in which recovery of swallowing function could be expected with immunosuppressive therapy and long-term rehabilitation.

W27-1

Differences in organ damage between juvenile, adolescent, and elderly-onset idiopathic inflammatory myopathies: a study using MYKO

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Conflict of interest: None

Objectives: To analyze differences in organ damage between age using Multicenter Myositis Registry (MYKO). Methods: Factors influencing organ damage (SDI) were determined by multivariate regression analysis. We classified patients into juvenile (<20 years old), adolescent (20-64), and elderly onset (>64). Results: A correlation was observed between age and SDI in 220 patients (ρ=0.28, p<.0001). Multivariate analysis showed that women (β=-0.54), onset age (β=0.036), disease duration (β=0.07), and steroid pulse (β=0.95) influenced on SDI. When patients were classified as juvenile (n=18), adolescent (n=168), elderly onset (n=44), total SDI was 1.0±0.76 vs. 1.3±1.61 vs. 2.16±1.94 (p=0.01), which was higher in patients with elderly onset. Organ-specific SDI items were high for eye, neuropsychiatric, renal, pulmonary, cardiovascular, peripheral vascular, gastrointestinal, skin, gonadal dysfunction, diabetes, and malignancy in the order of elderly, adolescent, and juvenile onset. SDI for musculoskeletal were higher for juvenile onset (juvenile vs. adolescent vs. elderly onset: 0.50±0.53 vs. 0.41±0.69 vs. 0.39±0.69, p=0.65, respectively). Conclusions: Older onset was associated with severe organ damage. Musculoskeletal damage was higher in patients with juvenile onset.

W27-2

Compatibility and modification of 2017 EULAR/ACR Classification Criteria for Myopathies in Anti-ARS patients -A Study Using the Kansai Multicenter MYKO cohort

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Conflict of interest: None

[Objectives] To evaluate and improve the 2017 EULAR/ACR classification criteria for idiopathic inflammatory myopathies (IIM) for anti-synthetase syndrome (ASS). [Methods] Anti-ARS-positive patients from the MYCO cohort were analyzed. Factors affecting the criteria's accuracy were identified, and an improved model for classification was developed. [Results] Of the 188 anti-ARS-positive patients, 67% met the criteria. Non-concordant group had similar high frequencies of mechanic's hands and interstitial lung disease (ILD), but a lower frequency of anti-Jo-1. Agreement improved to 72% with a change in dysphagia criteria to dysphagia or ILD, 96% with a change in anti-Jo1 to anti-ARS, and 99% with both changes. The agreement between clinical diagnosis and subclassification based on the criteria was 47%. Cases with mechanic's hands or mild muscle symptoms that were not included in the criteria tended to be classified as PM or CADM by clinical diagnosis. The agreement increased to 61% with the unification of DM or CADM with DM and 68% auditioning mechanic's hands to skin rash. [Conclusion] The 2017 EULAR/ACR criteria can be improved to classify ASS more accurately by revising antibody definitions and clinical manifestations.

W27-3

Clinical features of dermatomyositis and polymyositis that achieved glucocorticoid-free remission

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Conflict of interest: None

[Objectives] To clarify clinical features of dermatomyositis and polymyositis (DM/PM) achieving glucocorticoid (GC)-free remission. [Methods] A retrospective review of 98 DM/PM patients (64 DM, 34 PM) from 2017 to 2024. Factors analyzed included gender, age, maximum prednisone (PSL) dose (mg/kg/day) used to induce remission, myogenic enzymes (creatinine kinase (CK) and aldolase) before treatment, manual muscle test (MMT), CRP (mg/dl), disease-specific antibodies, interstitial pneumonia (%), observation duration, CK negativity, and GC-free status. Multivariate analysis was conducted for predictors of GC-free status. [Results] Mean diagnosis age was 58.5±15.5 years; male-to-female ratio was 32/66. The initial PSL dose for remission was 0.89±0.23 mg/kg/day, pretreatment CK was 1504.8±2252 U/L, MMT score was 4.0±0.89, and 66.3 % had interstitial lung disease. Twelve patients achieved GC-free status. Multivariate analysis indicated that pretreatment CK levels significantly predicted GC-free remission. [Conclusion] High CK levels before treatment are associated with difficulty achieving GC-free remission.

W27-4

Efficacy of Plasma Exchange Therapy and JAK Inhibitor for Anti-MDA5 Antibody-Positive Dermatomyositis

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Conflict of interest: None

[Objectives] Anti-MDA5 antibody-positive dermatomyositis often causes rapid progressive interstitial pneumonia, leading to poor prognosis and treatment resistance. Recent studies show that tofacitinib (TOF) and plasma exchange (PE), now covered by insurance in Japan, are effective. This study will assess these treatments at our institution. [Methods] A retrospective analysis was conducted on all cases diagnosed at our facility from

April 2014 to April 2024, examining patient backgrounds, treatment regimens, and outcomes. [Results] Among 14 cases (mean age 58.9 years; 5 males, 9 females), 7 received PE, and 8 received TOF. In the PE group, all patients also received TOF; PE+TOF was initiated in 6 cases for respiratory failure and in 1 for worsening interstitial pneumonia. Of the 14 cases, 11 survived, 2 were lost to follow-up, and 1 died early in treatment. The fatal case received TOF but not PE. Comparing PE vs. non-PE groups, median serum ferritin levels were 506.9 vs. 793.5 ng/mL at initiation, 697.6 vs. 1152.7 ng/mL at 1 month, and 53.6 vs. 958 ng/mL at 6 months. Daily PSL dose at 6 months was 10.0 vs. 11.5 mg. [Conclusion] In anti-MDA5 antibody-positive dermatomyositis, combining PE with JAK inhibitors may improve survival rates, enhance ferritin levels, and reduce steroid use.

W27-5

Investigation of Treatment Outcomes and Prognostic Factors in Anti-MDA5 Antibody-Positive Dermatomyositis (DM)

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Conflict of interest: None

[Objectives] Since the anti-MDA5 antibody test became covered by insurance, we evaluated the treatment outcomes and prognostic factors of anti-MDA5 antibody-positive DM diagnosed at Niigata University Medical and Dental Hospital and Nagaoka Red Cross Hospital. [Methods] We retrospectively reviewed the treatment outcomes of 43 patients diagnosed with anti-MDA5 antibody-positive DM after October 2016. [Results] Patients had a median age of 59 (47~70), 11 males, and 32 females, ferritin (223~1234) 466 ng/ml, CRP 0.81 (0.17~1.73) mg/dl, KL-6 661 (495~907) U/ml, and anti-MDA5 antibody titers 2400 (1085~3658) pg/ml. 5 patients had skin ulcers, 26 had inverse Gottron's sign, and 40 had interstitial lung disease. Three-drug combination therapy with high-dose steroids, calcineurin inhibitors, and intravenous cyclophosphamide was used in 35 cases, with additional therapies such as intravenous immunoglobulin (9), plasmapheresis (5), and others as needed. Survival rate was 74%. Ferritin, CRP, LDH, and anti-MDA5 antibody levels significantly decreased in surviving cases. Prognostic factors in fatal cases included age ≧60, ferritin ≧500 ng/ml, SpO_2 <95%, and CRP ≧1 mg/dl. [Conclusion] The three-drug combination therapy improved survival, but further therapies are needed for cases with poor prognostic factors.

W27-6

Optimal glucocorticoid maintenance dose for patients with anti-ARS antibody-positive polymyositis/dermatomyositis: a single-center retrospective study of 56 patients

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Conflict of interest: None

[Objectives] The clinical presentation of polymyositis/dermatomyositis differs according to myositis-specific autoantibodies. anti-ARS antibody-positive patients show good response to glucocorticoid (GC) therapy, but relapse following dose reduction is a concern. However, there is no adequate study on the appropriate maintenance dose to prevent relapse. [Methods] Among patients with positive anti-ARS antibodies measured at our hospital from April 2018 to September 2024, we retrospectively examined and statistically analyzed GC dose reduction and discontinuation. [Results] 56 patients, 32 of whom were female, and 50 with interstitial pneumonia were included in this study. Anti-Jo-1 antibody was positive in 11 cases, negative in 38 cases. In the remission induction phase, the mean initial dose of prednisolone (PSL) was 38 mg. The mean PSL maintenance dose at relapse was 1.9 mg and 4.3 mg (p=0.03) for anti-Jo-1 antibody-positive cases and negative cases, respectively (6 cases and 21 cases (p=0.97)). Relapse at 5 mg of PSL was observed in 0 and 9 patients. [Conclusion] It seems feasible to reduce the maintenance dose of GC in anti-Jo-1 antibody-positive cases to a lower dose than in negative cases, and the maintenance dose of PSL 5 mg/day seems to be an achievable goal without recurrence.

W28-1

Evaluation of the pathological characteristics of renal lesions and disease activity in adult Still's disease

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Conflict of interest: None

[Objectives] Renal manifestations in Adult-onset Still's Disease (ASD) present with diverse pathological features. We investigated the characteristics and outcomes of renal lesions in ASD patients. [Methods] We retrospectively analyzed clinical and pathological findings in ASD patients who underwent kidney biopsy or autopsy at our institution. [Results] Among 50 ASD patients, 6 (12%) underwent renal pathological evaluation. Mean age was 65.3±16.0 years, with equal gender distribution. Mean eGFR was 61.52±30.32 mL/min/1.73 m^2, with proteinuria in 5 cases (1.052 ±0.86 g/day). Pathological diagnoses included IgA nephropathy (n=2), nephrosclerosis (n=2), minor glomerular abnormalities (n=1), and AA amyloidosis (n=1). While five cases were diagnosed within 4 months of onset/relapse, the AA amyloidosis case occurred in a patient with 28-year disease duration, showing extensive amyloid deposits in the glomeruli, arterioles, and tubular basement. No cases progressed to end-stage renal disease. [Conclusion] Early ASD-related renal lesions are generally mild with favorable outcomes upon disease remission. However, prolonged high disease activity may increase the risk of secondary amyloidosis, suggesting that ASD disease control significantly influences renal structural integrity and prognosis.

W28-2

Risk Factors for Early Relapse Following Glucocorticoid Discontinuation in Adult-Onset Still's Disease Treated with Tocilizumab

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Conflict of interest: None

[Objectives] Tocilizumab (TCZ) with glucocorticoids (GC) has facilitated more frequent GC discontinuations in adult-onset Still's disease (AOSD), but early relapse after GC withdrawal on TCZ remains a concern. This study assessed factors for early relapse after GC discontinuation with TCZ. [Methods] From 81 AOSD patients treated from April 2010 to August 2024, 21 met Yamaguchi's criteria, received TCZ with GC, and discontinued GC. Patients were classified into relapse and non-relapse groups based on relapse within one year of GC discontinuation on TCZ monotherapy, and risk factors were retrospectively analyzed. [Results] Among 21 patients, 4 relapsed, and 17 did not. The median age at treatment initiation was 40 years in the relapse group and 31 years in the non-relapse group, with no gender difference. Clinical symptoms, organ involvement, and lab findings at treatment start and GC discontinuation were similar between groups. However, total GC duration was shorter in the relapse group (median 126 vs. 291 days, p=0.04). Patients with GC duration ≧136 days had a higher one-year relapse-free survival rate (p<0.001). [Conclusion] In AOSD patients stopping GC on TCZ, shorter GC duration is a risk factor for early relapse. Patients stopping GC within 135 days may need close monitoring.

W28-3

Improvement of the Activity Score for Behçet's Disease by Weighting BDCAF Items and Enhanced Prediction of Major Organ Events

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Conflict of interest: None

[Objectives] To modity the Behçet's disease (BD) activity score by weighting items in the Behçet Disease Current Activity Form (BDCAF) and assess the new score's utility in predicting major organ events. [Methods] We extracted 644 BDCAF from a BD registry at Yokohama City University, Hokkaido University, Kitasato University, and Niigata University. The 12 BDCAF items were weighted using Poisson regression with Lasso regularization, with physicians' disease activity evaluations on a 7-point scale as the outcome variable. The predictive performance of BDCAF and new scores for major organ events was compared for 209 patients aged ≧16, meeting Japanese diagnostic criteria, with a disease duration ≧6 months. [Results] Coefficients assigned were: 6 for new ocular symptoms and neurologic lesions, 4 for headache, oral ulcers, erythema, arthritis, and bloody diarrhea, 3 for arthralgia, and 1 for genital ulcers, pustules, and nausea/abdominal pain. The AUC for predicting major organ events up to 52 weeks was 0.6 for BDCAF and 0.7 for the new score. Combined with prednisolone ≦5 mg/day and serum IL-6, the new score's AUC was 0.83. [Conclusion] A novel score was developed by weighting BDCAF items. Combining the new score with treatment and serum IL-6 improved prediction of major organ events.

W28-4

Analysis of the Association Between Disease Activity Index BDCAF and Poor Prognosis Disease Types in Patients Registered in the Nationwide Behçet's Disease Registry

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Conflict of interest: None

[Objectives] This study aims to further validate the association between Behçet Disease Current Activity Form (BDCAF) scores and the onset or relapse of poor prognosis types defined as ocular, neurological, gastrointestinal, and vascular type among patients registered in a nationwide Behçet's disease (BD) registry in Japan. [Methods] Among 562 cases collected by October 25, 2024, we selected cases whose BDCAF at enrollment, major organ events, onset date of events, and follow-up period were available. Survival time analysis was performed for the first BDCAF=0 group (remission group) and the first BDCAF≧1 group (non-remission group). [Results] The median initial BDCAF of the 205 selected patients was 2 [1-3]. The mean follow-up was 115.7±47.3 weeks. 21 patients (10.2%, eye: 10, neurological: 2, intestinal: 7, vascular: 2) had major organ events, and the mean time to event was 55.0±39.9 weeks. Survival time analysis showed that the non-remission group tended to have a lower survival rate than the remission group. [Conclusion] This nationwide BD registry study suggests that maintaining a BDCAF score of 0 could potentially reduce the incidence or relapse of severe disease manifestations. We aim to update and present the latest data at the time of publication.

W28-5

Serum IL-6 in neuro-Behcet's disease

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Conflict of interest: None

[Objectives] In Behçet's disease, elevated serum IL-6 has been found to correlate with disease activity, leading to inflammatory organ lesions. In neuro-Behçet's disease (NB), elevated cerebrospinal fluid IL-6 is shown to reflect disease activity, while the role of serum IL-6 is unknown. We investigated serum IL-6 in acute NB (ANB) and chronic progressive NB (CPNB). [Methods] We measured serum IL-6 in the active phase of 16 patients with ANB (age 46.7±13.6 [mean±SD]) and 14 patients with CPNB (age 41.6±10.8), and 18 patients with non-inflammatory neurological diseases (age 47.4±10.7) as a control; the 3 groups were compared by the Kruskal-Wallis test. [Results] Serum IL-6 was significantly elevated in CPNB (5.897 ±1.333 pg/ml [mean±SEM]) compared with a control (1.189±0.295 pg/ml), but not with ANB. In ANB (3.451±0.880 pg/ml) serum IL-6 appeared higher than that in a control, but without significant difference. Of note, ROC analysis of serum IL-6 showed that CPNB could be differentiated from a control with sensitivity of 64.3% and specificity of 94.4% (AUC 0.7679, p=0.0104) with cut-off of serum IL-6 3.863 pg/ml. [Conclusion] The results indicate that serum IL-6 is involved in the pathogenesis of CPNB. Furthermore, it is suggested that serum IL-6 may be useful in the diagnosis of CPNB.

W28-6

Association of Clonal Hematopoiesis with Trisomy 8 in Intestinal Lesions

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Conflict of interest: None

[Objectives] Trisomy 8 is a chromosomal abnormality seen in myelodysplastic syndrome (MDS) and acute myeloid leukemia, and suggested association with clonal hematopoiesis of indeterminate potential (CHIP). Some patients with Trisomy 8 were affected with Behçet's disease-like intestinal lesions (ILs), which of pathology is unclear. In this study, we investigated association with CHIP in the mechanisms of inflammatory immune disease with Trisomy 8. [Methods] We analyzed 4 cases with ILs, and 4 MDS cases without ILs. [Results] Trisomy 8 cells were detected in bone marrow of all cases by G-band or FISH analysis. Among the 4 cases with ILs, 3 cases did not fulfill the diagnostic criteria for Behçet's disease. Two cases with ILs showed an increase of Trisomy 8 cells over time. Trisomy 8 cells were detected in the peripheral blood of 2 cases. In addition, FISH analysis confirmed the infiltration of Trisomy 8 cells into ILs in one case. The higher serum ferritin levels were shown in cases with ILs, while lower hemoglobin levels and a worse overall survival rate in cases without ILs. [Conclusion] Trisomy 8 cells are suggested to contribute to ILs. Further case accumulation and detailed molecular biological analyses are needed.

W29-1

Prognostic predictors of nintedanib for collagen disease-associated interstitial pneumonia

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Conflict of interest: None

[Background] Nintedanib is known to be effective SSc associated ILD. However, its efficacy and prognostic factors for other CTD-ILD is insufficient. [Objective] To explore factors predicting the efficacy of nintedanib against CTD-ILD. [Methods] We extracted CTD-ILD patients treated with nintedanib. Baseline information, KL-6 value, annual change KL-6 (ΔKL-6), and %VC before and after treatment were extracted. Patients whose KL-6 value showed a tendency to decrease were classified as effective group, and an increasing tendency were ineffective group. We explored factors that influenced the efficacy. [Results] 85 patients were identified, and 45 were effective group and 28 were ineffective group. Regression analysis showed that the change in %VC predicted the effective and ineffective groups ($p=0.029$). Regression analysis showed no significant differences in age, sex, steroid dosage, underlying disease, skin score, ILD pattern, or maintenance dose of nintedanib, but duration of disease ($p=0.0331$) and ΔKL-6 ($p < 0.01$) predicted effective group. Using the ROC curve, effective group could be predicted when cutoff value ofΔKL6 at 3 months -80 U/mL (OR; 24.9, $p < 0.01$). [Conclusion] Nintedanib can effective in CTD-ILD, and its efficacy may be predicted by KL6 levels.

W29-2

Effects of nintedanib in combination with immunosuppressive agents for CTD-ILD

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of combination therapy with nintedanib (NTB) and immunosuppressive drugs (IS) for progressive fibrosing connective tissue disease-associated interstitial lung disease (CTD-ILD). [Methods] CTD-ILD patients who fulfilled the criteria for PF-ILD at our hospital were divided into two groups: one received NTB alone (NTB group, n=16) and the other group received NTB and IS (NTB+IS group, n=17). Changes in FVC, DLCO, and serum KL-6 levels, and the incidence of adverse events (AEs) within 12 months were compared in the two groups. [Results] The pulmonary function at baseline in each group was as follows: mean FVC, 66.6%/64.4%; mean DLCO, 57.4%/41.4%. The main CTD was systemic sclerosis (8/6 cases in each group), and the most common IS in the NTB+IS group was rituximab (9 cases). Change in FVC after treatment was significantly greater in the NTB+IS group than in the NTB group (7.5% vs. -1.2%, $p=0.01$). The NTB+IS group showed an increase in DLCO and a decrease in KL-6 compared with the NTB group, with no significant differences. The most frequent AE was diarrhea, and the dose reduction of NTB was performed in 7/6 cases in each group. [Conclusions] NTB in combination with IS is an effective treatment option for progressive fibrosing CTD-ILD.

W29-3

A Case of Severe C1q Deficiency Presenting with Encephalopathy Associated with Hemophagocytic Syndrome

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Conflict of interest: None

[Case] A 47-year-old female patient was diagnosed with systemic lupus erythematosus and Sjögren's syndrome at age 12. She was treated with azathioprine during recent years. C3 and C4 levels remained normal, while CH50 levels continued to be low. Peripheral neuropathy and anemia were developed in June of Year X. She declined invasive examinations, and was treated with high-dose intravenous immunoglobulin. But her symptoms did not improve, leading to readmission in September. During this admission, she developed acute respiratory failure due to sputum obstruction, requiring intubation. Post-sedation, her consciousness remained impaired. A brain CT showed hypodense areas in the bilateral thalami, suggesting encephalopathy. In addition, pancytopenia, elevated ferritin, and hemophagocytosis in bone marrow led to a diagnosis of hemophagocytic syndrome (HPS) with encephalopathy. The low CH50 with undetectable C1q levels suggested C1q deficiency. Her pancytopenia, hyperferritinemia, and consciousness disorder were improved by glucocorticoid pulse therapy and cyclosporine. [Discussion] Complement deficiencies are rare pathology characterized by lupus-like symptoms. Here, we report a significantly rare and severe case involving HPS and encephalopathy.

W29-4

Inflammatory pseudo-tumor with multiple organ involvement, vasculitis, and autoantibody production

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Conflict of interest: None

Inflammatory pseudo-tumor (IPT) is a rare disease marked by benign mass formations characterized by inflammatory cell infiltration and fibrous tissue proliferation. Case: A 22-year-old woman first noticed an abdominal subcutaneous mass eight years ago. Four years later, she had seizures, leading to the discovery of a mass in her left parietal lobe. Three years ago, she was diagnosed with thrombocytopenic purpura, prompting steroid treatment that reduced the brain mass. After lowering her prednisolone dosage, new masses appeared in her abdominal subcutaneous tissue, thigh, lower leg, and right parietal lobe. She also experienced visual impairment due to a mass on her right optic nerve, along with right optic neuritis and retinal vasculitis. Her conditions included thrombocytopenia, elevated PAIgG, anti-thyroglobulin antibodies, and anti-CL-IgG. A biopsy confirmed lymphocyte inflammatory cell infiltration and fibrosis, leading to an IPT diagnosis. No genetic abnormalities for lymphoproliferative disorders were identified. Treatment with methylprednisolone pulse therapy and rituximab resolved the mass and markedly improved her optic neuritis, retinal vasculitis, and thrombocytopenia. There are no reports of IPT with multi-organ involvement, vasculitis, or autoantibody production.

W29-5

Analysis of risk of autoimmune diseases induced by type 2 inflammation inhibitors: An observational study using anonymized electronic medical record database

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Conflict of interest: None

[Objective] To investigate the association between biologics targeting type 2 inflammation (type 2i) and the onset of autoimmune diseases (AIDs). [Methods] We used an anonymized electronic medical record database in Japan. The study cohort included patients aged ≧18 years with diagnoses of bronchial asthma, chronic urticaria, eosinophilic sinusitis, or atopic dermatitis after April 2018. Exposures were anti-IL-5 agents (IL-5i), anti-IL-4 agents (IL-4i), and anti-IgE agents (IgEi). Outcomes included 11 AIDs as well as a composite of them. The risk of each exposure was analyzed using nested case-control (NCC) analysis and extended Cox regression (eCox), considering time-dependent exposure. [Results] A total of 27,164 patients were included. For the composite outcome, IL-4i had an adjusted RR of 1.91 (95% CI: 0.78, 4.68) in the NCC analysis and 2.07 (1.07, 4.00) in the eCox analysis. IL-4i in asthma patients showed an association with psoriasis, with an adjusted RR of 3.16 (0.37, 27.28) in the NCC analysis and

5.99 (1.81, 19.84) in the eCox analysis. No notable associations were found for other outcomes. [Conclusion] IL-4i was associated with the risk of AIDs, particularly psoriasis in asthma patients. This is the first large-scale study examining the association between type 2i and AIDs.

W29-6

9 cases of rheumatic irAE after initiation of immune checkpoint inhibitors

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Conflict of interest: None

[Objectives] Immune checkpoint inhibitors (ICIs) are now widely used in the perioperative period and in unresectable cases of multiple cancers. We report 9 cases of RirAE after initiation of ICI. [Patients] Nine patients with RirAE were diagnosed from 2020 to 2024. The mean age was 65.2 years (48-84), the proportion of female patients was 22.2%, the type of ICI was anti-PD-1 antibody in 8 patients (88.8%) and anti-PD-L1 antibody in 1 patient (11.1%). Continuation rate after RirAE: 11.1%, complication rate of irAE in other organs: 55.5%, rheumatoid factor (RF) positive rate: 33.3%, anti-CCP antibody (ACPA) positive rate: 22.2%, antinuclear antibody positive rate: 22.2%, prednisolone (PSL) use: 55.5%, mean dose at PSL start: 11.0 mg/day, csDMARDs use: 11.0 mg/day, csDMARDs use: 11.0 mg/day The csDMARDs used were methotrexate, salazosulfapyridine, iguratimod, and tacrolimus. [Conclusion] The rheumatologist's role is to alleviate RirAE symptoms and to help patients maintain effective cancer immunotherapy. The ICI continuation rate after RirAE in our hospital was 14.2%, which is low compared to previous reports. It is important for oncologists and rheumatologists to cooperate with each other from the early stage of oncology and rheumatology to identify and evaluate patients with RirAE.

W30-1

Involvement of IL-22/IL-22 binding protein in the pathogenesis of autoantibody-induced arthritis via modulation of inflammatory cytokine and chemokine expression in the inflamed synovium of a murine model

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Conflict of interest: None

[Objectives] Pathogenic role of IL-22 and IL-22 binding protein (IL-22BP) in inflammatory arthritis remains unclear. We investigated the role of IL22/IL-22BP in the arthritis development in mice. [Methods] C57BL/6 IL-22BP gene deficient (-/-) mice were used in K/BxN serum transfer arthritis. Murine fibroblast-like synoviocytes (mFLS) were stimulated with recombinant IL-1β and IL-22. mRNA levels of IL-22, IL-22BP, CXCL1 and IL-1β were analyzed in cultured cells and synovial tissues by qRT-PCR. CXCL1 and IL-1β protein were examined by ELISA. [Results] A significant upregulation of IL-22 and IL-22 BP mRNA was observed in inflamed synovial tissue compared to those of naive mice. mFLS expressed IL-22 and IL22BP mRNA and IL-1β stimulation increased IL-22 mRNA significantly. IL-22BP-/-mouse developed a more disease severity that was accompanied by elevation of IL-1β gene in the joints as compared to control mice. The infiltration of inflammatory cells was increased in IL-22BP-/-mice significantly with elevation of CXCL1 in inflamed ankle synovial tissues. IL-22 stimulation induced mFLS IL-1β and CXCL1 production at both RNA and protein levels. [Conclusion] IL-22BP deficiency exacerbated autoantibody-induced arthritis via upregulation of IL-1β and CXCL1 in the inflamed synovial tissues.

W30-2

The Research of intracellular signaling and cytokines in lung fibroblasts in neutrophil extracellular traps (NETs)

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Conflict of interest: None

[Objectives] In this study, we investigated the intracellular signaling involved in the production of cytokines in lung fibroblasts stimulated by NETs and the pathways involved in their production. [Methods] NETs were used to stimulate NHLF, and the levels of IL-6, IL-8, TNF-α, TGF-β, and VEGF in the cell supernatant were measured using ELISA. In addition, the phosphorylation of STAT1, STAT3, STAT5, NFκB, p38, and Src after stimulation was measured using Western blotting. [Results] Cytokines in co-culture of NETs and NHLF were IL-6 (1.64 ± 0.04 ng/ml, 11.9 ± 0.1 ng/ml), IL-8/CXCL8 (10.9 ± 0.02 ng/mL, 27.0 ± 0.1 ng/mL), TGF-β (338 ± 0.2 pg/mL, 528 ± 9.7 pg/mL), and VEGF (168 ± 13.2 pg/mL, 464 ± 2.8 pg/mL) production was enhanced. On the other hand, TNF-α did not increase (470 ± 8.7 pg/mL,554 ± 0.5 pg/mL). After 30 minutes of stimulation, intracellular signals, such as STAT3 and p38, were more phosphorylated than in undifferentiated HL-60 cells. On the other hand, there was no change in the phosphorylation of STAT1, STAT5, NFκB, or Src. [Conclusion] NETs were suggested to be involved in the expression of inflammatory cytokines and chemokines from NHLF via phosphorylation of STAT3 and p38, and cytokines such as IL-6 and IL-8, and factors involved in angiogenesis such as VEGF.

W30-3

Clinical Utility and Pitfalls of Serum Cytokine Panel screening for Cytokine Storm Syndrome

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Conflict of interest: None

[Objectives] Excessive cytokine production plays a key role in the severe pathology of rheumatic diseases. Measuring serum cytokines, such as IL-6 in sepsis, has become an important clinical tool. This study aimed to assess the utility and limitations of cytokine measurements in cytokine storm syndrome (CSS). [Methods] The study included 97 participants, comprising CSS patients with various underlying diseases and healthy subjects. Serum levels of 48 cytokines were measured using the Bio-Plex Pro™ 48-Plex Panel Kit. IL-6, IL-18, CXCL9, and IFN-α levels were also measured using ELISA kits to compare with the Bio-Plex results. [Results] CSS were divided into 5 subgroups based on cytokine profiles: IFN-α-dominant, IL-18-dominant, IL-6-dominant, CXCL9-dominant, and others. These profiles helped identify the underlying diseases. Strong correlations between the results of Bio-Plex and ELISA results were found for IL-6, IL-18, and CXCL9, but not for IFN-α. IL-18 levels of ELISA were approximately 4.7 times higher than those of Bio-Plex. [Conclusion] Serum cytokine panels are effective tools for identifying underlying diseases in CSS. However, inconsistencies across measurement methods highlight the need for standardization and correction formulas to ensure reliable clinical cutoff values.

W30-4

Deficiency of ADAR1 in macrophages exacerbates autoimmune arthritis in mice

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Conflict of interest: None

[Objectives] Our aim is to elucidate the role of a double-stranded RNA editor, ADAR1, in innate immune system cells in autoimmune diseases. [Methods] We utilized model mice of autoimmune arthritis, SKG mice, with macrophage-specific *Adar1* deficiency (Lyzs-*Adar1*-conditional knockout SKG mice; *Adar1*-cKO SKG mice). All mice were bred and manipulated under super-pathogen-free conditions, and arthritis was induced by intraperitoneal administration of mannan. Arthritis was evaluated by ar-

thritis score and joint histopathology in *Adar1*-cKO and *Adar1*-wild (WT) SKG mice. [Results] Joint swelling was observed significantly more frequently in *Adar1*-cKO SKG mice than in *Adar1*-WT SKG mice ($p<0.05$). The severity of joint swelling was also significantly more severe in *Adar1*-cKO SKG mice ($p<0.05$). Synovial hyperplasia, inflammatory cell infiltration and joint destruction were significantly more severe in *Adar1*-cKO SKG mice ($p<0.05$, $p<0.01$, $p=0.0345$, respectively). [Conclusion] Deficiency of ADAR1 in macrophages exacerbated autoimmune arthritis. ADAR1 in the innate immune system is suppressive in autoimmune diseases.

W30-5

Modulation of LRP4 and Agrin expression in articular cartilage degeneration and their effect on beta-catenin signaling

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Conflict of interest: None

Objectives: We aimed to explore the modulator of LRP4 and Agrin expression and investigate its functions in articular cartilage. **Methods:** IHC was used to determine the localization of LRP4 and Agrin in cartilage tissues obtained from patients. LRP4 and Agrin of normal human articular chondrocytes (NHAC) by IL-1β/TNFα stimulation and cyclic tensile stimulation (CTS) was evaluated by RT-PCR. The expression of LRP5/6, SOX-9, ACAN, RUNX-2 and ADAMTS-4 by LRP4 knockdown and Agrin treatment was evaluated by RT-PCR. The expression and localization of β-catenin were evaluated by ICC and WB. **Results:** LRP4 was upregulated in the early stage of OA and then decreased with cartilage degeneration, whereas Agrin was consistently increased. LRP4 in NHAC was decreased by TNFα stimulation, and increased by mild CTS. Agrin expression was increased by IL-1β/TNFα stimulation and intense CTS. LRP4 knockdown increased the expression of LRP5/6, RUNX2 and ADAMTS-4, but not SOX-9 and ACAN. Agrin treatment showed a similar trend in mRNA expression and increased nuclear translocation of β-catenin. **Conclusion:** LRP4 is thought to have an important function in cartilage maintenance. Since Agrin is thought to be associated with OA, inhibition of Agrin binding to LRP4 may lead to the treatment of early OA.

W30-6

***N*-acetylgalactosaminyl transferase 12 (GalNAc-T12) suppresses the hypertrophy and inflammation of chondrocytes**

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Conflict of interest: None

[Objectives] We previously showed that the SNP rs2295926 belonging to *GALNT12* gene (*N*-acetylgalactosaminyl transferase 12; GalNAc-T12) is strongly associated with rapid joint destruction in RA. We also found that GalNAc-T12 contributes to the survival and proliferation of chondrocytes. Here we examined the effect of GalNAc-T12 on the hypertrophy and inflammation of chondrocytes. [Methods] Normal human knee chondrocytes (NHAC-Kn) were induced the hypertrophy by culturing with ITS supplement and ascorbic acid in the presence of GalNAc-T12. Chondrocytes were also cultured with GalNAc-T12, followed by the stimulation with IL-6, TNF-α or IL-1β. The gene expression in chondrocytes was examined. [Results] GalNAc-T12 not only suppressed an increase in Type X collagen, MMP13, ADAMTS-5 and Runx2 but also improved a decrease in aggrecan, type II collagen and Sox9 in chondrocyte hypertrophy. Further, an increase in MMP3, MMP13, Runx2, iNOS and type X collagen was reduce, and a decrease in aggrecan, type II collagen and Sox9 was ameliorated by culturing with GalNAc-T12 in the stimulation with IL-6, TNF-α or IL-1β. [Conclusion] GalNAc-T12 may involve the joint destruction in RA by contributing to the hypertrophy and inflammation in addition to the survival and proliferation of chondrocytes.

W31-1

Safety of rituximab 1000 mg of remission induction therapy for microscopic polyangiitis and glanuromatosis with polyangiitis: a 2-year prospective cohort study

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Conflict of interest: None

Objective: To evaluate the risk of severe adverse event (SAE) of rituximab (RTX1000 mg) compared to cyclophosphamide (IVCY) in remission induction therapy for microscopic polyangiitis (MPA) and glanuromatosis with polyangiitis (GPA). Methods: MPA and GPA patients treated between January 2010 and July 2024 were observed from the start of induction therapy until SAE occurrence or 2 years later. Confounding factors were balanced between two groups by stabilized inverse probability weights (standardized mean difference < 0.1). We estimated weighted hazard ratio (HR) by Cox proportional hazards model. Restricted mean survival time (RMST) was calculated to quantify the time for SAE occurrence in 2 years. Results: Seventy-three patients (63 MPA and 10 GPA) were enrolled. Twenty received RTX and 53 received IVCY. Five severe infection and 3 deaths were observed in 2 years, whereas there was no significant difference of SAE risk between the groups (RTX 90.6% vs IVCY 90.1%, risk differencee 0.5% [95% confidence interval (CI): -17.0%, 16.1%], risk ratio 0.99 [95%CI: 0.83, 1.21], weighted HR 1.34 [95%CI: 0.39, 4.55]). RMST showed no significant difference (680.9 vs 673.3 days, the difference 7.52 [95%CI: -92.5, 107.5]). Conclusion: RTX1000 mg was not associatied with higher SAE risk compared to IVCY.

W31-2

A comparative study of methods for reducing glucocorticoid dosage in patients with ANCA-associated vasculitis who have been treated with rituximab as induction therapy for remission multicenter international cohort study

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Conflict of interest: None

[Objective] RCTs examining GC reduction methods in AAV patients treated with RTX support early GC reduction. We conducted a comparative study on GC usage methods during remission induction in AAV patients treated with RTX. [Methods] A cohort study was conducted in seven countries. The subjects were patients with MPA, GPA, or EGPA treated with RTX and GC. Patients were classified into three groups: 1) High-dose GC initiation and gradual reduction group, 2) High-dose GC initiation and early reduction group, and 3) Low-dose GC initiation group. The primary outcome was remission. Secondary outcomes included infection requiring hospitalization and death. Multiple logistic regression analysis was per-

formed. [Results] The number of patients in the 3 groups was 99, 28, and 33. At 24 weeks, remission rates were 81 (87.1%), 24 (88.9%), and 27 (81.8%) in the 3 groups. The 6-month remission showed an odds ratio of 0.74 (95% CI: 0.42-1.31) for the 1) group versus 2) group and an OR of 1.20 (0.30-4.76) for 1) group versus 3) group. No significant differences were observed in secondary outcomes. [Conclusion] Compared to the 1) group, 2) group, as well as 3) group, showed no differences in remission or adverse events, supporting the early reduction and low-dose steroid methods.

W31-3

Comparison of the Efficacy of Cyclophosphamide and Rituximab in Induction Therapy for Patients with ANCA-Associated Vasculitis: A Retrospective Cohort Study Using the J-CANVAS Multicenter Registry for ANCA-Associated Vasculitis

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Conflict of interest: None

[Objectives] To compare intravenous cyclophosphamide (IVCY) and rituximab (RTX) as induction therapies for microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). [Methods] J-CANVAS is a multicenter study in Japan tracking ANCA-associated vasculitis (AAV) patients since January 2017, with follow-up until March 2024. Patients with newly diagnosed or relapsing MPA/GPA who received IVCY or RTX within two weeks were included. Outcomes were remission at 24 weeks and remission with prednisolone ≦10 mg/day. IPTW with 23 variables was used for confounder adjustment, followed by logistic regression to estimate effects. [Results] A total of 429 patients were analyzed: 209 in the IVCY group and 220 in the RTX group. After IPTW adjustment, baseline characteristics were balanced. Remission at 24 weeks was 85% in the IVCY group and 82% in the RTX group, with an odds ratio (OR) of 1.28 (95% CI: 0.75-2.20). Remission with prednisolone ≦10 mg/day was 36% in the IVCY group and 69% in the RTX group, with an OR of 0.39 (95% CI: 0.26-0.57). [Conclusion] While remission rates were similar, RTX showed more favorable steroid-sparing potential compared to IVCY.

W31-4

Safety of glucocorticoid dose reduction in microscopic polyangiitis: A multicentre REVEAL cohort study

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Conflict of interest: None

[Objectives] A retrospective observational study was conducted using the REVEAL cohort to evaluate the safety of glucocorticoid (GC) dose reduction in microscopic polyangiitis (MPA). [Methods] Patients with newly diagnosed MPA were classified based on GC dose at 6 months: ≦10 mg/day vs. >10 mg/day (prednisolone equivalent). After propensity score matching, event-free survival rates for all-cause mortality, infection-related mortality, infection requiring hospitalisation, and relapse were compared using Kaplan-Meier and Cox proportional hazards models. Logistic regression was used to analyse factors associated with GC doses of ≦10 mg/day at 6 months. [Results] A total of 223 MPA patients were included in the analysis. Patients with GC doses ≦10 mg/day at 6 months (n=95) had significantly lower risks of all-cause mortality (HR: 0.38, 95% CI: 0.17-0.85), infection-related mortality (HR: 0.08, 95% CI: 0.01-0.58), and infection requiring hospitalisation (HR: 0.46, 95% CI: 0.23-0.92), although relapse was not statistically significant (HR: 0.73, 95% CI: 0.42-1.26). Rituximab treatment (OR: 3.71, 95% CI: 1.26-11.85) was associated with achieving a GC dose of ≦10 mg/day. [Conclusion] Reducing GC to ≦10 mg/day at 6 months in MPA is safe, and rituximab may help achieve this target.

W31-5

Predictive factors of relapse in microscopic polyangiitis treated with Rituximab as induction therapy

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Conflict of interest: None

[Objectives] Rituximab (RTX) has become available for induction therapy in microscopic polyangiitis (MPA). This study aimed to investigate the remission maintenance rate of MPA and identify predictive factors of relapse. [Methods] We enrolled MPA successfully treated with RTX as induction from 2018 to 2023. Predictors of relapse were explored using a Cox proportional hazards models. [Results] We enrolled 26 MPA including 15 females (58%), with a mean age of 74 [59, 80] years old (median [interquartile range]). At baseline, BVAS score was 12 [9, 8], glucocorticoid (GC) dose was 50 [40, 60] mg. Major organ involvement included rapidly progressive glomerulonephritis in 11 patients. As maintenance, 18 patients received RTX, and 8 patients received azathioprine (AZP). The 5-year remission maintenance rate was 80%. BVAS, GC dose, or major organ involvement were not identified as predictors of relapse, maintenance with RTX significantly reduced relapse (HR 0.33, 95% CI 0.07-0.96, p=0.042). No significant difference was observed in the incidence of infections requiring hospitalization between the RTX and AZP groups (p=0.87). [Conclusion] In MPA who achieved remission with RTX, regardless of age, disease activity, or GC dose, RTX should be chosen for remission maintenance due to its efficacy and safety.

W31-6

Comparison of relapsed and non-relapsed cases of ANCA-associated vasculitis after completion of Rituximab remission maintenance therapy

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Conflict of interest: None

Objective: To compare relapse and non-relapse cases of ANCA-associated vasculitis (AAV) who completed maintenance therapy after induction of remission with Rituximab (RTX). **Methods:** We studied AAV patients who treated with RTX in remission induction and maintenance therapy (RTX every 6 months for 2 and a half years) between 2015 and 2024. Patients who had no relapse during the 3 years after completion of maintenance therapy were defined as non-relapsed cases, and those who relapsed were defined as relapsed cases. **Results:** Eighteen patients completed maintenance therapy: 8 in the relapse group, 4 in the non-relapse group. Comparison of the relapse and non-relapse groups showed the following: age 72 years vs. 71 years; glucocorticoid (GC) dose at induction of remission 23 mg vs. 40 mg; duration of maintenance therapy 24 months vs. 20 months; total RTX dose used in maintenance therapy 2,550 mg vs. 2,060 mg; GC dose at the end of maintenance therapy 1 mg vs. 0.5 mg. As

for the relapse group, the time from the last RTX to relapse was 31 months, and all patients were accompanied by elevated/positive ANCA. **Conclusion:** There were no obvious differences between relapsed and non-relapsed cases, but relapsed cases had elevated/positive ANCA.

W32-1

Morphological differences between rheumatoid and osteoarthritis knees with varus deformity

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Conflict of interest: Yes

[Objectives] The objective of this study was to investigate whether there is a difference in bone morphology between the rheumatoid arthritis (RA) and knee osteoarthritis (OA) knees after adjusting for patient background and hip-knee-ankle angle (HKA angle). [Methods] In varus knees of 3° or greater, 1:1 matching was conducted by HKA angle, age, and gender. Subsequently, 47 knees for RA and 56 knees for OA were included. The femoral valgus angle, mechanical lateral distal femoral angle (mLDFA), femoral bowing in coronal and sagittal plane, medial proximal tibial angle (MPTA) and tibial posterior tilt were measured. On the axial plane, the angle between femoral surgical epicondylar axis (SEA)-posterior condylar axis (PCA) was measured. [Results] There were no significant differences between the RA and OA groups in femoral valgus angle, mLDFA, bowing in coronal and sagittal plane, and MPTA. Tibial posterior tilt was significantly greater in the RA group (11.4±6.4°) than in the OA group (7.6±6.5°) (p=0.007). Femoral SEA-PCA angle was significantly greater in the RA group (4.5±3.0°) than in the OA group (2.9±2.4°) (p=0.004). [Conclusion] There may be less difference in bone morphology between the RA and OA groups when alignment and other backgrounds are matched.

W32-2

Are there differences in function and living space after knee joint replacement surgery in patients with rheumatoid arthritis compared to patients with osteoarthritis of the knee?

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Conflict of interest: None

[Objectives] We compared the differences in motor function and living space between rheumatoid arthritis patients and knee osteoarthritis patients before and after TKA. [Methods] RA group 18 knees and OA group 45 knees undergoing TKA from 2019 to 2023 were included. The two groups were compared in muscle strength and motor function (10-m walk test, time up-and-go test (TUG)) on the operative side, 2 weeks postoperatively, and 3 months postoperatively, and in life space assessment (LSA) before and 3 months after surgery. [Results] At 2 weeks postoperatively, muscle strength decreased significantly in both groups ($p<0.05$), but motor function did not decrease significantly. At 3 months postoperatively, motor function improved significantly ($p<0.05$) in both groups, but there was no significant difference between the two groups. LSA improved significantly ($p<0.05$) in both groups at 3 months postoperatively, but there was no significant difference between the two groups. [Conclusion] The RA group improved in muscle strength, motor function, and spatial function without significant difference compared with the OA group. TKA in RA can be expected to be almost as effective as OA.

W32-3

Can the ACL tibial attachment be an intraoperative reference point to define the joint line for total knee arthroplasty in rheumatoid arthritis patients?

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Conflict of interest: Yes

Objective: In this study, we examined the relationship between the tibial attachment of the anterior cruciate ligament (ACL attachment) and the lateral articular surface of the tibia (Validation 1) and the clinical outcomes of RA TKA using the ACL attachment as a reference point for tibial osteotomy (Validation 2). (Validation 1) Material and Methods: 75 knees (mean age 74.9 years) that underwent TKA for medial OA were included. The distance between the center of the lateral tibial articular surface and the ACL attachment was measured by preoperative MRI images (Δ1) and intraoperative navigation system (Δ2). Results: Δ1 was 1.7±0.4 mm and Δ2 was 1.2±0.6 mm, indicating that the ACL attachment was almost as high as the lateral tibial articular surface. (Validation 2) Material and Methods: The joint line elevation before and after surgery was measured based on the fibular head from X-ray frontal images of RA 37 knees. Results: The joint line elevation was 15.5 mm preoperatively and 16.7 mm postoperatively, a difference of only 1.2 mm. Conclusion: The ACL attachment could serve as a reference point for determining the height of the tibial osteotomy when performing TKA in patients with no remaining cartilage on the tibial side.

W32-4

Investigate the flexion-extension gap after osteotomy in total knee arthroplasty using kinematic alignment for patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] In recent years, the usefulness of the kinematic-alignment (KA) method has been reported in total knee arthroplasty (TKA). The gap between RA knees may be larger than that of OA knees due to ligament laxity caused by preoperative joint synovitis. We investigated the gap after osteotomy in RA knees with those in OA. [Methods] Seventy-five patients (62 OA and 13 RA) underwent restricted KA-TKA (rKA-TKA). After osteotomy of the femur and tibia and the femoral trial was installed, the gap was measured using a tensor which preserved medial gap technique. Measurements were taken at 10, 30, 45, 60, 90, and 120 degrees of knee flexion. [Results] Mean age at the time of surgery was 76 years in the OA group and 67 years in the RA group. There was no statistical difference in gaps between the two groups on any knee flexion angles. The gasp for each angle was 14.2/14.3/14.5/14.4/14.5 mm in the OA group and 14.2/14.9/14.8/14.9/14.5/14.2 mm in the RA group. There was also no difference in extension (10° flexion) or flexion (90° flexion) gaps within each group. [Conclusion] We investigate the flexion-extension gap after osteotomy in rKA-TKA for RA and OA patients. There was no difference in the gaps after osteotomy between the two groups.

W32-5

Effectiveness of orthopaedic surgery for patients with difficult-to-treat rheumatoid arthritis

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Conflict of interest: None

[Objectives] Difficult-to-treat rheumatoid arthritis (D2T RA) is an emerging concept for RA patients with active disease despite multiple DMARDs. This study investigated the effect of surgical treatment for D2T RA. [Methods] We studied 120 RA patients treated with b/tsDMARD who underwent orthopaedic surgery from 2015 to 2022. Based on EULAR

definition, patients with moderate or high disease activity who had previously used ≧2 b/tsDMARDs were classified as D2T RA (group D, n=33), while others were non-D2T RA (group N, n=87). We compared patient characteristics, medications, surgical procedures, and CRP and DAS28-CRP values. [Results] Age, sex, disease duration, and comorbidities showed no significant differences between groups. MTX usage was similar (D: 55%, N: 58%), but glucocorticoid use was significantly higher in group D (67% vs 39%, $p<0.05$). DAS28-CRP improved in both groups. Preoperative CRP was significantly higher in group D (0.76 vs 0.28 mg/dL) but showed no significant difference at 6 months postoperatively (0.35 vs 0.24 mg/dL). Group D had more large joint surgeries (45% vs 31%), with these cases showing significant CRP improvement (from 0.91 mg/dL to 0.20 mg/dL). [Conclusion] The effectiveness of surgical treatment was demonstrated even in D2T RA patients.

W32-6

Long-term results of total hip and knee arthroplasty in the treatment of rheumatoid arthritis: infection, fragility fracture

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Conflict of interest: None

Objective: Compare outcomes of total knee arthroplasty (TKA) and total hip arthroplasty (THA) with rheumatoid arthritis (RA) versus non-RA. **Method:** We analyzed 1485 patients (1973 knees) and 1062 patients (1257 hips) who underwent primary TKA/THA from September 2009 to June 2022. We assessed revision surgery, infection, and fragility fractures, comparing outcomes between RA and non-RA, and examined RA treatment after infection. **Results:** TKA was performed on 367 RA knees and 1606 non-RA knees, with a revision rate of 1.8% and infection rate of 2.0%. RA had a significantly higher infection rate, with 12 cases (6 on steroids, 7 on biologics, 3 with recurrent infections, 3 resumed biologic). THA was performed on 117 RA hips and 1140 non-RA hips, with a revision rate of 2.7%, infection rate of 1.1%, and fracture rate of 3.7%. The revision rate was significantly higher in RA. RA tended to be higher infection rate, with 3 cases (2 on biologics, 1 resumed biologic). **Conclusion:** RA is a risk factor for infections in both TKA and THA, with higher revision rates in THA. Perioperative management of antirheumatic drugs is essential. Treatment for RA after infection is complex and requires individualized strategies. Further studies are needed to gather additional cases for analysis.

W33-1

Identification of Novel Blood Biomarkers for Disease Activity Indicators of ANCA-associated Vasculitis Using Proteomics

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Conflict of interest: None

[Objectives] To identify novel blood biomarkers that can serve as indicators of disease activity in ANCA-associated vasculitis (AAV) using proteomics. [Methods] Proteins were fractionated from stored plasma, and the SWATH method was performed using an LC-MS/MS system to identify and quantify proteins contained in the samples. First, disease activity marker candidates were selected using a screening sample set (11 AAV patients with pre- and post-treatment samples). Then, these marker candidates were evaluated using another sample set (48 AAV patients). [Results] As biomarker candidates, 5,061 proteins were identified using the screening sample set, and relative quantification values were measured for 3,471 of these proteins. Excluding common proteins such as CRP, 46 proteins were selected, including 34 types with relative quantitative values before treatment > after treatment and 12 types with relative quantitative values before treatment < after treatment. Reproducibility was confirmed in the evaluation sample set for 13 proteins, 2 types before treatment > after treatment and 11 types before treatment < after treatment. [Conclusion] Using proteomics, 13 novel blood biomarker candidate proteins that could serve as indicators of AAV disease activity were identified.

W33-2

The significance of TRECs and KRECs as immune indicators that reflect immunophenotypes and predict the risk of infection in systemic autoimmune diseases

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Conflict of interest: None

[Objectives] To clarify the role of T cell receptor rearrangement excision circles (TRECs) and Igκ-deleting recombination excision circles (KRECs) as immune indicators in systemic autoimmune diseases under immunosuppressive treatment. [Methods] Clinical data and peripheral blood (PB) samples from patients newly diagnosed with systemic autoimmune diseases were collected prospectively. TREC/KREC levels were measured with qPCR. Immunophenotypes of PB lymphocytes were analyzed with flow cytometry. Lymphocyte counts was evaluated. Each variable was assessed before immunosuppressive treatments (baseline), 3-, 6-, and 12-months post-treatment. Severe infections, defined as infections requiring hospitalization, were recorded. [Results] TREC/KREC levels were correlated positively with recent thymic emigrants and naïve T and B cells at all the timepoints. TREC/KREC levels decreased continuously after treatment. The ratios of TREC and KREC levels under treatment to baseline levels were significantly lower in patients with severe infection than those without. [Conclusion] TREC/KREC levels reflect immunophenotypes under treatment-naïve and immunosuppressive conditions. Changes in TREC/KREC levels serve as beneficial markers for predicting severe infection after treatment.

W33-3

Longitudinal analysis of changes in rheumatoid factor (RF) after treatment with bio/tsDMARDs in rheumatoid arthritis

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Conflict of interest: None

[Objectives] This study investigated changes in RF following the administration of bio-DMARDs with Fc. [Methods] Among 413 rheumatoid arthritis (RA) patients with a first visit to our department from April 2017 to April 2024, 53 patients who were prescribed bio/tsDMARDs and followable for at least 6 months with RF data over time were included. Changes in RF at 1, 3, and 6 months after treatment initiation, relative to baseline levels, were analyzed retrospectively. The analysis utilized a mixed model for repeated measures (MMRM), comparing patients treated with Fc bio/tsDMARDs to those without Fc. [Results] 79% were female, with a mean age (SD) of 63.4 years (19.3). Median CDAI (IQR) was 14.1 (0.8-27.9), median RF was 77.5 (21-1193), and 98% were anti-CCP antibody positive. 40 patients received Fc-positive agents (ABT: 15, ADA: 2, ETN: 3, GLM: 2, IFX: 1, TCZ: 15, SAR: 2), while 13 received Fc-negative agents (CZP: 6, BAR: 3, UPA: 2, PEF: 1, FIL: 1). The rate of change (slope) in RF over time was greater in the Fc-positive group compared to the Fc-negative at 3 months (P=0.006) and 6 months (0.001). [Conclusion] A decreasing trend in RF was observed after the administration of bioDMARDs with Fc, suggesting that RF may interact with the Fc region and decline as a result of consumption.

W33-4

IgG subclass distribution of serum anti-hinge peptide antibodies in patients with rheumatoid arthritis

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Conflict of interest: None

[Background] We have investigated the potential usefulness of anti-IgG hinge autoantibodies (AHAs), as a biomarker for seronegative rheumatoid arthritis (Arth Res Ther 2020, Clin Exp Rheumatol 2024). AHAs have been considered to show a deviation toward IgG3 subclass and play some effector functions, such as ADCC (J Immunol, 2008). [Objective] To confirm the IgG3 deviation of AHAs in human sera [Methods] DMARDs naïve RA patients within 2 years of onset and healthy controls (HCs) were included. We measured AHAs using four synthetic peptide analogues with MMP-3 or MMP-7 cleaved γ1 or γ4 chain epitope. Calibration curves were prepared using purified human myeloma protein and mouse anti-human IgG subclass antibodies. The IgG subclass concentrations of AHAs were obtained from the calibration curve. [Results] IgG3 deviation of AHAs could not be confirmed in HCs and RA patients. The IgG subclasses of many AHAs were present in IgG1>>IgG2>IgG3=IgG4. Interestingly, some cases showed higher proportion of IgG2 concentration of AHA against MMP-3 cleaved γ1 chain hinge peptide. No association between AHAs and joint destruction could be identified. [Conclusion] IgG subclass of AHAs was mainly IgG1.

W33-5

Significance of anti-Ro52 antibody measurement in anti-SS-A antibodies

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Conflict of interest: None

[Objectives] Some reagents for measuring anti-SS-A antibodies do not contain Ro52 antigen in the assay system, resulting in false-negative. We clarify the significance of measuring anti-Ro52 antibodies in actual clinical practice. [Methods] We included the serum samples of collagen disease patients in which anti-Ro52 antibodies were positive in immunoblotting (EUROLine (EURO IMMUN)). The presence of positive anti-SS-A antibodies measured by the MEBLux test SS-A and their association with antibody titer were analyzed retrospectively. We also examined the association with clinical characteristics. [Results] The mean age at examination was 55.9±17.1 years, and the ratio of males to females was 18:78. Of the 91 cases positive for anti-Ro52 antibody by immunoblotting, 51 (56.0%) were negative for anti-SS-A antibody. [Conclusion] We found that anti-Ro52 antibody-positive cases were frequently found even among anti-SS-A antibody-negative cases. Anti-Ro52 antibodies are useful not only for the diagnosis of Sjögren's syndrome, but also for assessing the risk of heart block, and for prognosis and monitoring of interstitial pneumonia. In addition, a system to measure anti-Ro52 and anti-Ro60 antibodies separately in actual clinical practice was considered necessary.

W33-6

Exploring the prevalence and clinical significance of anti-Stress Granule antibodies in healthy subjects and patients with rheumatic diseases

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Conflict of interest: None

[Objective] Stress granules (SG) are RNA aggregates that form in the cytoplasm induced by cellular stress. We developed a method to detect the autoantibodies against SGs and investigated their clinical significance in healthy subjects and patients with rheumatic diseases. [Methods] The prevalence of anti-SG antibodies in serum samples was investigated in 16 healthy controls (HC), 32 patients with rheumatoid arthritis (RA), and 9 with systemic lupus erythematosus (SLE). SG formation in the cytoplasm of U2OS cells was induced by sodium arsenite and detected by indirect immunostaining. [Results] The prevalence of anti-SG antibodies was significantly higher in HC compared to patients with RA (HC: 81.3% vs RA: 34.4%, $p<0.01$) and SLE (HC: 81.3% vs SLE: 11.1%, $p<0.001$). Among RA patients, patients with seronegative RA (SNRA) tended to have a higher prevalence of anti-SG antibodies compared to those with seropositive RA (SPRA) ($p=0.0627$). In SPRA patients, anti-SG antibody-positive cases tended to have lower RF and anti-CCP titers. [Conclusion] Anti-SG antibodies were frequently observed in healthy individuals, and in RA patients, their presence was associated with lower levels of RF and anti-CCP antibodies.

W34-1

Clinical Profile of IgG4-Related Disease in Japan based on the Rare Disease Data Registry

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Conflict of interest: None

[Objectives] Recently, a registry led by the research group to establish diagnostic criteria and guidelines for IgG4-related disease (IgG4-RD) with an "All-Japan approach" (Kawano group) was launched. This study aimed to utilize this registry to clarify the clinical features of IgG4-RD in Japan. [Methods] We comprehensively analyzed the clinical information of 854 cases registered in the Rare Disease Platform by institutions belonging to the Kawano group between December 2019 and February 16, 2024. [Results] Of the 854 cases, 808 were diagnosed with IgG4-RD. The average age at the registration (±SD) was 67.9±11.3 years, and 68.8% were male. A history or coexistence of malignancy was present in 4.2% of cases at the registration. The most frequently affected organ was the pancreas (49.8%), followed by the submandibular gland (46.2%) and the lacrimal gland (30.6%). Regarding imaging findings, pancreatic enlargement in autoimmune pancreatitis was diffuse in 53.0% of cases and localized in 44.6%. Depending on the organ, histopathological findings showed differences in the detection frequencies of storiform fibrosis and obliterative phlebitis. [Conclusion] We clarified the clinical, imaging, hematological, and histopathological findings of 808 Japanese patients with IgG4-RD.

W34-2

Successful differentiation of IgG4-related cardiovascular/retroperitoneal disease (IgG4-CV/RP) from mimickers based on clinical findings

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Conflict of interest: None

[Objectives] This study aimed to explore clinical findings other than those of cardiovascular/retroperitoneal (CV/RP) biopsy that may be useful for differentiating IgG4-CV/RP from mimickers. [Methods] We analyzed 75 patients diagnosed with IgG4-related disease (IgG4-RD) having CV/RP manifestations, along with 20 mimickers identified by experts. Clinical characteristics other than biopsy findings of CV/RP lesions related to the final diagnosis of IgG4-RD by experts were assessed by age-, sex-, and serum IgG4 level-adjusted logistic regression analyses. [Results] Age-, sex-, and serum IgG4 level-adjusted logistic regression analysis indicated that iliac artery involvement [odds ratio (OR) 8.701, 95% confidence interval (CI) 1.006-75.243], presence pf extra-CV/RP lesions (OR 9.097, 95% CI 1.055-78.419), and inclusion scores of the ACR/EULAR classification criteria for IgG4-RD (OR 1.155, 95% CI 1.025-1.301) were positively related to a final diagnosis of IgG4-RD. However, two cases of follicular lymphoma with periaortic, paravertebral, renal pelvic, and/or focal pancreatic lesions could be differentiated only based on biopsy. [Conclusion] The present study suggests that in the absence of CV/RP biopsy findings, some clinical findings are useful for differentiating CV/RP from mimickers.

W34-3

Examining the effect of sex differences on IgG4-related diseases

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Conflict of interest: None

[Objectives] To determine the effect of sex differences on the clinical presentation and course of IgG4RD. [Methods] Clinical outcomes such as patient background, flare, malignancy complications and death between men and women were compared in 221 patients. Background factors associated with flare and death were explored by Cox regression analysis. [Results] Men had higher IgG and IgE levels, lower C3 at diagnosis and more affected organs. Aortic, retroperitoneal, pancreatic and renal lesions were more frequent. During the observation period, 41 men and 22 women had flare, and sex was not associated with flare in a Cox regression model with sex, age, number of affected organs, IgG4, IgE and C3 levels and initial steroid dose as covariates. Malignancy development after IgG4-RD diagnosis was significantly more common in men. 9 men and 2 women died, and age- and sex-adjusted Cox regression analysis showed that the number of affected organs and the development of malignancy after IgG4-RD diagnosis were significantly associated factors, but sex was not associated with death. [Conclusion] Sex differences in clinical presentation at diagnosis were observed. The effect of sex differences on flare and death was not clear, but it should be noted that malignancies occur more frequently in men.

W34-4

Case series: Four cases of IgG4-related disease with cardiac lesion

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Conflict of interest: None

[Case] Four cases of IgG4-related disease with cardiac involvement treated at our department between January 2021 and September 2024. One case had coronary artery periarteritis and pericarditis, one another case had coronary artery pericarditis and persistent atrial fibrillation, while the remaining two cases presented with FDG-PET accumulation in the ventricular septum and complete atrioventricular block (CAVB). All three cases with arrhythmia had aortitis. Only one case presented with chest pain, and another two cases presented with syncope, but the remaining one case had no symptoms. The average age at the start of treatment was 70.3 years [48-80]. The average serum IgG4 level before treatment was 706.7 mg/dL [296-1118]. The mean prednisolone dose at treatment introduction was 37.5 mg/day [20-60]. Two cases of coronary artery periarteritis remitted quickly with initial treatment, but two cases of ventricular septal lesions achieved remission with rituximab, and a pacemaker was inserted for CAVB. [Discussion] Despite the fact that cardiac involvement can have a fatal outcome, there are cases where chest pain or high inflammatory response values are not present. We believe that prompt systemic examination and early use of immunosuppressants are desirable.

W34-5

Frequency and Characteristics of Cytopenia in IgG4-Related Disease

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Conflict of interest: None

[Objectives] To clarify the attributes of cytopenia in IgG4-related disease (IgG4RD). [Methods] We retrospectively analyzed 58 patients with IgG4RD who visited our hospital between April 2015 and July 2024. [Results] 37 out of 58 patients (64%) exhibited some form of cytopenia. The median age of these patients was 72 years (IQR 64-75), and 28 were men (76%). Among them, 3 cases (8%) had leukopenia. Anemia was present in 32 cases (86%) with a median hemoglobin level of 9.9 mg/dL (IQR 9.0-11.6). Additionally, 26 cases (70%) had thrombocytopenia with a median platelet count of $10.7\times10^4/\mu L$ (IQR 8.1-14.1). Pancytopenia was observed in 2 cases (5%), both of which had splenomegaly. Among the 37 cases, those with splenomegaly (n=7) showed a higher incidence of thrombocytopenia compared to those without splenomegaly (n=30) (85.7% vs. 66.7%, p=0.649). The platelet counts of patients with thrombocytopenia were significantly lower in the splenomegaly group (7.0 vs. $11.2\times10^4/\mu L$, p=0.024). No differences were observed in leukopenia, anemia, or IgG/IgG4 levels. [Conclusion] Cytopenia is a relatively common manifestation in IgG4RD, and in cases with splenomegaly, consideration should be given to the concomitant of thrombocytopenia.

W34-6

Clinical study of 19 cases of retroperitoneal fibrosis

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Conflict of interest: None

[Objectives] To clarify the clinical features and treatment course of retroperitoneal fibrosis (RF). [Methods] We retrospectively analyzed the clinical characteristics of 19 consecutive cases of RF at our department from March 2012 to October 2024. [Results] The mean age at RF diagnosis was 68.4 years, and the mean time from onset to start of treatment was 4.6 months. The sex ratio was 17 males to 2 females. The final diagnosis consisted of IgG4-related disease in 8 cases, 10 cases of idiopathic RF, and 1 case of malignant lymphoma. Glucocorticoids (GC) was administered at an initial dose of 0.6 mg prednisolone (PSL) per Kg of body weight, and the dose could be reduced to 5 mg PSL or less without any relapse, except for a case of lymphoma. In IgG4-related diseases, serum IgG4 levels were around 200 mg/dL in the absence of other organ involvements, but were higher (500-2000 mg/dL) when other organ lesions were present (3 of 8 patients) [Conclusion] In RF, 18 patients except one with lymphoma could be treated with GC as a single agent and did not relapse during dose reduction. Careful evaluation of malignant pathology was considered necessary

in cases of resistance to treatment.

W35-1

Risk factor analysis of serious infection, herpes zoster, and malignancy in Japanese patients with rheumatoid arthritis treated with baricitinib: 3-year data from an all-case post-marketing study

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Conflict of interest: Yes

[Objectives] This all-case post-marketing study of baricitinib (BARI) enrolled rheumatoid arthritis (RA) patients (pts) who received BARI from Sep 2017 to Apr 2019, with up to 3 yrs of follow-up. We examined risk factors for specified adverse events, namely serious infection (SI), herpes zoster (HZ), and malignancy, during BARI treatment. [Methods] A multivariate Cox hazard model was used for the risk factor analysis. [Results] Analyses included 4720 pts (mean age 64 yrs, 80% female, mean RA duration 12 yrs). Incidence rates (/100 pt-yrs) were SI 3.0, HZ 4.7, and malignancy 1.1. Risk factors (reference, hazard ratio [HR]) identified were: for SI, age ≧65-<75 yrs (vs <65 yrs, 1.4), ≧75 yrs (vs <65 yrs, 2.4), RA duration (incremental HR for each category [<2 yrs; ≧2-<5 yrs; ≧5-<10 yrs; ≧10-<20 yrs, ≧20 yrs], 1.2), and respiratory comorbidities (vs none, 2.1); for HZ, age ≧75 yrs (vs <65 yrs, 1.5), HZ history (vs none, 2.1), and 4-mg initial dose (vs 2-mg, 1.4); for malignancy, age ≧65-<75 yrs (vs <65 yrs, 1.7), ≧75 yrs (vs <65 yrs, 2.4), male (vs female, 2.3), and RA duration (incremental HR, 1.2). [Conclusion] Risk factors for SI, HZ, and malignancy were identified over 3 yrs of BARI treatment. These risk factors should be considered when treating RA pts using BARI.

W35-2

Comparative Evaluation of Herpes Zoster Risk Among Five JAK Inhibitors in Real-World Data: the ANSWER cohort study

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Conflict of interest: Yes

[Objectives] Herpes zoster (HZ) is a well-known adverse effect of Janus kinase inhibitors (JAKi). The aim of this study was to compare the incidence of HZ across five JAKi using real-world data. [Methods] This study included 1,096 patients with rheumatoid arthritis who were newly initiated on JAKi from the multicenter ANSWER cohort, and whose data on HZ incidence were available (Tofacitinib: TOF 223 cases, Baricitinib: BAR 364 cases, Peficitinib: PEF 128 cases, Upadacitinib: UPA 245 cases, Filgotinib: FIL 136 cases). A retrospective analysis was conducted to calculate incidence rates of HZ using the person-years method to compare across the five JAKi. [Results] The incidence rates of HZ per 100 person-years were 5.85 for TOF, 6.21 for BAR, 3.79 for PEF, 7.38 for UPA, and 1.73 for FIL. After adjustment for confounding factors (such as age, sex, disease duration, concomitant use of methotrexate or prednisone, and HZ vaccination status), the Cox proportional hazards model showed that the hazard ratio (HR) for HZ was significantly lower for FIL (HR: 0.11) compared to TOF (reference: 1.00). However, no significant differences were observed for BAR (HR: 0.70), PEF (HR: 0.16), or UPA (HR: 0.67). [Conclusion] FIL showed a significantly lower incidence rates of HZ compared to TOF.

W35-3

Safety of Upadacitinib Across Rheumatoid Arthritis, Psoriatic Arthritis, and Axial Spondyloarthritis Encompassing 15,000 Patient-Years of Clinical Trial Data (Encore)

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Conflict of interest: Yes

[Objectives] Describe the long-term integrated safety profile of UPA 15 mg across indications in rheumatology, in the context of active comparators, from the SELECT clinical program. [Methods] Safety data from 11 phase3 UPA trials were compiled for RA (6), PsA (2), AS (2), and nr-axSpA (1) for this analysis. [Results] In total, 4998 patients received ≧ 1 dose of UPA 15 mg, totaling 15,895.8 PYs of exposure. The rate of adverse events (AEs) leading to discontinuation of study drug was generally similar across treatment groups and diseases. Rates of serious infection and opportunistic infection were generally similar across treatment groups and diseases; however, the rate of serious infection was higher with UPA 15 mg versus ADA in PsA. Herpes zoster and elevated CPK were reported more often with UPA 15 mg versus active comparators in RA and PsA. Higher rates of NMSC were observed with UPA 15 mg versus active comparators in RA and PsA. [Conclusion] With the exception of serious infection (in PsA), herpes zoster, elevated CPK, and NMSC, the rates of TEAEs were generally similar between UPA 15 mg and active comparators in RA and PsA. Across RA, PsA, AS, and nr-axSpA, UPA 15 mg demonstrated a generally consistent safety profile, with no new safety risks identified with long-term treatment.

W35-4

Efficacy, Safety and Drug Continuation Rate of Naive or Second or Subsequent Doses of Janus Kinase inhibitors in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] To compare the efficacy, safety, and continuation of Janus kinase inhibitors (JAKi) between RA patients with JAKi-naïve and JAKi-exposed. [Methods] This retrospective study analyzed 143 RA patients who initiated JAKi from Oct. 2014 to Sep. 2023. Patients were classified into a JAKi-naïve and a JAKi-exposed group (patients switched to a second or later JAKi). [Results] JAKi-naïve group included 106 cases (74%). Patient backgrounds (JAKi-naïve/exposed) such as mean age (64/69 years), female (77/76%), RA duration (126/131 months), DAS28-CRP (4.15/4.51), RF positive (76/89%) and MTX use (35/30%) showed no significant differences between the groups. Compared with baseline, DAS28-CRP significantly improved in both groups three months after treatment ($p<0.001$/$p=0.010$). The 12-month continuation rates showed no significant difference (42/61%). Among the cases that discontinued JAKi within 12 months, there was no difference in the frequency of discontinuation due to lack of efficacy (27/22%) or adverse events (28/24%). [Conclusion] Switching to a second or later JAKi in RA demonstrated similar efficacy, safety, and continuation rates to those of JAKi-naïve, suggesting that switching to another JAKi may be effective for RA with an insufficient response to the first JAKi.

W35-5

Analysis of occurrence of herpes zoster due to JAK inhibitors and drug continuation after herpes zoster

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Conflict of interest: Yes

[Objectives] JAK inhibitor is a risk of herpes zoster (HZ). We studied occurrence of HZ during JAK inhibitor treatment for rheumatoid arthritis (RA), and JAK inhibitor retention during or after HZ. [Methods] HZ occurrence by JAK inhibitors were selected from RA patients. HZ occurrence and JAK inhibitor retention for 3 years were analyzed by Kaplan-Meier analysis. [Results] 318 patients were enrolled (74 tofacitinib, 96 baricitinib, 78 upadacitinib, and 70 filgotinib). There were 29 cases of HZ, and HZ-free survival rates were 83.4% in tofacitinib, 73.0% in baricitinib, 82.1% in upadacitinib, and 99.7% in filgotinib ($p=0.0748$). Among 29 cases with HZ, JAK inhibitors were continued or restarted after HZ in 22 (76%) and were stopped in 7 (24%). JAK inhibitor retention rates were 95.1% in tofacitinib, 94.8% in baricitinib, 97.0% in upadacitinib, and 100% in filgotinib ($p=0.612$). The reasons for JAK inhibitor stop include facial HZ, poor general status, and patient hope. [Conclusion] The incidence of HZ tended to be different by JAK inhibitors although no significance. The reason may be due to the difference in drug release date, HZ vaccination, and the effect of drug. There was no difference in JAK retention, indicating that JAK inhibitors can be continued or restarted in most of HZ cases.

W35-6

Safety of JAK inhibitors in elderly rheumatoid arthritis patients at our hospital

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Conflict of interest: None

[Objectives] We investigated the safety of JAK inhibitors in elderly RA patients at our hospital. [Methods] We investigated adverse events in 199 RA patients aged 65 years or older who started JAK inhibitors at our hospital between December 2013 and December 2022. [Results] The mean age of the target population was 74.3 years, and the mean duration of disease was 15.3 years. The JAK inhibitors used were tofacitinib in 94 patients, baricitinib in 42 patients, peficitinib in 14 patients, updacitinib in 30 patients, and filgotinib in 19 patients. The mean duration of treatment was 2.1 years. Adverse events were observed in 67 patients. [Conclusion] Although the use of JAK inhibitors in elderly RA patients showed some efficacy, adverse events such as malignancy and infection were observed. These risks may be associated with the risk of complications and decreased organ function in elderly patients compared with younger patients. Therefore, when using JAK inhibitors in elderly RA patients, the balance of advantages and disadvantages of treatment should be carefully evaluated. Early detection and management of adverse effects during treatment are required, and continuous observation and management are essential.

W36-1

Long-term prognosis of lupus nephritis in our hospital

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Conflict of interest: None

[Objectives] The aim of this study was to identify predictors of relapse, both judged by increased protein uremia and proven by rebiopsy, and predictors of progression to CKD in LN (lupus nephritis) patients. [Methods] Systemic lupus erythematosus patients with LN diagnosed and treated in our hospital with available pathological data were selected. We analysed the data to find out the prognostic factors predicting poor outcome such as e-GFR exacerbation rate, progression to CKD and relapse proven by rebiopsy. [Results] 109 LN patients with medical data on pathological findings were included in this study, and 22 patients underwent a total of 30 rebiopsies. Urine protein was not predictive of the rate of e-GFR deterioration, progression to CKD or relapse detected by rebiopsy. The results suggest that the neutrophil/lymphocyte ratio (NLR) before renal biopsy is associated with renal prognosis. [Conclusion] Recently, alternative predictors of response to treatment and progression to CKD in lupus nephritis patients have been identified, such as IFN signatures and urinary biomarkers, but their accessibility in clinical practice remains difficult. NLR is useful as a minimally invasive and easily accessible marker for predicting renal recurrence confirmed by rebiopsy.

W36-2

Renal and Patient Outcomes in Pure Lupus Nephritis in Japan: A Comparison with Proliferative Lupus Nephritis

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Conflict of interest: None

[Objective] To compare renal outcomes between membranous lupus nephritis (MLN) and proliferative lupus nephritis (PLN) in Japan. [Methods] We analyzed 90 MLN (V) and 362 PLN (III/IV±V), who were registered in the Japan Renal Biopsy Registry (2007-2012). Complete remission (CR) was defined as UPCR < 0.5 g/gCr and S-Cr ≦115% of baseline. [Results] Comparing MLN versus PLN: mean age at biopsy was 43.7±15.1 vs 41.3±15.0 years (ns), eGFR 90.2±32.7 vs 73.7±32.8 mL/min/1.73 m^2 ($P<0.001$), and UPCR 3.4±4.2 vs 3.3±3.1 g/gCr (ns). Initial PSL dose was 33.5±18.1 vs 40.5±15.2 mg/day ($P<0.001$), and mPSL pulse therapy was used in 18.9% vs 51.9% ($P<0.001$). During median follow-up of 62.4 months (IQR 50.5-81.8) vs 63.6 months (IQR 49.0-82.1) (ns), outcomes were: 1.5-fold increase in S-Cr 12.2% vs 16.3%, doubling of S-Cr or ESRD 4.4% vs 8.6%, and mortality 7.8% vs 5.5% (Log-rank test, ns). In the MLN group, CR rates at 6 and 12 months were 39.2% and 49.2%. No patients in the CR-achieved group experienced a 1.5-fold increase in S-Cr. [Conclusion] During the median follow-up period of 5 years, some MLN

patients experienced a decline in renal function or death, with no significant difference compared to PLN. MLN patients who achieved CR at 6 or 12 months had better renal outcomes.

W36-3

Renal Pathology Changes in Lupus Nephritis Undergoing Repeated Kidney Biopsies

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Conflict of interest: None

[Objectives] To clarify the renal pathological features and changes in patients with lupus nephritis (LN) who underwent multiple kidney biopsies. [Methods] We selected patients with LN who underwent kidney biopsies from 2008 to 2021 and evaluated clinical and renal pathological findings. We analyzed the changes and correlations over time. [Results] Out of 128 cases of LN that underwent kidney biopsy, 14 cases underwent repeat biopsies. The average age was 43.1 years, with 10 new-onset (71.4%) and 12 female (85.7%), and an average disease duration of 3.8 years. In the first biopsy, the pathological classification were II (14.3%), III (28.6%), IV (28.6%), III+V (0%), IV+V (7.1%), and V (21.4%). The average prednisolone dosage was 40.4 mg/day, and 12 cases received intensified immunosuppressive therapy. The second biopsy was performed after an average of 47.3 months due to flare or non-remission. Pathological changes occurred in 10 cases (71.4%), with progression of renal dysfunction. The chronicity index increased in 11 cases (78.6%), with four cases never achieving remission. [Conclusion] In cases of relapse in LN, approximately 70% of the repeated biopsies showed changes in histological type, with evident progression of chronic lesions in those who did not achieve remission.

W36-4

A Case of Systemic Lupus Erythematosus Complicated by Lupus Nephritis and Lupus Podocytopathy

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Conflict of interest: None

[Case]: A 28-year-old female was diagnosed with systemic lupus erythematosus (SLE) in X-12, presenting with fever, malar erythema, arthralgia, pancytopenia, and positive anti-ds-DNA and anti-Sm antibodies. Remission had been maintained with steroids, hydroxychloroquine, and tacrolimus. During a routine evaluation, she reported a 6 kg weight gain and exertional dyspnea. Lab showed serum albumin at 1.3 g/dL and urinary protein at 6 g/gCr, indicating nephrotic syndrome. Suspecting lupus nephritis (LN), the patient was hospitalized. Renal biopsy revealed ISN/RPS 2018 class II LN findings, with podocyte swelling and vacuolization, confirming lupus podocytopathy (LP). Steroid pulse therapy followed by 1 mg/kg/day of steroids and cyclophosphamide infusions was administered. By day 39, proteinuria resolved, and she was discharged. Electron microscopy showed no subendothelial deposits and 30-40% podocyte foot process effacement, consistent with LP. [Conclusion] LP, absent from ISN/RPS criteria, presents as a rapidly progressive nephrotic syndrome and is diagnosed by electron microscopy showing immune complex deposition and foot process effacement without glomerular proliferation. In stable SLE cases with no prior LN, sudden onset of nephrotic syndrome should prompt consideration of LP.

W36-5

Preventive effect of hydroxychloroquine (HCQ) desensitization on drug eruption in patients with anti-SS-A antibody (aSS-A) positive systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Objectives] We previously identified aSS-A positivity as an independent risk factor for drug eruptions by HCQ in SLE patients. We aimed to clarify preventive effect of HCQ desensitization on drug eruption in aSS-A positive SLE. [Methods] aSS-A positive 117 SLE patients who started HCQ between Sep 2015 and Sep 2024 were identified, and 21 cases assigned to desensitization group (starting at 50 mg/d, D group) and 96 cases to usual group (at 200 mg/d or more, U group). We retrospectively compared, 1) clinical features, 2) onset of drug eruption and discontinuation, and 3) odds ratio (OR) for drug eruption, between D and U groups. [Results] 1) Age, sex, history of allergy, skin lesions, and PSL dose at HCQ initiation were comparable between two groups. In D group, concomitant use of immunosuppressants was significantly less common, while initiation at hospitalization was significantly more common compared with U group. 2) In 49.2 ± 34.5 months of observational period, drug eruption occurred in 1 case in D group (4.8%), while in 11 cases in U group (11.5%). HCQ was discontinued in all 12 patients. 3) The adjusted OR for drug eruption in D group compared to U group was 0.39 (95% CI 0.02 -3.16). [Conclusion] In aSS-A positive SLE patients, HCQ desensitization might prevent drug eruption.

W36-6

Examination of factors associated with herpes zoster development in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is known to be frequently complicated by herpes zoster (HZ). This study aims to examine the frequency of HZ occurrence and its associated factors among SLE patients. [Methods] We retrospectively analyzed 208 SLE patients who visited Osaka Metropolitan University Hospital from April 2021 to March 2024. Baseline was set at the initial visit. Patients were categorized into three groups: no HZ, single HZ episode, and multiple (≧2) HZ episodes, and compared accordingly. [Results] The median age of the patients was 49 years, with a median disease duration of 18 years, and 87.5% were female. The overall prevalence of HZ was 47.5% of whom 39.3% experienced multiple episodes. Among the three groups, HZ-affected patients had a longer disease duration (P=0.038) and higher cumulative GC dosage (P=0.034) than those without HZ. Additionally, the usage of immunosuppressive and molecular-targeted agents was more frequent (P=0.010, P=0.017). Multivariate analysis identified molecular-targeted agents (OR=3.76), cumulative GC dosage (OR=1.01), azathioprine (OR=2.48), and mycophenolate mofetil (OR=2.91) as independent factors associated with HZ. [Conclusion] HZ is frequent in SLE patients, with immunosuppressive agents potentially increasing HZ risk.

W37-1

Association of age-related alterations in oropharyngeal microbiota and lymphocyte subsets with the pathogenesis of late-onset rheumatoid arthritis

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Conflict of interest: Yes

[Object] To identify the involvement of age-related alterations in oropharyngeal microbiota and lymphocyte subsets in the pathogenesis of late-onset rheumatoid arthritis (LORA) [Methods] Metagenomic analysis of oropharyngeal lavage fluid was performed in 47 patients with newly-diagnosed RA. The association between clinical presentation and bacterial species was analyzed by microbiome multivariable association with linear models ver. 2 (MaAsLin2). Age-associated helper T (ThA) cells, CD153-positive T peripheral helper (Tph)/T follicular helper (Tfh) cells, age-associated B cells (ABC), and terminally differentiated effector memory CD 45RA T cells (TEMRA) were analyzed by multicolor fluorocytometry. [Results] Four candidate bacterial species were identified in the oropharyngeal flora of RA patients that increased with age and were associated with increased CRP at baseline and complications of chronic lung disease. ThA, ABC, CD4-positive TERMA, and CD8-positive TERMA tended to be more frequent in LORA than younger-onset RA, and the percentage of CD153-positive Tph was associated with RA with bone erosion at baseline. [Conclusion] Age-related alterations in the oropharyngeal microbiota and an increased subset of lymphocytes with age may be associated with the pathogenesis in LORA.

W37-2

Pathogenic roles of KRAB zinc-finger protein, ZNF93, in rheumatoid arthritis synovial fibroblasts

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Conflict of interest: None

Objective: Synovial fibroblasts (SFs) in rheumatoid arthritis (RA) consist of multiple subsets involved in exacerbation or resolution of inflammation, as well as in destruction or repair of bone and cartilage, and are expected to be a drug target for difficult-to-treat RA. KRAB zinc-finger proteins (KZFPs), transcription factors repressing the transposons, are associated with pathological conditions such as cancer. In this study, we analyzed the functional roles of ZNF93 in RASFs. **Methods:** RASFs were stimulated with TNFα/IL1β/IFNγ/TGFβ (4 mix) and nuclear extracts were analyzed by data-independent acquisition (DIA) proteomoics. ZNF93 was knocked-down by siRNA and gene expressions were analyzed by RNA-seq and qPCR. **Results:** RASFs expressed 83 KZFPs. Among them, ZNF93 were up-regulated by 4 mix. siRNA knock-down of ZNF93 and RNA-seq revealed that ZNF93 regulated the pathways involved in proliferation, TNF signaling, and cancer. In addition, qPCR demonstrated that CSF2 and CSF3, involved in neutrophil proliferation and survival, and CXCL1 and CXCL2, involved in neutrophil migration, were down-regulated by the ZNF93 knock-down. **Conclusion:** ZNF93 in RASFs may participate in the synovial inflammation through the proliferation, survival, and chemotaxisis of neutrophils.

W37-3

Clonal hematopoiesis in patient with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Clonal hematopoiesis of indeterminate potential (CHIP) refers to somatic mutations in hematopoietic progenitor cells detectable in peripheral blood. CHIP has been linked to higher risks of hematologic malignancies, cardiovascular diseases, and diabetes. This study aimed to assess the prevalence of CHIP in rheumatoid arthritis (RA) patients. [Methods] A total of 28 RA patients (mean age: 75.6±8.7 years, 26 females) from Nagoya University Hospital were included. 17 CHIP-related genes were analyzed by using error-corrected targeted DNA sequencing with a variant-allele frequency (VAF) threshold of 0.5%. Additionally, patients with D2TRA, requiring two or more b/tsDMARDs were examined. [Results] CHIP-related mutations were identified in 14 of 28 patients (50%), involving seven genes (TET2: 7 cases, DNMT3A: 4 cases, CHEK2: 4 cases, ASXL1: 2 cases, TP53: 2 cases, CBL: 1 case, PPM1D: 1 case). Seven patients had mutations in multiple genes. Mutation prevalence increased with age (<60 years: 33.3%, 60-69 years: 50%, 70-79 years: 50%, ≧80 years: 54.5%). Among 15 D2TRA patients, mutations were detected in 7 cases, with TET2 being the most frequent (4 cases). [Conclusion] Using a VAF threshold of 0.5% and high-depth sequencing, CHIP was identified in 50% of RA patients.

W37-4

Biomarker exploration of PMR and EORA using novel proteomics on serum extracellular vesicles

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Conflict of interest: None

[Objectives] Polymyalgia rheumatica (PMR) is an inflammatory disease affecting individuals over 50 years, primarily targeting shoulder and hip joints. While PMR often responds to low-dose corticosteroids, distinguishing it from other diseases, particularly from elderly-onset rheumatoid arthritis (EORA), can be challenging, especially in cases with large joint involvement and seronegative results. Given the overlap in clinical features but differing management strategies, there is an urgent need for diagnostic biomarkers (BM). [Methods] To identify PMR-specific BMs, we performed proteomic analysis of serum extracellular vesicles (EVs) from 5 PMR patients, 5 seropositive RA patients, 4 seronegative RA patients, and 5 healthy controls. Statistical analysis was used to differentiate between PMR, RA, and healthy controls. [Results] The characteristics of patients were similar among the 4 groups. Proteomic analysis of EVs identified 2000 proteins, and statistical analysis revealed several BM candidates specific to PMR. Furthermore, the significance of these markers in the pathogenesis was investigated by integrated analysis of the proteome data and clinical information. [Conclusion] Using proteomic analysis of serum EVs, we identified novel BMs that distinguish PMR from RA.

W37-5

Frailty and nutritional status in patients with rheumatoid arthritis from a multicenter observational study (T-FLAG study)

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Conflict of interest: None

[Objectives] The aim of this study is to clarify the relationship between frailty and nutritional status in RA patients. [Methods] We enrolled 697 RA patients. Frailty was assessed using the KCL, while nutritional status was evaluated using the GNRI and CONUT. Multivariate analysis was used to identify factors associated with frailty, and the prevalence of frailty in each nutritional assessment group was examined. [Results] The background characteristics of the patients were as follows: mean age 69 years, disease duration 13 years, 73% female, SDAI 6.4, and KCL score 6.6. The prevalence of frailty was 33.4%. The GNRI nutritional levels were categorized as normal/mild/moderate/severe at 57.4/28.8/12.1/1.8%, while CONUT levels were 62.4/34.6/2.8/0.2%. In multivariate analysis, GNRI was found to be an independent factor associated with frailty. The prevalence of frailty across nutritional levels was as follows: for GNRI, normal/mild/moderate/severe were 29.6/42.8/48.1/66.7%; for CONUT, 32.6/40.5/64.7/100.0%, showing significant differences. [Conclusion] In RA patients, GNRI was identified as an independent factor associated with frailty, suggesting that nutritional status plays an important role in frailty management.

W37-6

Analyses of TIGIT and DNAM-1 expressions in GPI-induced arthritis

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Conflict of interest: None

[Objectives] TIGIT and DNAM-1 are checkpoint molecules mainly expressed on T cells, but their functional expressions on B cells have recently been reported. We analyze their expressions on B cells and T cells in mice with GPI-induced arthritis (GIA). [Methods] 1) Spleens and inguinal lymph nodes were collected on days 0 and 28 after GIA induction, and the expressions of TIGIT and DNAM-1 on CD4+ T cells, CD8+ T cells, regulatory T cells (Tregs) and follicular T cells were analyzed by flow cytometry. 2) On days 0, 7, 14, and 28 of GIA induction, memory B cells, naïve B cells, plasmablasts (PBs), plasma cells (PCs), and activated B cells were analyzed in the same methods as in methods 1. [Results] 1) On Tregs, TIGIT expression was increased on day 28 in the spleen and DNAM-1 was decreased on day 28. 2) In inguinal lymph nodes, TIGIT and DNAM-1 expressions increased over time on memory B cells and decreased in PBs. PCs had a trend to increase TIGIT expression, while DNAM-1 decrease. [Conclusion] In GIA, the expressions of TIGIT and DNAM-1 showed different kinetics on each subset of both T cells and B cells. We are investigating the functional effects of these molecules by in vitro assay.

W38-1

Development of rheumatoid vasculitis after COVID-19 vaccination in a patient with rheumatoid arthritis well controlled over the long term

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Conflict of interest: None

[Case] A 47-year-old woman with rheumatoid arthritis (RA) presented with worsening polyarthritis, along with nail fold infarctions. She had a highly elevated serum rheumatoid factor (RF) level (4130 IU/mL) and marked hypocomplementemia (CH50 <10 U/mL). She had been receiving treatment for RA for 31 years. Eight weeks earlier, she received her fourth dose of the COVID-19 vaccine (Moderna). Her disease activity has been well-controlled with etanercept and 3 mg/day of prednisolone. A diagnosis of rheumatoid vasculitis was made, despite the absence of serious extra-articular manifestations. At that time, her disease activity was moderate, with DAS28-CRP 2.87, DAS28-ESR 3.74. Disease activity gradually improved without intensifying treatment, with subsequent DAS28-CRP and DAS28-ESR scores of 2.97 and 3.50 one month later, and 2.52 and 3.63 three months later, respectively. Twenty months after the diagnosis of rheumatoid vasculitis, her disease activity remained well-controlled (DAS28-CRP 1.32, DAS28-ESR 2.53), although immunological abnormalities persisted (RF 2218 IU/mL, CH50 <10 U/mL). [Discussion] The gradual improvement in disease activity without intensifying treatment supports a possible link between CORVID-19 vaccination and the development of rheumatoid vasculitis.

W38-2

Impact of the Covid19 Pandemic on the Development of Herpes Zoster (HZ) in Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

[Background] Though there're previous reports for herpes zoster (HZ) incidence in the general population during the Covid19 pandemic, we don't have reports about them for rheumatoid arthritis (RA) patients. [Objective] To examine the incidence of HZ in RA patients before (pre-P: FY2017-FY2019) and during the Covid19 pandemic (P: FY2020-FY2022). [Methods] RA Patients who were registered in the NinJa database for 6-year (FY2017-FY2022) and investigated for HZ (9557~11877 patients per year) were analyzed, including RA drugs used and history of inactivated HZ vaccination. [Results] The incidence of HZ in FY2017-FY2019 (pre-P) was 1.32%-1.59% and 1.48% (FY2020), 1.86%,1.81% in FY2021, FY2022, respectively. The SIRs were 1.97 on average during pre-P, 2.00 on FY2020, and 2.48,2.42 on FY2021, FY2022, respectively. The incidence of HZ for JAKi non-users under 65 years old also increased during Covid 19 Pandemic (P): pre-P (0.88%-0.95%), P (1.15%-1.27%). The percentage of HZ vaccination usage in Japan increased only slightly to 1.32%, 3.2% in FY2021, FY2022 respecyively. The percentage of RA drugs used in patients with HZ weren't statistically significant compared between single years before and during Covid19. [Conclusion] Covid19 Pandemic may increase the percentage of HZ in RA patients.

W38-3

Coronavirus infections do not increase even if anti-rheumatic drugs are not discontinued when receiving a coronavirus vaccine -COVER-3 study-

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Conflict of interest: None

[Objective] At COVID-19 vaccination, RA patients have concerns for the effect of drugs on vaccine efficacy. And so, we searched for factors related to COVID-19 infection for one year. [Method] Among 420 RA patients (age 71.0 years, 76.2% female) who had anti-spike protein (S) and anti-nucleotide antibody titers measured, COVID-19 infection was confirmed in 72 patients (17.1%) during one year. A Cox proportional hazards analysis was performed with age, sex, BMI, use of molecular targeted medicines, MTX and PSL dosage, hypertension, disease activity, S antibody titer, and number of booster vaccinations as explanatory variables. [Results] The significant factors were age (HR 0.959 [95%CI 0.937-0.981], $p < 0.001$) and S antibody titer (HR0.998 [0.996-1.000], $p = 0.049$). The cutoff value for S antibody titer for infection suppression was 5035 U/ml (AUC 0.610, $p = 0.003$). [Discussion] We have not recommended that patients discontinue administration of anti-RA drugs, including MTX, at the time of vaccination. It was found that continued use of various medicines did not affect COVID-19 infection. A high S antibody titer was advantageous for preventing infection for the next one year. [Conclusion] There is no need to suspend RA medication before or after COVID-19 vaccination.

W38-4

Characteristics and risk factors of rheumatic disease patients hospitalized for COVID-19 infection

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Conflict of interest: Yes

Objective: We investigated the characteristics of rheumatic disease patients hospitalized due to COVID-19 infection. Methods: Sixteen cases analyzed with rheumatic disease hospitalized for COVID-19 infection from January 2021 to September 2024. Data were collected from medical records, including age, gender, underlying disease, treatments, comorbidities, diabetic status, vaccination history, blood test results, severity, hospitalization length, and prognosis. Result: Age was 66±17.5 years (10 males and 6 females) including 8 cases of rheumatoid arthritis (RA), 3 cases of systemic lupus erythematosus, and HbA1c >6% in 10 cases. Glucocorticoids were used in 14 cases, with a dosage of 5.8±3.5 mg/day. Each 7, 4, and 5 cases were mild, moderate, and severe, respectively, and 3 cases with RA treated with JAK inhibitors (JAKi) developed to severe stage and 2 unvaccinated cases required mechanical ventilation. One case died due to respiratory infection. Glucocorticoids have been previously reported as risk factors for severe COVID-19 infection. In our study, JAKi might be

identified as a risk factor. Conclusion: JAKi and diabetes were identified as risk factors for severe COVID-19 infection. We suggest it is important to control not only rheumatic diseases but also comorbidities.

W38-5

Two cases of HTLV-1-related myelopathy with suspected rheumatic disease

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Conflict of interest: None

HTLV-1 is the cause of HTLV-1-related diseases, including adult T-cell leukemia. HTLV-1 carrier is also known to develop rheumatic diseases such as rheumatoid arthritis (RA) and Sjogren's syndrome, and have been implicated in chronic inflammatory and pain disorder. Here, we present two cases of HTLV-1-associated myelopathy (HAM), which were suspected to be rheumatic diseases based on clinical symptoms. (case 1) A woman in her 70s became aware of periarthral pain in both thighs in October X-1. She first visited our department in July X with suspected RA and polymyalgia rheumatica (PMR). She had no evidence of synovitis or bursitis, and was diagnosed as having active HAM with intermediate disease due to spastic paraplegia, positive blood and CSF HTLV-1 antibody, increased provirus level and CSF CXCL-10. (Case 2) A woman in her 60s became aware of bilateral leg muscle pains in November X-1. Based on family history, she was suspected HTLV-1 carrier and diagnosed with intermediate active HAM, although she lacked spastic paraplegia. (Discussion) The current diagnostic algorithm for HAM requires the presence of spastic paraplegia, but in some cases does not become apparent early phase. We were able to identify the early symptoms of HAM, leading to a relatively early diagnosis.

W38-6

Survey of human T-cell leukemia virus type 1 positive patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] We attempted to clarify the reality of human T-cell leukemia virus type 1 (HTLV-1) positive systemic lupus erythematosus (SLE). [Methods] We included 216 SLE cases that were followed up at our department and six other medical institutions from January 2023 to January 2024. Clinical information was collected retrospectively using the medical records. [Results] A total of 197 cases with a confirmed anti-HTLV-1 antibody assays (particle agglutination method) were analyzed. Ten patients were diagnosed as HTLV-1 carriers and one as adult T-cell leukemia. 5.1% of all cases were HTLV-1 carriers. We categorized the entire group into HTLV-1 carrier and non-HTLV-1 carrier groups. The carrier group was older than the non-carrier group. There was no difference in the complication rate of Sjogren's syndrome. Because HTLV-1 carriage rates vary with age, we compared HTLV-1 carriage rates in the national general population with those in the SLE population. In almost all age groups, the latter showed higher carriage rates. [Conclusion] These results suggest that there is some association between HTLV-1 infection and SLE. The impact of HTLV-1 infection and SLE on each other is not yet known. Accumulation of future cases is considered important.

W39-1

Development of a Phase IIIb Trial Design for Nerandomilast (BI 1015550) in Patients with Systemic Autoimmune Rheumatic Disease-Related Interstitial Lung Diseases

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Conflict of interest: Yes

Objective: Nerandomilast, a preferential PDE4B inhibitor, is being evaluated in Phase III trials in IPF and PPF (FIBRONEER™). As some immunosuppressants (ISs) are used as standard therapy for patients with systemic autoimmune rheumatic disease-related interstitial lung diseases (SARD-ILDs) but are restricted in the FIBRONEE™ trials, evaluation of nerandomilast under IS therapy is needed. **Methods:** A steering committee of 7 rheumatologists, 3 pulmonologists and 1 radiologist met several times to discuss the study design development, and advisory boards were held in countries including Japan. This trial aims to enroll patients with SARD-ILDs using ISs, whilst exploring new endpoints in a shorter study duration. **Results:** Eligible patients have any of the following SARD-ILDs: ILD associated with RA, SSc, IIM, Sjögren's syndrome, or MCTD, with no lung function improvement or clinically significant ILD improvement despite treatment with IS therapy for ≧6 months (≧3 months for IIM). The primary endpoint is absolute change from baseline in quantitative ILD score (%) on quantitative HRCT at Week 26. **Conclusion:** This trial will provide key information on the real-world use of nerandomilast in SARD-ILD with broader ISs, with evaluation of a novel imaging-based outcome measure as an endpoint.

W39-2

Association of rare single nucleotide variant MUC5B rs35705950 with interstitial lung disease in Japanese rheumatoid arthritis

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) is sometimes complicated by interstitial lung disease (ILD) with a poor prognosis. A single nucleotide variant (SNV) in *MUC5B* was associated with ILD in European RA patients. But its frequency in Japanese populations is very low, thus, associations of this SNV were not detected in Japanese RA patients. We analyzed the associations of candidate SNVs including the *MUC5B* variant with ILD in Japanese RA. [Methods] Genotyping of *MUC5B* rs35705950, *MUC2* rs7934606, *MAD1L1* rs12699415, and *PPFIBP2* rs6578890 in Japanese RA patients was conducted for association analyses. [Results] *MUC5B* was associated with usual interstitial pneumonia (UIP) (*P*=0.0039, *P*c=0.0156, OR10.66, 95%CI2.05-55.37) or ILD (*P*=0.0071, *P*c=0.0284, OR7.33, 95% CI1.52-35.44) in Japanese RA under the allele model. *MUC2* was associated with UIP (*P*=0.0072, *P*c=0.0288, OR29.55, 95%CI1.52-574.57) or ILD (*P*=0.0037, *P*c=0.0148, OR22.95, 95%CI1.27-416.13) in RA. Haplotype analyses suggested the primary association of *MUC5B* with UIP in Japanese RA. No significant association of *MAD1L1* or *PPFIBP2* with UIP, nonspecific interstitial pneumonia, or ILD in RA was observed. [Conclusion] *MUC5B* rs35705950 is associated with, and might be involved in the pathogenesis of ILD, especially UIP, in Japanese RA.

W39-3

Achieving rapid clinical remission and sustaining remission after starting treatment with molecular targeting drugs suppress the progression of interstitial lung lesions in rheumatoid arthritis

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Conflict of interest: None

Object: This study aimed to analyze the association between the duration of controlling disease activity with molecular targeting drugs and the changes of pulmonary abnormality including interstitial lung disease (ILD) in patients with rheumatoid arthritis (RA). Methods: Participants were 115 patients with RA under molecular targeting drugs therapy who underwent chest HRCT scans before and during treatment. We calculated DAS28-ESR at 3 months after starting molecular targeting drugs and the average DAS28-ESR during observation period. Based on these values, we compared changes of pulmonary lesions including ILD on HRCT between patients who achieved clinical remission (3Mo/average CR group) and those who did not (3Mo/average non-CR group). Results: The 3Mo CR group showed significantly less worsening of pulmonary lesions as compared with the 3Mo non-CR group although there was no significant difference in ILD lesions. Both pulmonary and ILD lesions were significantly less worsened in the average CR group than the average non-CR group: 36.4% vs 63.3% (p=0.0051) and 20.0% vs 38.3% (p=0.0409), respectively. Conclusion: Achieving clinical remission within 3 months after starting treatment with molecular targeting drugs and sustaining remission can suppress the progression of ILD in RA.

W39-4

The Therapeutic Efficacy of Abatacept for Rheumatoid Arthritis-Associated Interstitial Lung Disease

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Conflict of interest: None

[Objectives] Our aim was to evaluate the therapeutic efficacy of abatacept for RA-ILD. [Methods] This observational retrospective study included patients with RA-ILD treated with abatacept be tween 2012 and 2021. Indices of RA disease activity and interstitial lung disease (Disease Activity Score in 28 joints using C-reactive Protein [DAS28-CRP], Simplified Disease Activity Index [SDAI], Clinical Disease Activity Index [CDAI], serum Krebs von den Lungen-6 levels, % forced vital capac ity [%FVC], and semi-quantified chest high-resolution computed tomography scores) were evaluated before and 1 year after the start of abatacept administration. [Results] Overall, 38 patients were included. DAS28-CRP, SDAI, and CDAI were significantly improved (all with $p < 0.0001$). Total ground-glass opacity scores were decreased in both patients with usual interstitial pneumonia (UIP)-like patterns and with non-UIP-like patterns ($p = 0.008$ and < 0.002, respectively). Total fibrosis scores were also decreased in the UIP-like pattern group ($p < 0.042$). The %FVC remained stable. [Conclusion] Abatacept significantly improves RA disease activity and reduces pulmonary inflam mation in patients with RA-ILD.

W39-5

Is it possible to administer bDMARD while treating pulmonary MAC disease? Long-term observation of pulmonary MAC disease associated with rheumatoid arthritis

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Conflict of interest: None

Objectives: We investigated the possibility of treating MAC-PD and simultaneously administering bDMARD (Bio). Methods: Among 1123 RA patients from 2011 to 2022, 28 patients with nodular bronchiectasis (NB) were retrospectively analyzed. Result: MAC-PD observation period was 54 months, age at MAC diagnosis was 63 years, BMI 18.0, smear positive 11 cases. Chest CT revealed interstitial lung disease (ILD) in 6 cases, cavitary lesions in 8 cases. Bio was stopped in all patients and CAM, RFP, EB was administered in 23 patients (82%). 14 patients (50%) continued for more than 12 months, and 79% were sputum negative conversion. RA treatment was 13 patients (6 resumed, 7 initial induction) in Bio group, 8 patients in non-Bio group were treated with MTX, 7 patients with csDMARD (SASP, IGR). Of the 28 patients, 9 died (age 82 years), 2 in the Bio group, 1 in the MTX group, and 6 in the csDMARD group due to inadequate MAC therapy. All-cause mortality was not significantly different between Bio and non-Bio group (MTX, csDMARD) (Log-rank, P=0.08). There was no significant difference in the time to first pneumonia hospitalization between the Bio group and the non-Bio group (P=0.91). Cavitary lesions and ILD had poor prognosis. Conclusion: Bio administration is possible if RECAM can be continued.

W39-6

Factors associated with progression of chronic kidney disease and carviovascular events in rheumatoid arthritis

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) have a higher risk of progression to chronic kidney disease (CKD) and cardiovascular events (CVD) compared to the general population. This study aims to identify factors associated with these risks. [Methods] We compared clinical backgrounds and risk factors between 27 patients who progressed to CKD (G3b or higher, G3a or higher A2 or higher, and A3 or higher), 16 patients who developed CVD, and a group without these conditions. [Results] Significant differences were observed in the incidence of CVD events based on the presence of CKD. Progression to CKD showed significant differences based on the presence of hypertension. Logistic regression analysis for CVD events showed significant associations with hypertension, NSAID use, diabetes, GC use, and proteinuria 2+. No significant correlations were found with CRP levels or RF levels. Logistic regression analysis for CKD progression showed significant associations with hypertension, GC use, CRP levels, MTX use, and RF 155 IU/mL. [Conclusion] While the risk of CVD complications in RA has limited association with disease activity,

the risk of CKD complications is related not only to lifestyle-related diseases but also to RA disease activity, including high RF levels.

W40-1

Self-injection instruction for rheumatoid arthritis (RA) patients ~Issues in Nursing Intervention from the Self-Injection Check Sheet~

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Conflict of interest: None

[Objectives] The advantages of AI are that it is safe, easy to administer and requires fewer hospital visits. The disadvantage is that it may be administered with incorrect. technique or drug administration. We examined nursing intervention during instruction using a seif-injection checklist at our center. [Methods] Guidance was provided every 2-3 months to 52 patients who self-injected at the RA center from February 2019 to March 2024, using a self-injection checklist developed in collaboration with the Pharmacy Department. [Results] Of the 529 patients attending our RA center, 66.5% (352/529) were using biological agents and 14.8% were self-injecting patients. In the first round 53.8% of patients could be vaccinated without any problem, and in the sixth round, 87.5% of the patients could be vaccinated without any problem. However, 63.6% of patients were able to be vaccinated after the seventh round without any problems. The reasons for this were forgetting to give injections due to not using a notebook, ambiguity in how to handle problems, and not using a cold bag. [Conclusion] During seif-injection instruction, nurses need to understsnd the patient's level of comprehension, functional disability, and social background, and then provide self-injection instruction appropriate for each RA patient.

W40-2

Development of a Nursing Support Evaluation Scale for Foot Care in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To develop a scale to evaluate the knowledge and practice of nurses in supporting foot care for patients with RA. [Methods] The subjects were RA nurses from all over the country. I sent a request form to the head of the nursing department at all 605 educational facilities of the JCR and asked them to recommend eligible participants. The request form included a QR code that nurses could use to voluntarily respond to the web survey. [Results] We extracted 116 items from previous research and teaching materials, and examined the validity of the items with eight RA nurses. We then conducted a web-based questionnaire with 47 questions and a five-point scale for implementation. There were 167 respondents (91% female, 22% public hospital, 32% outpatient, average age 39,7 years of RANs experience), and responses were received from all prefectures. The average score and standard deviation for each item were calculated, and 38 items were selected, excluding the 9 items that were too high or too low. The results of factor analysis (Varimax rotation) were "Knowledge (12 items)" and "Practice (26 items)". Cronbach's alpha was 0.977. [Conclusion] We have been able to develop a scale that can evaluate "the knowledge and practice of nurse foot care support" consisting of 38 items.

W40-3

Efficacy of Hospitalization under the Clinical Pathway When Initiating Biologic and Targeted Synthetic DMARD

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Conflict of interest: None

[Objective] Our hospital has introduced a clinical path as part of patient education at the start of b/tsDMARDs. The purpose of study was to clarify the medical needs of patients admitted with the clinical path by conducting a satisfaction survey. [Methods] 56RA patients hospitalized under the clinical pathway from 2022 to 2024 were enrolled. Drug persistence rates and patient satisfaction survey results were compared by year. [Results] A total of 56RA patients were analyzed. There were no significant differences in age, gender, or introduced b/ts DMARDs between the three groups. Drug persistence rates at three months after initiation tended to be higher in the 2024 group compared to the other two groups. In the patient satisfaction survey, scores related to the daily life guidance and the duration of hospitalization were lower in the 2024 group. Decision tree analysis identified age under 67.5 years as a factor associated with lower scores (over 67.5 years old vs. under 67.5 years old: 4.65 vs. 4.19, 4.48 vs. 4.12). [Conclusion] Clinical pathway hospitalization improved the early drug persistence rate. However, it is suggested that a more thorough explanation of the significance and importance of clinical pathway hospitalization is needed for patients aged under 67 years.

W40-4

About the feeling of using Ozoralizumab Auto Injector~From a survey of nurses (Ns)~

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Conflict of interest: None

[Objectives] We conducted a survey of Ns who had used OZRAI to investigate their impression of using the syringe. Methods] Ns who were administered O Z R A I for the first time were surveyed on (1) whether they had any anxiety before administration, (2) the simplicity of the administration procedure, and (3) whether they had any concerns about O Z R A I self-injection instruction [Results] The overall mean age was 46.1±10.1 Ns, with a history of 22.5±10.1 Ns, a history of working in rheumatology 7.4±7.8 R A Care Ns qualifications were none for 15 patients (52%). (1) 8 were not at all anxious, 5 were not very anxious, 5 were somewhat anxious, and 0 were very anxious; (2) the mean score for simplicity was 0.7± 0.7; (3) 7 were not at all anxious, 16 were not very anxious, 6 were somewhat anxious, and 0 were very anxious regarding self-injection instruction. (1) There was no difference between the two groups in the percentage of no worries before administration and in the rating of ease of administration. (3) Worry about self-injection instruction was more in the no group ($P<0.05$) [Conclusion] O Z R A I was administered easily and without anxiety even in situations where Ns with a short history of rheumatoid arthritis work were administering it for the first time.

W40-5

The practice and challenges of shared decision-making in the nursing of rheumatoid arthritis

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Conflict of interest: None

[Objectives] The 2018 update of the EULAR recommendations for nurses' roles proposed that rheumatology nursing is based on shared decision-making (SDM) with patients. This study's objective was to clarify the levels of acceptance and practice of this principle and identify potential barriers to its practice. [Methods] Data were collected from August 1 to December 31, 2022. Nurses and doctors engaged were asked to answer

questions about the levels of agreement and nurses' implementation of this principle using numerical rating scales (0-10). They were also asked to give reasons for inadequate implementation of SDM. [Results] 215 nurses and 94 doctors participated, of which 69 nurses and 33 doctors provided a total of 113 comments. Both groups of the participants showed high levels of acceptability (median: 10). Perceived levels of nurses' implementation showed significantly lower in both groups ($p<0.001$), citing lack of knowledge, staff, time, support systems, collaboration, and patient cooperation as barriers. [Conclusion] Nurses and doctors both perceived that nurses' practice was lower with matching views on its barriers. To successfully practice SDM, support systems for nurses should be established in the workplace, and full comprehension and cooperation of doctors are required.

W40-6

Preventing Accidental Live Vaccine Administration in Rheumatoid Arthritis Patients: Findings from Pre- and Post-Education Surveys on Herpes Zoster Prevention

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Conflict of interest: None

Objective: This study investigates awareness of herpes zoster (HZ) prevention in rheumatoid arthritis (RA) patients and evaluates the effectiveness of patient education, addressing issues of vaccine misadministration. **Methods:** From February to April 2024, we surveyed 30 RA patients on HZ prevention awareness, with a six-month follow-up. The survey included interviews and guidance on HZ prevention and immunosuppressive medications. **Results:** The follow-up showed increased awareness that RA treatment raises the risk of HZ, from 33% to 57%, and that live vaccine administration is prohibited, from 20% to 30%. Recognition of the recombinant zoster vaccine rose from 43% to 70%, but interest in receiving it decreased from 27% to 13%. Among 202 municipalities, only 25% provided warnings for immunosuppressive therapy, and just 3.5% explicitly stated the "prohibition of live vaccine". Of 20 biological agents and JAK inhibitors, only one mentioned this prohibition on patient cards. **Conclusion:** Patient education enhanced awareness of HZ prevention, but challenges remain in communicating the prohibition of live vaccines. Expanding vaccine subsidies and collaboration among healthcare providers, government, and pharma company are essential to prevent misadministration.

W41-1

Clinical and pathological features of ANCA-associated vasculitis presenting as IgA nephropathy histologically

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Conflict of interest: None

[Objectives] To elucidate the characteristics of ANCA-associated vasculitis (AAV) presenting as IgA nephropathy (IgAN) on renal biopsy. [Methods] Among 92 patients diagnosed with AAV and who underwent renal biopsy from 2000 to 2023, we compared the clinical and pathological features of 8 patients with IgAN (AAV/IgAN overlap group) and 84 patients without IgAN (AAV group). [Results] All 8 patients in the AAV/IgAN overlap group were diagnosed with MPO-ANCA positive microscopic polyangiitis (MPA). Univariate analysis showed that the AAV/IgAN overlap group had significantly higher serum IgA (P=0.04), lower CRP (P=0.01), fewer systemic symptoms (P=0.009), and fewer pulmonary lesions (P=0.05). BVAS score was lower (P=0.15), with no differences in renal function. Pathologically, the AAV/IgAN overlap group had more adhesions (P=0.07) and significantly fewer crescents (P=0.04). Renal function and eGFR improvement rates at 3 months were similar. There was no significant difference in the 10-year survival rate and renal survival rate. [Conclusion] AAV presenting as IgAN on renal biopsy had lower CRP, fewer systemic symptoms, and fewer pulmonary lesions, with fewer crescents pathologically. Renal and overall prognosis were similar to those of AAV alone.

W41-2

Efficacy of IL-23 inhibitors for axial involvement in pustulotic arthro-osteitis (PAO); a case series

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Conflict of interest: None

[Objective] To evaluate the efficacy of iIL-23 inhibitors for axial involvement in pustulotic arthro-osteitis (PAO). [Methods] Five PAO patients with axial involvement treated with IL-23 inhibitors were enrolled. We evaluated clinical symptoms, disease activity (ASDAS-CRP, mBASDAI) and MRI findings before and after treatments with IL-23 inhibitors. [Results] The patients' age was 22 to 69 years (median: 58 years) and male/female was 1/4. All patients had back pain, and some patients presented with neck, shoulder, elbow and ankle pain. Spinal MRI revealed bone marrow edema in all cases. All cases had received dental treatment, antibiotics, NSAIDs, csDMARDs, or TNF inhibitors prior to initiation of IL-23 inhibitors, but showed poor response. After starting IL-23 inhibitors, skin lesions and back pain improved in all cases. Within 3 weeks to 6 months, bone marrow edema on spinal MRI dramatically improved in all cases. The ASDAS-CRP scores before treatment showed 1.8 to 3.5 (median: 2.12). While post-treatment scores showed significant improvement; 0.6 to 2.0 (median: 0.96). [Discussion] This case series highlights the potential efficacy of IL-23 inhibitors for axial involvement in PAO. We would like to discuss about the differences of pathophysiology between PAO, PsA and axSpA.

W41-3

Screening methods and diagnostic procedures for adult-onset hypophosphatasia in our hospital

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Conflict of interest: None

Objectives: Hypophosphatosis (HPP) is a genetic disorder that causes osteoporosis due to an abnormality in the alkaline phosphatase (ALP) enzyme, and is one of the designated incurable diseases. In this study, we report the results of a screening test for HPP at our hospital. Methods: Patients with multiple ALP levels below 37 U/l from April 2021 to March 2023 were screened. Patients with low ALP after initiation of steroids or bone resorption inhibitors were excluded. Patients were asked about the presence of premature loss of deciduous teeth, repeated fractures, and musculoskeletal pain that was difficult to treat, and the possibility of HPP was explained to each patient. Genetic testing was proposed for those patients who showed further elevated levels. Results: Ten patients showed multiple low ALP levels. Among them, 2 patients did not wish to undergo close examination, and 8 patients underwent urinalysis. One of them showed abnormally high levels, which led to genetic testing, which showed a genetic abnormality in that patient. Conclusion: We performed HPP screening at our hospital. As a result, we were able to diagnose one patient with HPP.

W41-4

Pathological findings of Relapsing polychondritis in our hospital

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Conflict of interest: None

[Objectives] Relapsing Polychondritis (RP) is a rare disease marked by cartilage inflammation. Diagnosis relies on clinical symptoms and pathology, but consolidated reports are limited due to its rarity. This study investigates the role of pathological testing in our RP patients. [Methods] We reviewed 25 RP patients from October 2004 to April 2023, all having documented pathological findings. [Results] Samples were taken from auricular cartilage (17 cases), nasal septum (1), trachea (5), and costal cartilage (2). Inflammation was confirmed in 10 auricular, 1 nasal septal, 4 tracheal, and 1 costal case. Six auricular cases showed inflammation around the cartilage. Degeneration was noted in 8 auricular and 1 tracheal case, with fibrosis in 1 auricular case. Notably, 30% had no inflammatory cell infiltration. Only 2 cases needed pathology for a definitive diagnosis. [Conclusion] While cartilage biopsy is useful, its effectiveness is limited by site availability and timing. Many chondritis symptoms occurred in multiple organs, suggesting possible diagnoses without biopsy. Atypical RP presentations underscore the need for comprehensive evaluations, including pathology.

W41-5

A case of VEXAS syndrome complicated by nephrotic syndrome

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Conflict of interest: None

75 year-old male developed relapsing itchy erythema in his legs 3 years before presentation. The erythema worsened and he developed redness and periorbital edema in the left eye after receiving COVID-19 vaccination. The patient presented to the previous hospital with fever >38°C, swelling of the cheeks, nasal mucosa, and right ear, and scrotal and leg edema. Investigations revealed progressive macrocytic anemia, pericardial and pleural effusion, and pulmonary infiltration. Bone marrow examination revealed myelodysplastic syndrome and vacuoles in the myeloid and erythroid progenitor cells. He was referred to our hospital and hospitalized. For severe proteinuria, hypoalbuminemia, and decreased renal function, a renal biopsy was attempted but not performed due to progressive anemia and hypertension. UBA1 gene analysis was performed, which revealed a missense somatic mutation (c. 122T>Cp. Met41Thr) with a variant allele frequency of 0.673. A diagnosis with VEXAS syndrome was made. Treatment with prednisolone 1 mg/kg/day improved clinical symptoms, blood, urine, and imaging findings, and the patient was discharged on the 61st day of hospitalization. The association between VEXAS syndrome and nephrotic syndrome, which has rarely been reported, will be discussed.

W41-6

A case of thrombocytopenia caused by VEXAS syndrome successfully treated with baricitinib

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Conflict of interest: None

[Chief Complaint] Fever [History of Present Illness] Diagnosed with myelodysplastic syndrome (MDS) in year X-10 due to leukopenia. In year X, presented with fever, left auricular redness, panniculitis in both thighs, and multiple interstitial lung shadows. Bone marrow examination showed vacuolated granulocyte cytoplasm, leading to a clinical diagnosis of VEXAS syndrome. He maintained remission with prednisolone (PSL) and tocilizumab (TCZ), but in year X+1, interstitial pneumonia worsened, requiring hospitalization. Platelet count dropped below 20,000, making him transfusion-dependent. Without signs of immune or thrombotic thrombocytopenic purpura, thrombocytopenia was attributed to VEXAS syndrome. Despite high-dose steroids improving pneumonia, transfusion dependency for platelets persisted. On day 10 of hospitalization, baricitinib was initiated to control VEXAS syndrome. Two weeks later, platelet counts gradually rose, and by one month, he achieved transfusion independence. However, baricitinib showed limited control of recurrent fever and pneumonia upon steroid tapering. [Discussion] No established treatment exists for VEXAS syndrome; high-dose steroids, TCZ, and JAK inhibitors are commonly used. This case discusses the potential role of JAK inhibitors in VEXAS syndrome management.

W42-1

Characteristics of HLA-E-expressing macrophages and NKG2A/CD94 expression in adult-onset Still's disease

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Conflict of interest: None

[Objectives] To investigate the characteristics of human leukocyte antigen (HLA)-E-expressing macrophages and NKG2A/CD94 expression in T and natural killer (NK) cells in patients with adult-onset Still's disease (AOSD). [Methods] Isolated monocytes, from peripheral blood mononuclear cells, were differentiated into M0, M1, and M2 macrophages. HLA-E and NKG2A/CD94 expression levels were evaluated using quantitative RT-PCR and flow cytometry. [Results] HLA-E expression in M0 and M2 macrophages was significantly higher in AOSD than in healthy controls (HC) and had positive correlations with serum C-reactive protein levels and erythrocyte sedimentation rate. NKG2A/CD94 expression in CD4+ and CD8+ T cells was significantly higher in AOSD than in HC. In AOSD, NKG2A expression in CD4+ T cells positively correlated with HLA-E expression in M0, M1, and M2 macrophages. CD94 expression in CD8+ T cells inversely correlated with HLA-E expression in M1 and M2 macrophages. NKG2A and CD94 expression in NK cells inversely correlated with HLA-E expression in M0, M1, and M2 macrophages. [Conclusion] Increased HLA-E in macrophages and NKG2A/CD94 in T cells may be attributed to the inflammation in AOSD. HLA-E-expressing macrophages may be differently associated with NKG2A/CD94 expression in T and NK cells.

W42-2

The association between the serum caspase-1 and inflammatory cytokines in adult-onset Still`s disease

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Conflict of interest: None

[Objective] Caspase-1 is a crucial component of the inflammasome cascade. This study investigated whether serum caspase-1 could be a reliable inflammatory marker in adult-onset Still's disease (AOSD) patients. [Methods] We included 51 patients diagnosed with AOSD, 66 patients with rheumatoid arthritis (RA) as disease controls, and 36 healthy controls (HCs). Serum caspase-1 levels were measured using ELISA. Serum cytokine concentrations in AOSD patients were analyzed via the multiplex suspension array, with cluster analysis conducted to determine specific cytokine networks. [Results] Serum caspase-1 levels were significantly elevated in AOSD patients compared to RA patients ($p < 0.001$) and HCs

($p < 0.001$). Furthermore, serum caspase-1 levels were positively correlated with AOSD disease activity score (Pouchot score, r = 0.59, $p < 0.001$) and serum ferritin (r = 0.54, $p < 0.001$). In AOSD patients, serum caspase-1 levels were significantly correlated with inflammatory cytokines, including IL-18. Immunoblot analysis detected the active form of caspase-1 (p20) in the sera of untreated AOSD patients but not in inactive AOSD patients under immunosuppressive therapy. [Conclusion] This study suggests that caspase-1 can be a valuable biomarker for diagnosing and monitoring AOSD.

W42-3

Identification of novel cytokine to judge the diagnosis and clinical phenotype of adult-onset Still's disease

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Conflict of interest: None

[Objectives] To identify biomarkers to distinguish adult-onset Still's disease (AOSD) and to predict disease phenotypes. [Methods] In total, 49 patients diagnosed with AOSD and 200 patients with common diseases (controls) were included in the analysis. The levels of 69 cytokines were analyzed using a multi-suspension cytokine array. Cytokine cluster analysis was performed to identify specific molecular networks. Random forest analysis and logistic regression analysis were used to rank cytokines based on their importance and to determine specific biomarkers for identification of AOSD patients and phenotypes. [Results] Patients with AOSD demonstrated significantly higher macrophage migration inhibitory factor (MIF) and interleukin (IL)-12 (p40) serum levels than controls and patients with rheumatoid arthritis. Serum levels of chemokine (C-C motif) ligand (CCL) 8 and CCL22 were significantly lower in AOSD patients with a polycyclic systemic disease phenotype and could be differentiated with high accuracy from the other phenotypes. [Conclusions] Combined MIF and IL-12 (p40) levels may represent a biomarker for differentiating patients with AOSD from those with other diseases. The chemokine profiles of AOSD with a polycyclic systemic disease phenotype may differ from other phenotypes.

W42-4

Adult-onset Still's disease after COVID-19: case report and literature review

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Conflict of interest: None

[Case] A 59-year-old man was diagnosed with SARS-CoV-2 infection (COVID-19) in August 20X, and 11 days later, he developed urticarial rash on his face and upper limbs, arthralgia, and fever. He showed high fever of >39°C, generalized arthralgia, sore throat, increased white blood cell count with neutrophilia (WBC 10880/μl, Ne 87.3%), and hyperferritinemia (25989 ng/ml), then he was diagnosed with adult-onset Still's disease (AOSD). The patient improved with prednisolone (maximum dose 80 mg/day) and methotrexate. [Discussion] There have been eight reports of cases of AOSD developing after COVID-19, and we examined the clinical characteristics of all nine cases, including our case. The median age was 42 years (range 19-59 years), 7 female and 2 male patients, the median time from onset of COVID-19 to onset of AOSD was 14 days (range 3-182 days), and the median serum ferritin level was 6108 ng/ml (range 1750-25989 ng/ml). One case each of serositis and myocarditis was reported, but no patients developed MAS or DIC. [Conclusion] AOSD develops relatively early after COVID-19 infection. And although ferritin levels are high, there have been no reports of severe complications such as MAS or DIC, suggesting that the prognosis is not poor.

W42-5

Investigation of Risk Factors for Macrophage Activation Syndrome During IL-6 Inhibitor Treatment in Adult-onset Still's Disease

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Conflict of interest: None

[Objectives] While IL-6 inhibitors effectively treat Adult-onset Still's Disease (AOSD), IL-6 inhibitor-induced Macrophage Activation Syndrome (MAS) is a concerning adverse event. This study investigates risk factors for MAS development in AOSD patients receiving IL-6 inhibitor therapy. [Methods] We analyzed 22 AOSD patients (24 episodes) treated with IL-6 inhibitors between 2012-2024, comparing 6 MAS cases with 18 non-MAS cases. We evaluated demographic data, laboratory markers (CRP, ferritin, LDH), steroid doses, and timing of treatments. Logistic regression analyzed the relationship between MAS development and two factors: CRP <1 and ferritin decrease to <50% of peak value at IL-6 inhibitor initiation. [Results] Univariate analysis showed no significant differences between groups. Logistic regression revealed OR=0.2289 (95%CI: 0.0122-4.2771, p=0.3236) for CRP <1 and OR=11.3654 (95%CI: 0.9102-141.9148, p=0.0592) for ferritin <50%. [Conclusion] While ferritin reduction showed correlation with MAS development, no parameters reached statistical significance, possibly due to small sample size.

W42-6

Impact of plasma exchange in adult-onset still's disease

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Conflict of interest: None

[Objectives] To investigate the impact of plasma exchange (PE) in patients with adult-onset still's disease (AOSD). [Methods] The clinical records of 74 patients who were newly diagnosed with AOSD were reviewed. Clinical information was compared between patients who underwent PE (PE group) and those without PE (non-PE group). In the PE group, PE-related efficacy, including remission (REM), partial response (PR), and no response (NR), prognosis, and adverse events were evaluated. [Results] PE and non-PE groups were classified into 10 (mean 63 years, 8 women) and 64 patients (54 years, 42 women), respectively. Higher frequency of macrophage activation syndrome (MAS) (100% vs. 34.4 %) and serum ferritin levels, and lower platelet counts were significantly observed in the PE group than in the non-PE group ($P < 0.01$). In the PE group, out of the 10 patients, 4 had REM, 5 had PR, and 1 had NR without any deaths. One had a drug eruption and 2 had hemorrhage at the catheter insertion. [Conclusion] MAS was significantly observed in the PE group. Our study suggests that PE may contribute to improving prognosis, although previous reports indicated increased mortality under MAS existence.

W43-1

Efficacy, Safety and Radiographic Outcomes from the Phase 3 SELECT-AXIS 2 Study of Upadacitinib in Patients with Active Ankylosing Spondylitis and an Inadequate Response to Biologic DMARD Therapy: 2-Year Data with overall and Japanese Subjects Sub-analysis

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Conflict of interest: Yes

[Objectives] To assess the 2-year efficacy and safety of Upadacitinib (UPA) 15 mg 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 once daily for up to 90 wks. [Results] Of 420 randomized pts including 12 Japanese pts who received the study drug, 331 (78.8%) completed 104wks of treatment. Response rates were maintained or improved from wk14 to wk104 in the continuous UPA group and at wk104 similar responses were achieved in the group those who switched from PBO to UPA at wk14, including ASAS40 (As observed with non-responder imputation analyses; 64.9% and 61.7%, respectively). Safety was reported in 414 pts (687.2 pt-years [PY]) who received ≧1 UPA dose. Treatment emergent adverse event rates were 165.2 events/100 PY. Efficacy and safety of Japanese pts were generally consistent with overall pts. [Conclusion] UPA showed sustained efficacy up to wk104 in bDMARD-IR pts with active AS. UPA was generally well tolerated, with no new safety signals identified.

W43-2

Factors associated with sacroiliac joint ankylosis in patients with inflammatory bowel disease

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Conflict of interest: None

[Objectives] Inflammatory bowel disease (IBD) often has extraintestinal complications, but reports on axial spondyloarthritis (axSpA) in Japanese IBD patients are limited. IBD patients with inflammatory back pain and sacroiliitis (e.g., sacroiliac joint ankylosis) may be diagnosed with axSpA. This study examined the prevalence and factors related to sacroiliac joint ankylosis in IBD patients. [Methods] A retrospective study was conducted on 880 IBD patients (374 with ulcerative colitis [UC], 506 with Crohn's disease [CD]) who underwent CT for their primary disease. [Results] The cohort was 69% male, with an average age of 45±16 years and disease duration of 13±11 years. Ankylosis was found in 41 cases (4.7%). The ankylosis group had more males (90% vs. 68%), was older (60±16 vs. 44±16 years), and had a longer disease duration (17±11 vs. 13±11 years) (all $p<0.001$). Multivariate analysis showed CD [3.57 (1.47-8.67)], male gender [6.87 (1.97-23.96)], and age [1.09 (1.06-1.12)] were independent risk factors. [Conclusion] A 2019 survey reported axSpA prevalence in Japanese IBD patients as 1.3-1.6%. This study suggests axSpA may be underdiagnosed. In addition to back pain, screening the sacroiliac joints via CT performed for evaluating the primary disease could be useful for diagnosing axSpA.

W43-3

Sacroiliac joint changes in patients with lumbar spinal stenosis

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Conflict of interest: None

[Objective] The purpose of this study was to examine changes in the SIJ in cases of lumbar spinal stenosis (LSS) in which axSpA cannot be diagnosed, using pelvic XP, MRI, and CT, and to contribute to the diagnosis of axSpA. [Method] The study included 48 patients who underwent surgery in LSS. There were 12 men and 36 women, and the average age was 71 years. In these cases, 96 SIJ joints were examined. Pelvic XP was classified according to New York criteria. MRI was examined for the presence of high signals on STIR. CT was classified into 4 types, type 0: normal, type 1: mild degeneration, type 2: severe degeneration, and type 3: ankylosis. [Results] Pelvic XP showed 0° in 10 joints (10%), 1° in 23 joints (24%), 2° iin 47 joints (49%), 3° in 12 joints (13%), 4° in 4 joints (4%). 57% met the radiographic criteria. MRI: Only 6 joints (6%) showed high signals on STIR. CT showed type 1: 3 joints (5%), type 2: 14 joints (23%), Type 3: 37 joints (58%), Type4: 8 joints (13%). [Conclusion] SIJ changes in cases that could not be diagnosed as axSpA were examined using 3 imaging tools, and more than half of the cases, including those who were older, showed radiographic abnormalities. Further detailed investigation is needed so that axSpA can be considered as a single disease.

W43-4

The incidence and HLA phenotype of infection-related arthritis in Japanese patients with bladder cancer following intravesical BCG therapy

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Conflict of interest: None

[Background] Intravesical instillation of Bacillus Calmette-Guerin (iBCG) is used as an effective immunotherapy of bladder cancer. However it may have, as adverse event, an infection-related arthritis (IRA) and the frequencies are known as about 0.5 to 5.7%. [Objectives] To prospectively evaluate the incidence and HLA typing of IRA in Japanese patients with bladder cancer following iBCG therapy. [Methods] The clinical findings of Japanese patients who received iBCG ($n = 125$) for bladder cancer from 2018 to 2023 were prospectively assessed, with specific attention to patients with IRA and/or uveitis/conjunctivitis. We also looked at HLA typing of patients with IRA and/or uveitis/conjunctivitis. [Results] Patient age was 75 ± 9 and male/female ratio was 105/20. Of the 125 cases, IRA, uveitis and conjunctivitis were revealed in 4 (3.2%), 1 (0.8%) and 6 (4.8%), respectively. Notably, HLA-B27 was not detected in IRA patient in this study. [Conclusion] In this study, the incidence of ReA in Japan was 3.2% as same as that in previous study from Western countries and Japan. The frequency of HLA-B27 in Japanese is lower than Western countries, and therefore we need to assess the other genetic and environmental factors as large-scale and long-term prospective study.

W43-5

Fecal calprotectin in patients with spondyloarthritis

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Conflict of interest: None

[Objectives] To clarify the relationship between bowel inflammation and fecal calprotectin (fCAL) in patients with spondyloarthritis (SpA) and those without SpA [Methods] Thirty-four patients with SpA and 33 patients with other RMDs at Kagawa University Hospital from November 2020 to March 2024 were included. fCAL was measured by fluorescence enzyme immunoassay. Colonoscopy (CS) was performed in 13 patients with SpA and 11 patients with other RMDs to determine whether there was any inflammation. [Results] In patients with inflammation observed by CS, no difference in fCAL was observed between SpA group and other RMDs group. In the group excluding patients with inflammation observed by CS, fCAL in SpA group was significantly higher than that in other RMDs group. In other RMDs group, fCAL in patients with inflammation observed by CS was significantly higher than that in the group excluding patients with inflammation. In SpA group, however, no difference was observed among these patient groups. [Conclusion] fCAL in SpA patients was high even when there was no bowel inflammation and no difference was observed between the presence or absence of inflammation. Studies with more patients are needed to clarify the relationship between fCAL

and bowel inflammation in SpA patients.

W43-6

Four Cases of Reactive Arthritis Associated with Chlamydia trachomatis Infection

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Conflict of interest: None

[Objective] Reactive arthritis (ReA) due to *Chlamydia trachomatis* (Ct) is a form of non-septic arthritis primarily linked to urogenital chlamydia. We report four cases of Ct-associated ReA with their initial clinical findings and treatment progress. [Methods] We reviewed four cases (three men, one woman) diagnosed with Ct-associated ReA in our department between May 2018 and July 2024. [Results] Patients ranged from 22 to 31 years (mean, 26). All had unilateral knee pain, and one also had sternoclavicular pain. None showed urethritis symptoms. Initial tests showed high WBC in one patient and positive CRP in three. All were negative for RF/ACPA, positive for Ct-IgG, and two for Ct-IgA. Urinary Ct-DNA was positive in all, and one was positive for Ct-rRNA in vaginal secretions. Synovial fluid was cloudy across cases, with negative culture and crystal results. Treatment included antibiotics (AZM or LVFX) and NSAIDs for all. One patient discontinued follow-up, two had symptom resolution within 2.5 and 6 months, and one began csDMARDs after one month. [Conclusion] With rising Ct infections, especially in those in their 20s, Ct-associated ReA should be considered in young patients with non-septic arthritis, with Ct antibody and urinary DNA tests recommended for evaluation.

W44-1

The clinical features of systemic sclerosis patients with late-onset interstitial lung diseases: a retrospective observational study

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Conflict of interest: None

[Objective] The purpose of this study is to evaluate the clinical features of systemic sclerosis (SSc) patients with late-onset interstitial lung diseases (ILD). [Methods] Patients diagnosed with SSc without ILD at our department from April 1, 2012 to July 31, 2024 and followed for at least 12 months were retrospectively reviewed for clinical characteristics. Late-onset ILD was defined as the development of ILD during the follow-up period in SSc patients who did not have ILD at the initial diagnosis. [Results] One hundred sixty-two patients were diagnosed as SSc, and 71 (44%) were SSc without ILD. Of these, 38 patients were enrolled. The median observation period was 50 months, median age was 57 years, 32 (84%) were female, 31 (82%) were limited cutaneous SSc, and 29 (76%) were positive for anticentromere antibody (ACAs). Five patients (13%) were developed late-onset ILD, and four developed ILD within five years of the initial diagnosis. Four were limited cutaneous SSc; three were positive for ACAs. The patients with late-onset ILD had no or mild respiratory symptoms and none were progressive or fatal. [Conclusions] Thirteen percent of SSc patients were identified as late-onset ILD. Even if ILD was not present at initial diagnosis of SSc, periodic evaluation of ILD is necessary.

W44-2

Evaluation of Nintedanib Effectiveness in Connective Tissue Disease-Associated Interstitial Lung Disease

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Conflict of interest: None

[Objectives] To assess the effectiveness of nintedanib (NTB) in connective tissue disease-associated interstitial lung disease (CTD-ILD) compared to non-NTB users. [Methods] CTD-ILD patients treated with NTB from May 2020 to September 2023 were retrospectively analyzed. CTD-ILD patients who were not treated with NTB were also evaluated as a control group. Outcomes included KL-6, %FVC, and %DLCO over 52 weeks, focusing on those treated for ≧6 months. [Results] The NTB group included 19 patients (12 females) and the control group included 137 patients (97 females). Systemic sclerosis was the most common in the NTB group (9 cases). Rheumatoid arthritis (46 cases) and dermatomyositis (44 cases) were common in the control group. Among the 15 patients who continued NTB, improvements were significantly shown in KL-6 (877.0 [567.0-1301.5] U/ml to 688.5 [512.5-999.5] U/ml, p=0.03) and %FVC (73.5 [71.7-85.6]% to 80.25 [73.4-91.7]%, p<0.01). %DLCO changes were not significant (54.1 [44.3-72.6]% to 59.9 [56.0-65.3]%, p=1.00). In the control group, %FVC improved (86.9 [76.3-102.8]% to 91.9 [80.5-105.9]%, p=0.02), but KL-6 reduction was not significant (551.5 [370.3-874.3] U/ml to 527.0 [340.5-774.5] U/ml, p=0.299). [Conclusion] NTB demonstrated potential therapeutic benefits in CTD-ILD.

W44-3

Lung Cancer Incidence rate and Risk Factors in Patients with Interstitial Lung Disease Associated with Systemic Sclerosis (SSc-ILD)

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Conflict of interest: None

[Objective] To investigate incidence rate of lung cancer and its risk factors in patients with SSc-ILD. [Methods] Patients with SSc-ILD with no history of lung cancer at the time of SSc diagnosis were selected from a single-center prospective registry. Baseline characteristics associated with future diagnosis of lung cancer were evaluated using univariate Cox regression analysis. [Results] Of 169 patients with SSc-ILD, 8 patients were newly diagnosed with lung cancer during median of 83 months of follow-up, resulting in annual crude rate of lung cancer of 2.3%. Patients who received diagnosis of lung cancer during follow-up had a higher prevalence of anti-topoisomerase I antibody (75% vs. 52.8%) and history of smoking (87.5% vs. 37.9%) compared to those who did not. On the other hand, baseline ILD severity and follow-up ILD progression showed no differences between groups. Longer duration between SSc onset and lung cancer diagnosis was the only baseline feature associated with lung cancer incidence (P = 0.02). Of 8 patients with lung cancer, 5 were classified as stage IV at diagnosis, and 4 of them died due to lung cancer. [Conclusion] A regular follow-up of lung cancer is necessary in patients with SSc-ILD, particularly those with anti-topoisomerase I antibody or smoking history.

W44-4

Initial Combination Therapy of Mycophenolate Mofetil (MMF) and Tocilizumab (TCZ) in Patients with Diffuse Cutaneous Systemic Sclerosis (dcSSc) and Interstitial Lung Disease (ILD)

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Conflict of interest: None

[Objectives] In the 2023 update of EULAR recommendations for treatment of systemic sclerosis, individual treatment modalities, such as MMF and TCZ, are recommended for skin fibrosis and ILD. This study was aimed to explore potential roles of their initial combination therapy in patients with dcSSc and ILD. [Methods] We selected 62 patients with dcSSc-ILD from a single-center registry, based on a disease duration shorter than 6 years at referral and those who had received treatment with MMF and/or TCZ for over 6 months. The patients were categorized into 37 with MMF alone, 18 with TCZ alone, and 7 with initial combination of MMF and TCZ (MMF/TCZ). Serial clinical data were retrospectively collected by a chart review. [Results] At baseline, TCZ and MMF/TCZ groups

had higher mRSS and EULAR activity index scores, and lower DL_{CO} compared to MMF group. Over 48 weeks, TCZ and MMF/TCZ group experienced greater reduction of modified Rodnan skin score compared with MMF group (P<0.001), and there was a trend toward less forced vital capacity decline in TCZ and MMF/TCZ groups than in MMF group (P=0.2). [Conclusion] MMF/TCZ initial combination therapy might be a treatment option for dcSSc-ILD patients with high disease activity.

W44-5

Validation of a predictive model for progressive pulmonary fibrosis (PPF) in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

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Conflict of interest: None

[Objectives] Using our single-center registry (derivation cohort), we have developed a predictive model for PPF in SSc-ILD patients; total number of 3 factors (anti-topoisomerase I antibody, KL-6, and UIP pattern) in patients with limited disease. This study was aimed to validate our model using a specialized respiratory center's prospective registry. [Methods] SSc-ILD patients with limited disease selected from Tosei General Hospital registry (validation cohort) were applied to our prediction model. [Results] Of 50 patients with SSc-ILD, 29 (58%) developed PPF during median of 97 months of follow-up. The patients in the validation cohort were older, and showed higher proportions of males and UIP pattern, lower proportions of anti-topoisomerase I antibody and diffuse cutaneous SSc, shorter disease duration, higher KL-6, and lower DL_{CO}, compared to those in the derivation cohort. The cumulative probability of PPF in patients with the number of 0, 1, 2, and 3 factors were 38%, 58%, 64%, and 100%, respectively (P = 0.03). The optimal cut-off was set at 1.5 with area under the curve of 0.61. [Conclusion] Utility of our prediction model was confirmed generally in patients with baseline characteristics different from the derivation cohort.

W44-6

The preferential PDE4B inhibitor nerandomilast (BI 1015550) exhibits antifibrotic and anti-inflammatory effects in human in vitro SSc models (encore presentation)

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Conflict of interest: Yes

Objectives: To investigate the effect of nerandomilast on cell proliferation, fibrosis marker expression, proinflammatory mediator release and IFN response gene expression. **Methods:** Effect on proliferation of SSc dermal fibroblasts was measured using Ki-67 staining. Antifibrotic effects were examined by expression of fibrosis markers IGFBP3, sICAM-1 and PAI-1 and with an in vitro fibrosis model (Scar-in-a-Jar assay). Anti-inflammatory effects were examined by measuring TNF-α secretion from PBMCs and TNF-α and IL-6 secretion and expression of type 1/2 IFN markers from macrophages. The effect of nerandomilast and/or mycophenolate mofetil (MMF) was evaluated. **Results:** Nerandomilast reduced SSc dermal fibroblast proliferation ($p<0.05$) and IGFBP3, sICAM-1 and PAI-1 expression, and decreased the level of α-SMA expression in a Scar-in-a-Jar assay ($p \leqq 0.0001$). The effect of nerandomilast alone was greater compared with MMF alone. Nerandomilast reduced TNF-α secretion from SSc patient PBMCs ($p \leqq 0.0005$), suppressed TNF-α and IL-6 secretion from macrophages, and attenuated type 1/2 IFN responses. **Conclusions:** Nerandomilast had significant antifibrotic and anti-inflammatory effects on cell types relevant to SSc in vitro, indicating that it could attenuate the underlying disease pathology in SSc.

W45-1

Safety of mepolizumab spacing and dose reduction in patients with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: Yes

[Objectives] This study aimed to assess the safety of spacing or reducing mepolizumab (MEP) for the treatment of eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] A total of 48 patients with EGPA who were initiated on MEP 300 mg at three institutions between May 2018 and July 2024 were included in the study. Patient records were collected at the initiation of MEP and at the time of and following spacing or reducing MEP. [Results] The mean age at the initiation of MEP was 56.2 ± 13.5 years, 27 (56.3%) of the patients were female, and the median disease duration was 13 months. Fifteen patients modified the regimen, with ten spacing and five reducing doses. There were no significant differences in patient background at the initiation of MEP between the standard and modified groups. The BVAS at the time of spacing or reducing of MEP was 0 [0-3], the eosinophil count was 28 [12-59], and the PSL dose was 0.5 [0-3] mg. The fluctuations in eosinophil counts and PSL doses, relapse, MEP discontinuation, adverse events, and infections were similar before and after spacing or reducing of MEP. [Conclusion] MEP may be used as a safe and effective method for spacing and reducing doses in patients with EGPA.

W45-2

Efficacy of mepolizumab for eosinophilic granulomatosis with polyangiitis and possible discontinuation of glucocorticoids: a retrospective study of 35 cases

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Conflict of interest: Yes

[Objectives] MPZ treatment for EGPA has been reported with a focus on GC reduction and remission maintenance. We previously reported a mean PSL dose of 1 mg and a GC discontinuation rate of 48% in a study of 27 patients. Here we report the subsequent treatment course and the results of detailed analysis. [Methods] We searched for patients who received the combination of MPZ and GC ≧48 weeks. Patients were divided based on the achievement of GC discontinuation, ANCA status, the use of concomitant IS, and their characteristics were statistically analyzed. [Results] 35 patients were included. After a mean of 197±83 weeks MPZ, 26 (74%) patients discontinued GC; 31% were ANCA-positive and 60% had concomitant IS; ANCA-positive patients had significantly more renal lesions, and the initial PSL dose in patients with concomitant IS was significantly higher than in patients without IS. There was a strong correlation between time from disease onset to MPZ induction and total GC duration ($r=0.691$, $p<0.001$). 3 patients had minor relapse, but no discontinuations of MPZ. [Conclusion] MPZ allows a high rate of GC discontinuation regardless of the presence of ANCA or concomitant IS, and can shorten the duration of PSL administration by initiating early in the disease course.

W45-3

Possible Discontinuation of Glucocorticoid by Mepolizumab in Eosinophilic Granulomatosis with Polyangiitis with Sinonasal Lesions

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Conflict of interest: None

[Objectives] To investigate whether glucocorticoid discontinuation is achieved by mepolizumab (MPZ) in patients with eosinophilic granulomatosis with polyangiitis (EGPA) with sinonasal lesions that can otherwise remain despite the standard of care. [Methods] The medical charts of patients with EGPA treated in our hospital during the past six years were reviewed to determine whether MPZ-treated patients can be characterized by the clinical symptoms and parameters related to vasculitis. [Results] Forty-one patients (32 females, 9 males, average age; 54, disease duration; 6.5 years) were eligible for this retrospective study. MPZ was introduced in 19 patients (46.3%), and 70.6% of them had sinonasal lesions at the onset, whereas 18.8% of the patients without MPZ use did. Prednisolone was reduced to less than 5 mg/day in 11 (61.1%) of 18 patients using MPZ for more than 12 months. Eight (66.7%) of 12 patients with sinonasal lesions used 5 mg/day or less prednisolone, and five (41.7%) discontinued prednisolone. [Conclusion] Half of the patients with EGPA with sinonasal lesions possibly discontinue prednisolone by concomitant MPZ.

W45-4

Analysis of clinical outcomes in eosinophilic granulomatosis with polyangiitis treated with mepolizumab for remission induction on early or late administration

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Conflict of interest: None

[Objectives] We investigated whether mepolizumab (MPZ) should be started early after the onset of Eosinophilic granulomatosis with polyangiitis (EGPA) and its long-term use. [Method] Forty EGPA patients (12 male, 28 female, 17 MPO-ANCA-positive) who started treatment with MPZ at our hospital since 2018 (up to Sept 2024) were analyzed for clinical course. They were divided into those who started MPZ within 6 months from the onset of EGPA (Early group: E-group) and the others (Late group: L-group). [Results] Of the 40 patients administrated MPZ, 16 patients were categorized as the E-group and the other 24 patients in the L-group. Mean ages at initiation of E-group and L-group were 59.3 and 64.3 years old, and days from onset to initiation of MPZ were 76.3±60.2 and 4467± 8356 days, respectively. The PSL dose (mg/day) at the administration of MPZ was 30.8/5.6, but at 24 and 36 months (M), the PSL dose was significantly lower in the E-group than in the L-group (24M: 1.6/3.4, 36M: 1.4/4.2). The remission rate (%) was significantly higher in the E-group after 24 months (24M: 90/43, 36M: 86/47, 48M: 100/47). Bone-related adverse events were more common in the L-group. [Conclusion] It was suggested that the use of MPZ early from onset may result in GC sparing and remission.

W45-5

Clinical characteristics of patients with early induction of mepolizumab after induction of remission for EGPA: from the KVAS cohort

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Conflict of interest: None

[Objectives] Mepolizumab (MPZ) treatment for eosinophilic polyangiitis granulomatosa (EGPA) has been shown to be effective in achieving remission and reducing glucocorticoids (GC) in relapsed or refractory cases. We investigated the benefit of induction of MPZ at a relatively early stage after initial remission induction therapy. [Methods] Cases diagnosed with EGPA and enrolled in the multicentre study on ANCA-associated vasculitis (KVAS) during the period 2011-2023 were included in the study. Patients followed up for at least one year after remission induction therapy were included in the analysis. [Results] The analysis included 53 patients; 10 patients were in the MPZ early induction group (MPZ within six months of the start of remission induction therapy) and 43 in the conventional treatment group. There were no significant differences in remission and relapse rates, GC dose or dose reduction rates in either period, but the rate of concomitant immunosuppressive drugs was lower in the early MPZ group. There was also a significantly lower trend for increased Vascular Damage Index (VDI) in the early MPZ group compared with the conventional treatment group. [Conclusion] Early induction of MPZ may be effective in maintaining remission, and inhibiting organ damage progression.

W45-6

Efficacy of Eosinophil-Targeting Therapies on Specific Disease Manifestations of Eosinophilic Granulomatosis with Polyangiitis in the Phase 3 MANDARA Trial

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Conflict of interest: None

[Objectives] EGPA is characterized by small- to medium-vessel vasculitis, asthma and eosinophilia. In the MANDARA trial (NCT04157348), benralizumab was non-inferior to mepolizumab in patients with EGPA. Here, we analysed changes in individual items of disease activity and damage. [Methods] Adults with relapsing or refractory EGPA receiving standard of care were randomized to benralizumab 30 mg (n=70) or mepolizumab 300 mg (n=70) SC Q4W for 52 weeks. Findings for BVAS and VDI assessments are reported for the combined trial population. [Results] Among the 140 patients, airway-related manifestations commonly reported at baseline included wheeze (24.3%), paranasal sinus involvement (17.9%), and bloody nasal discharge/crusts/ulcers/granulomata (14.3%), all of which affected <5% of patients by Week 52, despite substantial OGC reductions. The frequency of non-airway-related manifestations also decreased to <2% of patients. Cutaneous manifestations disappeared. No cardiovascular manifestations were reported. Three central nervous system manifestations were reported. There were 22 new items of damage

recorded. [Conclusion] Eosinophil-targeting biologic agents appear to be rapidly effective at reducing and controlling both airway- and non-airway-related manifestations of EGPA.

W46-1

Longitudinal changes in remission-induction treatment and outcomes in eosinophilic granulomatosis with polyangiitis: A multicenter cohort study using J-CANVAS

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Conflict of interest: None

[Objectives] The study aimed to describe the changes in remission-induction regimens and outcomes in eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] The J-CANVAS registry enrolled patients with new-onset or severe relapsing ANCA-associated vasculitis diagnosed after January 2017 at 29 sites, followed until March 2024. New-onset EGPA patients were divided into two phases: Phase I (until June 2020) and Phase II (from July 2020). They were analyzed for clinical characteristics, mepolizumab (MPZ) usage, remission rates at 24 and 48 weeks, and prednisone (PSL) dosages. Continuous variables were summarized as medians (interquartile range), and categorical variables as percentages. [Results] There were 113 patients in Phase I and 68 in Phase II. The median age was 61 (48-69) vs. 64 (49-69) years; MPO-ANCA positivity was 37% vs. 44%; Birmingham Vasculitis Activity Score was 15 (12-21) vs. 16 (13-22); and the initial PSL dose was 50 (40-50) vs. 50 (30-50) mg/day. MPZ use within 1-year was 17% in Phase I and 56% in Phase II, with 38% vs. 71% use during the entire period. Remission rates at 48 weeks were 90% vs. 94%. PSL doses at 48 weeks were 7.5 (5-7.5) vs. 5 (3-5) mg/day. [Conclusion] MPZ usage increased over time, suggesting reduced PSL doses and improved patient outcomes.

W46-2

Longitudinal changes in remission-induction treatment and outcomes in microscopic polyangiitis/granulomatosis with polyangiitis: A multicenter cohort study using J-CANVAS

Satoshi Omura[1,2], Takashi Kida[1,2], Takahiro Seno[1], Masataka Kohno[1], Daiki Nakagomi[2], Yoshiyuki Abe[2], Makoto Wada[2], Naoho Takizawa[2], Atsushi Nomura[2], Yuji Kukida[2], Yasuhiko Yamano[2], Hirosuke Takagi[2], Koji Endo[2], Shintaro Hirata[2], Naoto Azuma[2], Tohru Takeuchi[2], Shoichi Fukui[2], Toshiko Ito-Ihara[2], Nobuyuki Yajima[2], Takashi Kawaguchi[2], Yutaka Kawahito[1,2]

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Conflict of interest: None

[Objectives] This study aimed to describe the changes in remission-induction regimens and outcomes in microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). [Methods] The J-CANVAS registry enrolled patients with new-onset or severe relapsing ANCA-associated vasculitis diagnosed after January 2017 at 29 sites, followed until March 2024. New-onset MPA or GPA patients were divided into two phases: Phase I (until June 2020) and Phase II (from July 2020). They were analyzed for clinical characteristics, RTX and CY usage within 12 weeks, remission rates at 48 weeks, prednisone (PSL) dosages, survival rates, and the incidence of infection requiring hospitalization. [Results] There were 477 patients (MPA 369, GPA 108) in Phase I and 250 (MPA 185, GPA 65) in Phase II. Age was 75 (68-81) vs. 75 (69-81) years; serum creatinine 0.9 (0.7-1.7) vs. 0.9 (0.6-1.5) mg/dL; and the initial PSL dose 42 (35-42) vs. 40 (30-40) mg/day. RTX use was 22% vs. 42%; CY use 40% vs. 30%; and non-use 42% vs. 31%. Remission rates at 48 weeks were 79% vs. 83%, with PSL doses 7.5 vs. 5 mg/day. 1-year survival rates were 93% vs. 96%, and infection rates were 18.2 vs. 10.6 per 100 person-years. [Conclusion] RTX usage increased over time, suggesting reduced PSL doses and improved patient outcomes.

W46-3

Differences in efficacy and safety of different treatments for microscopic polyangiitis and granulomatosis with polyangiitis

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Conflict of interest: None

Purpose: In recent years, the use of glucocorticoids in microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) has decreased with the use of RTX and avacopan from early onset. The purpose of this study was to clarify the differences in efficacy and safety in clinical practice due to recent changes in treatment. Methods: Propensity score matching was performed in 50 patients treated from 2017-23. Clinical findings at admission, treatment, and one-year post-treatment outcomes were compared between 15 patients treated from 2017-20 (group A) and 15 from 2021-23 (group B). Results: There was no difference in initial PSL doses or IVCY use, but RTX and avacopan were used more frequently in group B. In group B, PSL doses at 2 weeks, 1, 2, 3 and 6 months after the treatment was significantly lower, had higher CRP level at 1 month and more positive urinary blood at 2 months. There was no difference in relapse within 1 year or number of CKD patients, and the incidence of infections other than CMV was lower in group B. Conclusion: In Group B, RTX and avacopan were administered to more patients to quickly reduce the dose of PSL. It took longer to improve CRP and hematuria, but there was no difference in relapse and CKD within 1 year, and fewer infections occurred in group B.

W46-4

Comparison of Cyclophosphamide pulse therapy and Rituximab therapy for ANCA-related vasculitis in our department

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Conflict of interest: None

[Objectives] RTX has become available for the treatment of AAV and is increasingly used as an initial remission induction therapy (RIT). We compared the therapy of IVCY or RTX as RIT for AAV in our department. [Methods] In this study, we analyzed 25 patients diagnosed with AAV and treated with RIT between January 2020 and June 2024. These cases were reviewed for differences in patient background and organ involvement. [Results] The mean average at diagnosis was 73.2 years old, all 25 cases were MPA with MPO-ANCA positive in 24 cases. Lung involvement occurred in 18 cases, RPGN in 8. All patients were treated with GC therapy, and initial prednisolone was 1 mg/kg in 20 patients and 0.5 mg/kg in 5. IVCY was performed in 8 patients and RTX in 10. In the IVCY group, 5 out of 8 patients had lung involvement and 7 had RPGN. In the RTX group, 9 out of 10 patients had lung involvement and 1 had RPGN. GC pulse therapy was used in 6 patients in the IVCY group and in only 1 patient in the RTX group. [Conclusion] In cases with RPGN, IVCY and GC pulse therapy were more frequently selected. Although there are limitations due to the retrospective analysis, treatment progressed relatively well in both groups. Further case accumulation and detailed analysis are needed.

W46-5

Clinical Features of Granulomatosis with Polyangiitis with neurological involvement: multicenter REVEAL cohort study

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Conflict of interest: None

[Objectives] To elucidate the clinical features of patients with Granulomatosis with Polyangiitis (GPA) with neurological involvement (NI). [Methods] We focused on patients newly diagnosed with GPA based on the EMA algorithm or the ACR/EULAR 2022 classification criteria in REVEAL cohort study. Meningitis, cerebrovascular accident, spinal cord lesion, cranial nerve palsy, sensory peripheral neuropathy, mononeuritis multiplex, and hypertrophic pachymeningitis were defined as NI. We compared the clinical features of patients with GPA with and without NI. [Results] Out of 84 patients with GPA, 65 met the inclusion criteria. The median age was 69.0 years, 46.2% were male, 50.8% were PR3-ANCA positive, and NI was observed in 24.6%. In the group with NI, the history of ischemic stroke, total BVAS, administration of IVCY and AZP, and the PSL dose at 3, 6, 12, and 24 months after remission induction therapy were significantly higher ($p = 0.034$, 0.0029, 0.0078, 0.026, 0.0080, 0.012, 0.017, and 0.036, respectively), compared to the group without NI. The VDI at 6 and 24 months were significantly higher ($p = 0.027$ and 0.011, respectively). [Conclusion] The prognosis of neurological involvement in GPA patients might be poor despite intensive treatment.

W46-6

The investigation of risk factors for thrombocytopenia induced by Rituximab in ANCA-Associated Vasculitis

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Conflict of interest: None

[Objective] To retrospectively examine the risk factors for thrombocytopenia induced by rituximab (RTX) administration in patients with ANCA-associated vasculitis (AAV). [Methods] Patients treated with RTX for AAV at our institution between January 2017 and September 2024 were evaluated. Thrombocytopenia was defined as a platelet count of < 150,000/μL within 28 days after RTX administration. 1) Background, 2) BVAS and 3) laboratory findings were examined in the patients with thrombocytopenia retrospectively. [Results] 1) The study included 29 cases (mean age 70.8 years; 20 with microscopic polyangiitis and 9 with granulomatosis with polyangiitis). Eleven cases had thrombocytopenia and 18 did not. There were no differences in age, sex, type of vasculitis, or prednisolone doses between two groups. 2) BVAS scores were significantly higher in patients with thrombocytopenia at remission induction (14.6 vs. 10.1, $p = 0.049$) and after 1 month of RTX (3.8 vs. 2, $p = 0.014$). 3) eGFR at RTX initiation was significantly lower in patients with thrombocytopenia (33.1 vs. 70.5, $p < 0.001$). [Conclusion] Higher disease activity and renal impairment may be potential risk factors for thrombocytopenia after RTX administration in AAV patients.

W47-1

Association of NCF2 missense variant with systemic lupus erythematosus in a Japanese population

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Conflict of interest: Yes

[Objectives] *NCF1* and *NCF2* genes encode components of NADPH oxidase (NOX2) complex. We previously reported association of *NCF1* missense variant, p. Arg90His, with systemic lupus erythematosus (SLE) in a Japanese population. To comprehensively analyze the contribution of NOX2 complex variants to SLE, this study examined association of *NCF2* with SLE in a Japanese population. [Methods] Association studies were performed for three *NCF2* missense variants, p. Lys181Arg, p. Thr279Met, p. Arg395Trp, in 456 SLE patients. Allele frequency data of 60KJPN registered in the Japanese Multi Omics Reference Panel (jMorp) were used as controls. [Results] *NCF2* p. Arg395Trp was significantly associated with SLE (P: 0.0035, odds ratio [OR]: 1.63, 95% confidence interval [CI]: 1.17-2.27). When association of *NCF2* with clinical symptoms of SLE was analyzed, significant association with early onset (age of onset<20 years) of SLE was observed (case-control analysis, P: 6.8×10^{-4}, OR: 2.77, 95%CI: 1.50-5.11, case-case analysis, P: 0.036, OR: 2.22, 95%CI: 1.04-4.77). [Conclusion] Association of *NCF2* missense variant with SLE was detected in the Japanese population, which was more striking in early onset SLE. These findings are consistent with *NCF1* variant, and support the importance of NOX2 complex variants in susceptibility to SLE.

W47-2

Difference in gut microbiota diversity by fecal sampling locations in NZB/NZW F1 mice

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Conflict of interest: None

[Objectives] Advances in next-generation sequencing have associated with gut microbiota dysbiosis to various diseases. *Lactobacillus* spp. culture supernatants have shown inhibition of bacteria associated with SLE. Although microbiota changes are known in MRL/lpr mice, NZB/NZW (B/W) F1 mice remain uncharacterized. We used 16S amplicon sequencing to analyze gut microbiota in B/W F1 mice. [Methods] Five 8-week-old female B/W F1 mice were dissected, and fecal samples collected from 1 cm upper (U1), 1 cm (L1), and 4 cm (L4) lower the cecum. DNA was extracted using the ISOSPIN Fecal DNA Kit, with library prep using the 16S Metagenome Kit and Ion Plus Fragment Library Kit, and sequencing on the Ion Chef & S5 system. [Results] No differences in microbiota composition were observed at identical sampling sites. L1 and L4 showed similar microbiota and higher diversity than U1 in all mice. In β-diversity analysis, L1 and L4 clustered closely, distinct from the U1. [Conclusion] Our results indicate distinct microbiota diversity between the ileum and colon of B/W F1 mice, with reduced diversity in the ileum consistent with antimicrobial peptide activity. These findings underscore the impact of sampling location in microbiota studies, as B/W F1 mice show unique microbiota in the ileum and colon.

W47-3

Identification of ribosomal P protein-expressing immune cells on the cell surface andanalysis on immunoreactive mechanism based on IgG subclasses of anti-ribosomal P antibody

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Conflict of interest: None

[Objectives] Anti-ribosomal P protein antibody (anti-P Ab) is an autoantibody specific to SLE. Previous studies reported that anti-P Ab consists of IgG2 (low Fcλ receptor affinity) and IgG3 (high Fcλ receptor affinity), with elevated IL-6 levels in patients. This study aims to identify peripheral

blood mononuclear cells (PBMC) expressing ribosomal P protein antigens on their surface and clarify cytokine production by anti-P Ab. [Methods] 1) The expression of P protein antigen on the cell surface of PBMC from healthy donors was analyzed with mouse anti-P monoclonal Ab 4H11 using flow cytometry (FCM). 2) Recombinant forms of 4H11-IgG2 and 4H11-IgG3 were reacted with human PBMC, and cytokine production was measured by real-time RT-PCR, ELISA, and intracellular FCM. [Results] 1) Peripheral blood B cells and $CD8^+$T cells expressed P antigens on their cell surfaces. 2) Co-culture of PBMC with 4H11-IgG3 enhanced IL-6 production in monocytes, while 4H11-IgG2 and 4H11 F $(ab')_2$ did not. IL-6 production increased further when monocytes co-cultured with B or $CD8^+$T cells and 4H11-IgG3. [Conclusion] While anti-P Ab would bind cell surface P antigens on B cells and $CD8^+$T cells through its Fab portion, interaction between its Fc portion and Fcλ receptors on monocytes would require high affinity IgG3 subclass.

W47-4

Analysis of the mechanism of early onset of lupus nephritis via circulating Kim1

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Conflict of interest: None

[Objective] Circulating Kim1 has been linked to CKD progression and CVD onset. We hypothesized that circulating Kim1 might be involved in lupus nephritis pathogenesis and conducted a study to verify this. [Methods] We created an AAV encoding the extracellular domain of mouse Kim1 (Kim1-AAV) and administered 1x10^11 genome copies via tail vein injection to 8-week-old B6-MRL/lpr mice (male and female). Control mice received the same amount of control AAV. Mice were sacrificed 16 weeks post-administration, and samples were collected for analysis. [Results] Kim1-AAV infected the liver and expressed Kim1, with no expression in the kidneys or spleen. The Kim1-AAV group showed increased blood Kim1 concentrations, some leaking into urine. While body weight was unchanged, the Kim1-AAV group exhibited enlarged spleens with expanded white pulp and increased fragmented TUNEL-positive cells. Male mice showed increased proteinuria, while some female mice had elevated serum urea nitrogen and creatinine levels. [Conclusion] Overexpression of circulating Kim1 in B6-MRL/lpr lupus model mice, without inducing kidney injury, resulted in spleen enlargement and kidney dysfunction. We are investigating the underlying mechanisms and will report these findings along with the results.

W47-5

The impact of serum CGRP and type I interferon on headache in SLE patients

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Conflict of interest: None

[Objective] To investigate the implications of calcitonin-gene related peptide (CGRP) and type I interferon (IFN) as the biomarkers of headache (HA) in systemic lupus erythematosus (SLE). [Methods] We involved 144 patients with SLE from the LUNA cohort who provided information on HA. Serum levels of CGRP, IFN-α and IFN-β, which were measured using ELISA, were compared between patients with HA (HA group), those without HA (nonHA group), and 20 healthy controls (HC). [Results] Of the 144 patients, 60 were classified in HA group (mean 44 years, 55 women), who were significantly younger than those in nonHA group (mean 50 years, 77 women) ($p<0.005$). Median SLEDAI-2K scores were 4.0 in both groups, not significantly different. Serum levels of CGRP and IFN-α were not significantly different between HA, nonHA groups, and HC (CGRP: 27 pg/mL vs. 26 pg/mL vs. 33 pg/mL; IFN-α: 6.9 pg/mL vs. 5.5 pg/mL vs. 5.0 pg/mL). Serum levels of IFN-βwere significantly higher in HA group than in nonHA group (12.5 pg/mL vs. 9.5 pg/mL, $p <0.005$), while being significantly lower in both HA and nonHA group than in HC (18.2 pg/ml, $p <0.005$). [Conclusions] Our study suggests that CGRP, IFN-α, and IFN-β may not be implicated in headache in SLE patients.

W47-6

Investigation of the usefulness of leucine-rich alpha 2 glycoprotein (LRG) in evaluation of disease activity in systemic lupus erythematosus (SLE)

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Conflict of interest: None

Objectives: In systemic lupus erythematosus (SLE) where CRP often remains low, disease activity is comprehensively evaluated using general, organ-specific, and serological indicators. LRG, an inflammatory biomarker identified in our lab, is used in clinical practice for inflammatory bowel disease and proved to detect IL-6-independent inflammation, unlike CRP. This study examined LRG's usefulness as an activity marker of SLE. **Methods:** Fifty-four SLE patients were enrolled to measure anti-ds-DNA antibodies, C3, CRP, and LRG before and 6 months after intervention. SLE activity was indicated by SLEDAI. **Results:** After intervention, upon the decrease in SLEDAI, anti-ds-DNA antibody and C3 levels improved. Both CRP and LRG levels decreased, but LRG ($rs=0.463$, $p<0.01$) showed a better correlation than CRP ($rs=0.337$, $p>0.01$) with SLEDAI. ROC curve analysis discriminating low disease activity (SLEDAI≦4) showed that the AUC of LRG (0.7178) was better than those of CRP (0.7013) and anti-ds-DNA antibody (AUC 0.6755). In patients with CRP<0.2, LRG decreased significantly after treatment, maintaining good correlation with SLEDAI ($rs=0.476$, $p<0.01$). **Conclusion:** LRG reflects SLE activity even in low-CRP cases, likely due to its induction by various cytokines and production at inflammation sites.

W48-1

Relationship between the long-term progression of deterioration at the wrist joint and disease activity in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: To examine the relationship between the secular change of radiographic deterioration at the wrist joint and the disease activity in patients with rheumatoid arthritis (RA). Methods: A total of 320 wrists in 172 patients (median age 56 years, 72.1% women), who started treatment within the first year of onset of RA and were followed up for 10 years at

our hospital. The annual mean DAS28-ESR and HAQ-DI, and carpal: metacarpal ratio (c/MC) every 2 years were investigated. Based on the radiographic findings at the last follow-up, the wrists were classified into three groups: Larsen grade (LG) 0, LG I-II, and LG III-V. Results: The 10-year annual mean of DAS28-ESR and HAQ-DI, and the magnitude of change of c/MC for ten years were highest in LG III-V. The c/MC every two years had a weak positive correlation with the annual mean DAS28-ESR (r=0.339). Rapid decrease in c/MC was noted in the first two years. The cut-off value of the annual mean DAS28-ESR during the first two years indicating progression to LG III-V at the last follow-up was 3.59. Conclusion: It is important to control disease activity as early as possible after the onset of RA to prevent further deterioration at the wrist joint and the impairment of physical function.

W48-2

Factors contributing to the overdiagnosis in the examination of wrist joints in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Joint examination is essential in managing rheumatoid arthritis (RA), but findings often differ between physical examination and ultrasound (US). We investigated factors contributing to overdiagnosis in wrist examinations of RA patients. [Methods] We evaluated 235 RA patients who underwent bilateral wrist US and compared the results with physical examination. Joints with swelling and/or tenderness on examination but no US abnormalities were classified as overdiagnosed joints (OJ), while those with no findings on both examination and US were defined as non-synovitis joints (NJ). [Results] Among 470 wrist joints, 19 (4%) were classified as OJ, and 142 (30%) as NJ. Disease activity score (DAS28-CRP) was significantly higher in OJ (median 2.47 vs. 1.97, p=0.019), with no significant differences in age, gender, disease duration, body size, or treatment. Tendon involvement was more frequent in OJ (10% vs. 5%, p=0.193). In a generalized linear mixed model, DAS28-CRP was a significant factor (odds ratio 1.9, p=0.018), while tendon involvement was not. [Conclusion] Overdiagnosis in RA wrist joint examination may be associated with higher disease activity.

W48-3

Implementation and Evaluation of a Deep Learning Model to Infer Early Rheumatoid Arthritis from Digital Camera Images of Both Hands

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Conflict of interest: None

[Objectives] To provide a resource that allows individuals to self-assess the presence and treatment necessity of rheumatoid arthritis (RA), a deep learning model was developed and evaluated for inferring early RA from digital images of both hands. [Methods] Digital images of both hands were taken from 180 patients at first consultation for joint pain, swelling, and stiffness (97 undiagnosed RA, 83 non-RA), with backgrounds removed and images resized and normalized. These images were fed into deep learning models (vit_base_patch16_224_in21k and ResNet50. tv_in1k) to predict final diagnoses and evaluate loss values and accuracy. [Results] Using vit_base_patch16_224_in21k with epoch 120, batch size 16, learning rate 0.01, and update rate 0.7, the model predicted RA with CRP values above 0.30 mg/dl resulting in training loss of 0.4964, training accuracy of 0.7865, evaluation loss of 0.5283, and evaluation accuracy of 0.7708. For CRP values above 1.00 mg/dl, training loss was 0.4903, training accuracy 0.7746, evaluation loss 0.4933, and evaluation accuracy 0.7917. ResNet50. tv_in1k showed overfitting. [Conclusion] The results demonstrate that it is feasible to use the vit model to infer RA requiring treatment even with a small sample size.

W48-4

Ultrasound Image Alignment Using AI-Based Robotic Mapping Technology (SLAM)

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Conflict of interest: Yes

[Objectives] In rheumatoid arthritis (RA) management, achieving consistent cross-sectional imaging remains challenging. We investigated an AI-based approach to identify identical cross-sections by employing Simultaneous Localization and Mapping (SLAM) technology, a robotic mapping technique that has seen significant advancements in autonomous driving. [Methods] We enrolled 77 healthy participants (144 wrists) and recorded continuous longitudinal ultrasound images of the dorsal wrist in horizontal cross-sections. Using these images, we created SLAM maps via UMAP-based topological mapping. We then visually evaluated the alignment of the radioulnar joint and dorsal carpal bones within each individual and between individuals to assess the capability of cross-sectional alignment for RA ultrasound diagnostics. [Results] SLAM mapping allowed for consistent alignment of identical cross-sections within each individual in all cases. However, alignment between different individuals was unsuccessful. [Conclusion] Applying autonomous driving's mapping technology to ultrasound examinations demonstrated that creating individual-specific maps facilitates accurate cross-sectional alignment.

W48-5

Radiographic prevalence of osteoarthritis of thumb carpometacarpal joint in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The purpose of this study was to investigate the prevalence of radiographic OA of thumb CM joint in the patients with RA. [Methods] A retrospective electronic medical record survey was performed for the patients with RA whose dorsopalmar radiographs of bilateral hands were taken from 2021 at our institution. The prevalence of radiographic OA of thumb CM joint in the dorsopalmar radiographs of both hands and the stage of Eaton's classification were evaluated. The correlation between the Eaton's stage, age, and the duration of RA was calculated. [Results] 160 patients with RA were included in this study (mean age 71.8 years, 38 males, 122 females, mean disease duration 16.9 years). Radiographic OA of thumb CM joint was found in 60 patients (37.5%) on the right hand and 79 patients (49.4%) on the left hand. The Eaton classification stages (2, 3, and 4) were 22, 19, and 19 cases for the right hand and 31, 31, and 17 cases for the left hand, respectively. A weak correlation between the stage of Eaton's classification and the duration of RA (right hand r=0.41, left hand r=0.35). [Conclusion] Considering the correlation with the duration of RA, it was suggested that the effect of RA on the carpal bones might have influenced the arthritic changes of the thumb CM joint.

W48-6

Assessment of the chest and abdominal regions screening by computed tomography and magnetic resonance imaging in rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] It is known that patients with rheumatoid arthritis have an

increased concern for malignancy. In particular, the use of JAK inhibitors is recommended to include risk assessments for malignancy. CT is often used for cancer screening; however, repeated CT scans during each treatment change raise concerns about radiation exposure. The aim of this study is to compare the imaging findings of chest-to-pelvis CT and MRI with DWIBS. [Methods] The subjects were 526 patients who underwent both CT and DWIBS scans. Radiologists evaluated the images, and if a malignancy was suspected, further investigation was conducted by the relevant department to confirm the diagnosis of malignancy. [Results] Sixteen cases (3.0%) were diagnosed with malignancy. These included six cases of prostate cancer, four cases of lung cancer, two cases of breast cancer, two cases of uterine cancer, and one case each of ovarian cancer and fallopian tube cancer. All cases with suspected malignancy were detected by DWIBS, whereas 13 cases (81.3%) were detected by CT. In contrast, CT was able to identify other findings useful for RA treatment, such as lung disease, colonic diverticula, and kidney stones. [Conclusion] DWIBS can be a viable option for cancer screening, but CT remains valuable in certain cases.

W49-1

Characteristics of spinal alignment in hip osteoarthritis with acetabular dysplasia: comparison of healthy patients and pre- and postoperative patients

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Conflict of interest: None

[Objective] Secondary osteoarthritis (OA) of the hip associated with acetabular dysplasia (DDH) is said to be common in Japan, but there is little data comparing alignment changes after total hip arthroplasty (THA) with healthy controls. In this study, we aimed to compare spinal alignment changes before and after THA with healthy controls. [Method] A healthy group of 509 patients and an OA group of 323 patients who underwent THA for OA were included. Propensity score matching was performed for age, height, weight, and sex, and 110 patients from each group were measured for spinal alignment on standing lateral whole spine plain radiographs before and after surgery. [Results] There were significant differences in PI-LL and SVA, with PI-LL increasing significantly in the pre-op group compared to the healthy group, but there was no difference before and after surgery. SVA decreased significantly in the healthy group compared to the pre-op and post-op groups, but there was no difference before and after surgery. [Conclusion] In this study, OA cases showed increased PI-LL and SVA before surgery, but after surgery tended to approach the alignment of the healthy group. It is possible that spinal alignment changed due to improvement in pain and range of motion after THA.

W49-2

Radiographic study of hip morphology

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Conflict of interest: None

[Background] Our facility has developed a purely domestic implant and use it in total hip arthroplasty (THA). The purpose of this study is to three-dimensionally analyze the hip bone morphology in Japanese people with osteoarthritis of the hip (OA) from CT images in order to further improve the compatibility of stems. [Method] The OA group consisted of 82 cases and 84 joints in which THA was performed for OA at our hospital in 2023. The healthy group consisted of 21 cases and 37 hips in which CT scans were performed from the pelvis to the knee joint at our hospital's emergency room. Propensity score matching was performed for age, sex, and BMI for both groups, and 20 cases and 21 hips in the OA group and 14 cases and 21 hips in the healthy group were included. For all cases, CT scans were measured and compared using 3D template software (zed hip, Lexi). [Results] There were significant differences in the CE angle, lateral opening angle, femoral length, femoral offset, neck-shaft angle, anteversion angle, and CCI ($p<0.05$), but no significant differences were observed in the other areas. [Conclusion] In the OA group, the effects of acetabular dysplasia were observed, and the offset, neck-shaft angle, and anteversion angle were large on the femoral side.

W49-3

Investigation of crosstalk in chondrocytes and synovial cells regarding tenascin-C and syndecan-4 using co-culture system

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Conflict of interest: None

[Objectives] Interaction with human chondrocytes (AC) and synovial cells (SC) were evaluated focused on tenascin-C (TNC) and syndecan-4 (SDC4) [Methods] Human cartilage and synovium were obtained from patients who underwent total knee arthroplasty, and cells were isolated. CD68 expression levels in SC were examined using western blot and divided into two groups: a high expression group (n=6) of macrophage-like synovial cells (MLS) and a low expression group (n=5) of fibroblast-like synovial cells (FLS). Co-cultures were performed for 7 days using transwell inserts. Real time PCR was used to evaluate the expression levels of TNC, SDC4, anabolic and catabolic factor. Flow cytometry was used to examine the ratio of M1/M2 macrophages in SC after isolation, 7 days monoculture and coculture (n=10). [Results] In the high expression group, TNC and MMP3 in AC co-cultured was significantly increased compared to AC alone, SDC4 in SC co-cultured was significantly increased compared to SC alone. The ratio of M1 macrophages were higher in SC immediately after isolation and co-culture compared to monoculture. [Conclusion] MLS increased TNC in chondrocytes and might be involved in the pathology of OA. M1/M2 imbalance in synovial cells might be maintained by their crosstalk with chondrocytes.

W49-4

Association Between Synovial Pathology and Preoperative Ultrasonography Findings in OA Patients Undergoing TKA

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Conflict of interest: None

[Objectives] To evaluate the synovial thickness and power Doppler (PD) level of patients who underwent total knee arthroplasty (TKA) using US (Ultrasonography). [Methods] TKA patients who underwent preoperative US and intraoperative synovial biopsy between July 2023 and October 2024 were included. US was used to obtain the maximum synovial thickness (MST) and power Doppler (PD) grade on the affected and healthy sides of the medial, lateral, and suprapatellar knee joint. Next, the patients were divided into an RA group, which had RA-like synovitis findings in synovial pathology examination (RAPE), and an KOA group, which did not, and the maximum synovial thickness and PD grade of both groups were compared. [Results] Of the 17 patients (mean age 75 years, 4 men), 2 had RAPE (RA group), and the patients' medical history indicated that they had highly active RA. The mean MST in the two groups was 5.6 mm (RA)/3.1 mm (KOA), and the grade of the PD method (median of the representative value on the affected side) was 3 (RA)/1 (KOA). In this study, when a MST of 4.2 mm or more was considered to be positive in US findings, the sensitivity was 1.0/specificity was 0.87. [Conclusion] The results of this study suggest that US may be helpful in distinguishing between KOA and LORA.

W49-5

Association of Forgotten Joint Score with locomotive syndrome and physical frailty in patients after total knee replacement

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Conflict of interest: None

[Objective] To clarify the relationship between Forgotten Joint Score (FJS), locomotive syndrome (LS), and physical frailty in patients after total knee arthroplasty (TKA). [Methods] Patients who underwent TKA between July 2020 and June 2022 and whose preoperative LS, frailty, and FJS at 1 year postoperatively could be assessed were included; LS was calculated by the rise test, 2-step test, and locomo 25, respectively (none, 1, 2, 3); The frailty was evaluated based on the presence or absence of frailty. Statistical analysis was conducted on the relationship between sex, age, body mass index, knee joint range of motion, flexion force, and extension force and FJS. [Results] 124 patients (12 males and 112 females) were included in the study. The mean FJS at 1 year postoperatively was 56 points, correlating with preoperative frailty (Spearman correlation coefficient r=-0.35, p<0.01) and preoperative locomo 25 (Spearman correlation coefficient r=-0.27, p<0.01). Multivariate analysis revealed that preoperative locomo 25 and physical frailty were relevant factors. [Conclusion] FJS is one of the indicators of postoperative satisfaction after TKA surgery, and in this study, preoperative locomo 25 and physical frailty were found to be favorable factors related to FJS at 1 year postoperatively.

W49-6

Short-term outcome of Cooled Radiofrequency Ablation (CRFA)

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Conflict of interest: None

[Objectives] Cooled Radiofrequency Ablation (CRFA) is an innovative treatment for knee osteoarthritis. We started using it from May 2024 and investigated its short-term outcome and the relationship between outcome and duration of the test block effect. [Methods] The subjects were 26 patients with 27 knees (mean age 71.7±9.3 years) who were diagnosed with knee osteoarthritis and underwent CRFA from May to September 2024. We examined the change in VAS values for test block and CRFA, and the change in VAS%. We examined whether the effect time of the test block (VAS% less than and greater than 50% after 1 week) would change the postoperative outcome. [Results] VAS values (test block (before→immediately after→1 week after) →CRFA (before→next day→1 week after→1 month after) changed (61.3±19.9→12.5±12.3→31.9±18.9) → (41.9±20.9 →7.9±13.9→14.4±17.5→12.5±12.8), VAS% changed (100→19.9± 20.3 →50.1±25.7) → (76.4±51.8→14.4±26.6→22.2±27.7→18.7±17.6). There was no significant difference in VAS value and VAS% at 1 month of CRFA between the different of duration of effect of the test block. [Conclusion] 1-month VAS% after CRFA was about 20%. There was no relationship between the duration of effect of the test block and the 1-month CRFA outcome.

W50-1

Bone turnover markers corrected by physics are more reliable

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Conflict of interest: None

[Objectives] The correlation between YAM and bone turnover markers corrected by physics was assessed. [Methods] The hip %YAM and TRACP-5b and BAP were measured in total 533 cases that underwent total knee arthroplasty and cases that underwent treatment of osteoporosis. The mean age, heigh and weight were 75.8 years old, 151.0 cm and 54.5 kg, respectively. The correlation between %YAM and TRACP-5b and BAP, and TRACP-5b /BW (TRACP-5b divided by body weight) and BAP/BW, and TRACP-5b/BH (TRACP-5b divided by body height) and BAP/BH was calculated. [Results] The correlation coefficient was -0.16 and -0.09 -0.29 and -0.27, -0.21 and -0.13, respectively. %YAM did not have correlation with TRACP-5b or BAP. %YAM had correlation with TRACP-5b /BW, TRACP-5b /BH and BAP/BW. Bone is significantly larger than other organs. Therefore, bone turnover marker in the unit quantity is thought more reliable. The bone quantity correlates with physics. Bone turnover marker divided by the body weight was more reliable. [Conclusion] TRACP-5b and BAP devided by body weight are more reliable in the assessment of the osteoporosis.

W50-2

Is Semiquantitative (SQ) grading appropriate as a risk factor for incident vertebral fractures?

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Conflict of interest: None

Objectives We examined whether semiquantitative (SQ) grading is appropriate as a risk factor for incident vertebral fractures (VFs). Methods Outpatients who were followed up for ≦ 2 years were recruited for the study. All of them were tested with X-ray images of the lateral thoracolumbar view, bone mineral density, and blood at baseline. Patients were classified according to the SQ grade, and each group's mean values of potential risk factors were compared. Cox regression analysis (COX) was performed regarding the incident VFs for the potential risk factors. The prevalence of incident VFs in the SQ was compared in the population whose propensity scores of potential confounding factors among SQ groups were adjusted using a propensity-based inverse probability treatment weighting (IPTW) technique. Results The prevalence of incident VFs in SQ Grade 3 was significantly higher than in the other SQ grades. No significant difference was observed in the other groups or after the IPTW. COX indicated that SQ grade was the only significantly higher risk factor. However, it was stated only for Grade 3. Conclusion These results suggest that the SQ classification is available for screening to predict incident VFs. However, it is only valid for SQ Grade 3.

W50-3

Comparative study of bone mineral density evaluation using Dual-Energy CT and DXA

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Conflict of interest: None

Purpose: This study compares Dual Energy CT (DECT) and Dual-energy X-ray Absorptiometry (DXA) for bone density measurement. DXA can be affected by osteoarthritis in elderly patients, while DECT can potentially evaluate cortical and trabecular bone strength separately. Methods: DECT was performed on 20 pre-total hip arthroplasty patients. 3D ROIs were set on the lumbar spine and femoral neck. HAP-enhanced images were obtained by removing water and fat components. Evaluations were made for combined and trabecular bone alone, comparing correlations with DXA. Results: DECT evaluations of combined bone showed strong correlations with DXA. For the lumbar spine, HAP-water correlation was 0.914 and HAP-fat was 0.868 (p<0.01). For the femoral neck, HAP-water was 0.824 and HAP-fat was 0.853 (p<0.01). Trabecular bone-only DECT evaluations showed lower correlations: 0.729 and 0.696 for the lumbar spine, and 0.525 and 0.573 for the femoral neck, suggesting DXA may not accurately assess trabecular bone density. Conclusion: DECT shows superior material differentiation and site-specific analysis compared to DXA, potentially offering higher accuracy in trabecular bone evaluation. It may assess localized bone strength that DXA cannot, indicating its potential as a valuable bone density measurement tool.

W50-4

Prevalence of osteoporotic vertebral fractures in female patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) patients are considered to have a higher fracture risk than non-RA patients. In this study, we report the prevalence of osteoporotic vertebral fractures (OPVF) in female RA patients. [Methods] Subjects were 424 female RA patients (mean age 68.4 years, mean disease duration 15.6 years) from the Orthopaedic Surgery Department of Okayama City Hospital. The prevalence of OPVF was investigated and examined by age group and prednisolone (PSL) administration history. [Results and Conclusion] 17.7% of RA patients had OPVF, most of which were in the thoracic-lumbar junction. The prevalence increased in those over 70 years old. In addition, the prevalence of fractures was higher in those who continued PSL administration.

W50-5

Patient characteristics of contralateral hip fracture in rheumatoid arthritis

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Conflict of interest: None

[Objectives] To investigate patient characteristics of contralateral hip fracture in rheumatoid arthritis (RA). [Methods] A retrospective study was conducted on 20 RA patients with hip fractures who underwent surgical treatment in our hospital from April 2019 to March 2021. Patients with a history of contralateral fracture at the time of surgery and those who suffered a contralateral fracture during follow-up were defined as bilateral fractures. Patients were divided into two groups, the bilateral group and the unilateral group, and the baseline characteristics were statistically examined. [Results] The mean age was 75.9 years, the mean disease duration was 21.1 years, the rate of MTX use was 45%, the rate of biological agents or JAK inhibitors use was 35%, and the rate of steroid use was 25%. Fifty percent had a history of osteoporosis treatment, the mean bone mineral density was YAM60 at femoral neck. Three patients had a history of contralateral fracture, and one patient suffered a contralateral fracture within 2 years after surgery. Univariate analysis was performed, age ($p=0.012$) and rate of steroid use ($p=0.032$) were significantly higher in the bilateral group. [Conclusion] Contralateral hip fractures in RA patients were more common in older patients and those using steroids.

W50-6

Study of bone density in female surgical patients undergoing proximal femur and distal radius fracture at our hospital

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Conflict of interest: None

[Objectives] We recommend early bone mineral density analysis (DEXA) for patients with fragility fractures due to osteoporosis, and have performed bone mineral density analysis of the forearm, femur, and lumbar spine. In this study, we compared the usefulness of forearm DEXA. [Methods] Bone density testing was performed using the DEXA method, and results were tabulated and compared retrospectively. There were 235 proximal femur fractures (PFF) and 59 distal radius fractures (DRF) cases with a mean age of 80.4 years. [Results] The mean YAM values of the forearm, femur, and lumbar spine were 57.0%, 61.7%, and 69.0%, in the PFF patients. The mean YAM values of the forearm, femur, and lumbar spine were 68.7%, 75.0%, and 75.6%, in the DRF patients. When the cases were sorted by forearm YAM values of 70% or less, fewer PFF patients had YAM values of 71% or more for both the femur and lumbar spine, while more DRF patients had YAM values of 71% or more for both, suggesting that the forearm bone mineral density test is useful for early intervention in osteoporosis treatment. [Conclusion] Forearm YAM values tend to decrease earlier in postmenopausal women, and forearm bone mineral density test may be useful for early osteoporosis treatment intervention and may lead to primary fracture prevention.

W51-1

Issues in the current glucocorticoid tapering strategy in patients with polymyalgia rheumatica: Descriptive epidemiology using group-based trajectory modeling

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Conflict of interest: Yes

[Objectives] To identify glucocorticoid (GC) treatment patterns in polymyalgia rheumatica (PMR) patients and to determine populations that may benefit from GC-sparing therapy. [Methods] This study used an electronic medical record database in Japan. PMR patients who initiated GC from 2010 to 2019 were included. The patients were classified using group-based trajectory modeling based on their GC treatment patterns over 52 weeks, and clinical characteristics were analyzed. [Results] Among 452 eligible PMR patients, 4 groups were identified: rapidly-declining (19.0%), low-dose (36.9%), intermediate-dose (32.5%), and high-dose (11.5%). The rapidly-declining and low-dose groups included more patients aged over 80 years and with comorbidities, while the high-dose group included younger patients with a lower prevalence of comorbidities. Inadequate reductions in GC doses in the low-dose, intermediate-dose, and high-dose groups resulted in higher cumulative GC doses and were associated with GC-related toxicities. [Conclusion] The results suggest the high risk of GC-related toxicity even in the low-dose group, indicating that GC-sparing therapy should be considered from the low-dose to the high-dose group.

W51-2

Analysis of gender differences in the Health Assessment Questionnaire-Disability Index (HAQ-DI) using the NinJa database

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Conflict of interest: None

[Objectives] To examine gender differences in physical function based on Health Assessment Questionnaire-Disability Index (HAQ-DI) scores in rheumatoid arthritis patients, and whether the differences vary by age group. [Methods] A cross-sectional analysis of 2021 NinJa data was conducted using a geometric mean model for gender and HAQ-DI relationship, and ordinal logistic regression for gender and individual domain relationship. Covariates included age, disease duration, disease activity, and Steinbrocker's stage. Patients were divided into two groups (age 70+/70-) for the age analysis. Significance was set at $p<0.05$. [Results] Of 17243 cases, 10403 were analyzed. Females had HAQ-DI scores 1.37 times higher than males [95%CI: 1.32-1.43]. Gender differences were found in all domains, with notable gaps in "Grip", "Eating", "Reach", and "Activity" (odds ratios: 2.99 [2.66-3.36], 2.49 [2.22-2.80], 2.10 [1.89-2.35], and 1.93 [1.72-2.18], respectively). In both age groups, females had higher scores (1.41 [1.33-1.50] times higher in 70+ and 1.29 [1.22-1.36] times higher in 70-) with similar trends across domains. [Conclusion] Significant gender differences in HAQ-DI scores were found, consistent across age groups, indicating that gender should be considered in assessing physical function.

W51-3

Factors associated with accumulation of comorbidities in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] Increased number of comorbidities was a key component in a cumulative deficit model of frailty. Our aim was to assess multi-comorbidities in patients with rheumatoid arthritis (RA) and factors associated with multi-comorbidities. [Methods] Data from the multicenter prospective cohort study (ATOMM) and the KURAMA cohort of Kyoto University were combined, and 44 comorbidities were counted for 883 patients with a mean age of 72.5 years. The comorbidity score was defined as the number of comorbidities. Using baseline data, factors associated with comorbidity scores were evaluated by multiple regression analysis. [Results] MTX was used in 60.2%, bDMARDs in 51.2%, and glucocorticoids (GC) in 31.7%. Ischemic heart disease was observed in 3.9%, interstitial lung disease in 10.4%, and osteoporosis under treatment in 37.0% of the patients. The mean comorbidity score was 3.75 and the mean rheumatic disease comorbidity index was 1.82. Multiple regression analysis showed that age and GC use were associated with increased comorbidity scores, while disease activity, physical function, depression, and bDMARD use were not associated. [Conclusion] In a cross-sectional analysis, aging and GC use may be associated with frailty of RA in terms of an increased number of comorbidities.

W51-4

Effect of distance to hospital on RA care: A cross-sectional study

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Conflict of interest: None

[Objectives] The distance to rheumatology specialists may influence treatment decisions in RA patients due to the burden of hospital visits and medication concerns. This study investigated how access to specialists affects disease activity and treatment choices in RA patients. [Methods] A cross-sectional study analyzed 489 RA patients at Sapporo Medical University Hospital (April-July 2024). Patients were grouped by straight-line distance to hospital: Group A (over 40 km, n=30) and Group B (under 40 km, n=459). We collected data on complications, autoantibodies, medications (PSL, MTX, other csDMARDs, biologics, JAK inhibitors), and joint assessments. Statistical analysis used R v4.2.0 for between-group comparisons and correlation analysis (significance level: $p<0.05$). [Results] Group A showed higher tender joint counts (1.23 vs 0.52, $p<0.001$) and PSL doses (2.78 vs 1.84 mg/day, $p=0.037$) than Group B. JAK inhibitor use trended higher in Group A (20.7% vs 8.9%, $p=0.057$). No between-group differences were found in complications, MTX use, biologic use, or swollen joints. Group A showed weak correlation between tender joints and JAK inhibitor use ($r=0.4$, $p<0.02$). [Conclusion] Distance to hospital may affect RA treatment outcomes and further longitudinal studies are needed.

W51-5

The Trends in Work Status in NinJa Over a 10-Year Period

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Conflict of interest: None

[Objective] To examine long-term trends in the work status of patients with rheumatoid arthritis (RA). [Methods] RA patients with consecutive work status data from NinJa (2013-2022) were included. The following variables were described: age, gender, disease duration, work status, employment turnover, disease activity, HAQ-DI, and treatment. [Results] A total of 2828 patients were identified, of which 2361 (83%) were women, with a median age of 63 years and a median disease duration of 9 years in 2013. The percentage of employed patients declined over time from 2013 to 2022: 41.9, 40.7, 40.5, 39.4, 38.9, 38.3, 37.6, 36.6, 35.8, and 34.1%. The rates of leaving work and finding employment from 2014 to 2022 were 4.2/3.0, 2.4/2.1, 3.0/1.8, 2.1/1.6, 2.7/2.1, 2.3/1.5, 2.4/1.5, 2.3/1.6, and 2.5/0.8%, indicating that job separations consistently exceeded new employment. There was a gradual decline in disease activity markers, and the percentage of patients using GC/MTX over time, alongside an increase in the use of bDMARDs and tsDMARDs. [Conclusions] The population was found to maintain good disease control over an extended period with appropriate treatment. The primary cause of turnover was believed to be the effects of aging.

W51-6

Prospective study of the development of rheumatoid arthritis in residents health check-ups; Nagasaki Island Study

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Conflict of interest: None

Objective: Rheumatoid arthritis (RA) progresses from asymptomatic to arthralgia to undifferentiated arthritis. Anti-citrullinated protein antibodies (ACPA) positivity is a strong risk factor for the development of RA. We conducted a prospective follow-up of RA progression in healthy subjects. Methods: From 2014 Serum ACPA measurements and interviews were conducted the community health check-ups in Goto City, Nagasaki Prefecture, and those at high risk of developing RA were selected for secondary check-ups at the main hospital. High-risk subjects were defined as those who were (1) ACPA-positive or (2) had finger joint symptoms and a family history of RA by interview, and RA was diagnosed based on both of the 2010 and 1987 RA classification criteria. Results: 70 (1.9%) of 3564 (8290 total) examinees were ACPA-positive, 1031 (28.9%) had HLA-DRB1*04:05, and ACPA positivity was significantly higher in those with HLA-DRB1*04:05 (2.8% vs. 1.6%, $\chi 2$ test $p<0.05$). 34% had a history of smoking. 116 (40%) of those eligible for secondary screening were examined, with a median follow-up of 12 months, and 21% developed RA during follow-up periods of 6-117 months. Conclusion. The ACPA-positive rate and RA progression rate were similar to those previously reported.

W52-1

Certolizumab pegol (CZP) inhibits radiographic progression even in rheumatoid arthritis (RA) patients (pts) with high rheumatoid factor (RF) levels: A pooled, post-hoc analysis of two phase 3 trials (encore)

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Conflict of interest: Yes

[Objectives] Assess radiographic progression in CZP+MTX vs placebo (PBO)+MTX-treated pts with RA, stratified by RF level. [Methods] Pooled post-hoc analysis of pts with early moderate-to-severe RA with poor prognostic factors in C-EARLY (NCT01519791)/C-OPERA (NCT 01451203) (full analysis set). Week (Wk) 24: PBO non-responders switched to CZP for next 28wks (early escapers). Baseline (BL) RF stratified (low: <200 IU/mL; high: ≧200) for outcomes reported: modified total sharp score (mTSS) change from BL, % with Wk24 & Wk52 mTSS minimum clinically important difference (worsening; >5), mTSS over time. [Results] BL RF measured in 813 CZP (low RF: N=571/high: N=242), 367 PBO (N=242/N=125) pts; 56 early escapers. Pts with high vs low RF had more severe BL disease (higher mean CRP, ACPA, mTSS, erosion scores). By Wk52, mean mTSS increased from BL in PBO pts with high & low RF, but was comparable to BL in CZP pts. % pts with meaningfully worsening radiographic progression higher in PBO pts with high vs low RF at Wk24 & Wk52. Smaller % of CZP pts experienced meaningful worsening; this was similar between pts with high/low RF. [Conclusion] Consistently lower radiographic progression with CZP vs PBO regardless of BL RF levels, suggesting RF does not adversely influence radiographic response to CZP.

W52-2

Comparison of efficacy between tocilizumab and upadacitinib in patients with rheumatoid arthritis: Switching from JAK inhibitors

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Conflict of interest: None

[Objectives] Various bDMARDs and JAKi are available for the treatment of RA, though there is little evidence regarding switching. In this study, we evaluated the effectiveness of switching from a JAKi to tocilizumab (TCZ) or upadacitinib (UPA). [Methods] The background of 45 patients with TCZ and 49 with UPA was adjusted using the propensity score inverse probability weighting, and the efficacy was retrospectively evaluated using CDAI, and ACR response rate. We also evaluated factors associated with ACR20 at 12 weeks. [Results] Both drugs significantly reduced the mean CDAI at weeks 12 and 24. There was no difference in the rate of low disease activity (TCZ56.4% vs. UPA52.8% at week 12, TCZ55% vs. UPA49.4% at week 24). However, the CDAI remission rate at week 12 was significantly higher with TCZ (TCZ 19.2% vs. UPA 7.4%, P<0.05). Additionally, the ACR20 at week 12 was higher with TCZ (TCZ 50.2% vs. UPA 34%, P<0.05), but the ACR50 at week 24 was higher with UPA (TCZ 12.1% vs. UPA 32.3%, P<0.01). Factors associated with achieving ACR20 at 12 weeks were identified as high ESR for TCZ and non-concomitant use of MTX for UPA. [Conclusion] Half of those treated with TCZ or UPA were effective, and the effectiveness was associated high ESR for TCZ and no-concomitant MTX for UPA.

W52-3

Consistent efficacy of sarilumab in patients with active rheumatoid arthritis with varying disease activity

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Conflict of interest: Yes

Objective: To investigate the efficacy of sarilumab (SAR) in rheumatoid arthritis (RA) patients (pts) with various disease activities (DAs). Methods: A post-hoc analysis of the KAKEHASI trial (NCT02293902) evaluated the efficacy of SAR in groups classified by BL-CDAI score. Other factors at BL affecting SAR efficacy were also evaluated. Results: The efficacy analysis population was stratified to high DA (HDA) 84.7% (205/242), moderate DA (MDA) 15.3% (37/242), and low DA (LDA) 1 pt, based on BL-CDAI scores. Mean CDAI scores (n) at BL for HDA and MDA groups who received SAR were 37.8 (133) and 18.6 (27), reaching 8.8 (105) and 5.6 (17) at W52 in both groups, respectively. The percentage change in CDAI scores (absolute) at W52 was comparable between groups [BL-HDA -75.1% (-28.4); BL-MDA -68.3% (-12.7)]. More than half of SAR-treated pts achieved LDA or remission [56.4% (75/133), BL-HDA; 55.6% (15/27), BL-MDA]. Other DA/PRO parameters such as DAS28-CRP and pt and physician global assessment showed similar trends to the CDAI changes. In the BL-HDA group, pts still in HDA after SAR treatment (20 at W24, 9 at W52) had higher BL DA than those who improved. Conclusion: SAR showed consistent efficacy across pts with various DA at BL, suggesting potential use in a broad range of RA pts.

W52-4

Evaluation of ozoralizumab in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To analyse of the efficacy and safety for the rheumatoid arthritis (RA) patients treated with ozoralizumab (OZR) at our hospital. [Methods] We investigated a retrospective survey of RA patients who started OZR from August 2023, and examined the patient characteristics, disease activity, retention rates and safety. [Results] There were 19 patients (13 females), with mean age of 74.5 years, mean disease duration of 10.3 years, 79% receiving MTX with dose at 7.9±2.2 mg/week, 32% using prednisolone. 47% was b/tsDMARDs naïve, and 16% had prior exposure to ≧2b/tsDMARDs. CDAI and SDAI at baseline were 14.2 and 16.8, and at 12, 24, 36, 48 weeks were as follows, 8.5-6.5-4.3-4.5 and 9.7-6.7-4.3-4.5. Disease activity was improved significantly. The retention rate was 79 % at 24 weeks. 2 patients (10%) with prior exposure to ≧3 b/tsDMARDs discontinued OZR due to inadequate response within 6 months. There were no obvious adverse effects. [Conclusion] In this study, OZR showed effective and safety expect patients with prior exposure to ≧3b/tsDMARDs.

W52-5

24-week, Post-Marketing Surveillance Analysis of Upadacitinib in Japanese Patients with Rheumatoid Arthritis (Encore)

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Conflict of interest: Yes

[Objectives] To evaluate the safety and effectiveness of Upadacitinib (UPA) for rheumatoid arthritis (RA) in all-case post-marketing surveillance (PMS). [Methods] All patients (pts) treated UPA were included in this PMS, which started in Apr 2020. Pts' backgrounds, adverse events (AE), and effectiveness were evaluated for 24 weeks. [Results] As of May 2024, 2,771 pts were enrolled (Female=80.6%). 73.0 and 26.3% of pts were initiated UPA 15 and 7.5 mg, respectively. The mean ages were 64.7 (15 mg) and 68.4 years (7.5 mg), respectively. In overall, 80.1% continued UPA for 24 weeks. AEs were reported in 596 (21.5%) and serious AEs (SAEs) in 138 (5.0%). AEs of special interest included herpes zoster (3.2%), hepatic disorder (2.6%), serious infection (2.2%, including 11 PCP cases), death (0.5%), malignancy (0.5%), renal failure (0.5%), interstitial pneumonia (0.4%), cardiovascular event (0.3%), serious cytopenia (0.1%), HBV reactivation (0.1%), and venous thromboembolism (0.04%). In the effectiveness analysis set of 1,411 pts started on 15 mg, 872 were assessed for DAS28-CRP at week 24: 708 (50.2%) reached DAS28-CRP<3.2. [Conclusion] The safety and effectiveness profile were consistent with clinical trial results and no new safety signals were identified.

W52-6

Evaluation of the early efficacy of ozoralizumab in elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] Ozorarizumab (OZR) is the newest BIO-DMARDS, launched in December 2022. We will report the background, efficacy and adverse events of elderly RA patients treated with OZR at our institution. [Methods] This study included patients aged > 64 years with RA who received OZR. We collected patient background and treatment data. Efficacy was evaluated based on the number of swollen and tender joints and the CDAI before and 12 weeks after OZR administration. [Results] Thirty-six patients (29 females and 7 males) with an average age of 79 years and a median disease duration of 13 years were included in the analysis. Six patients were biologic-naïve and the median number of previously used BIO agents was one. At the start of OZR therapy, 17 patients were on concomitant MTX and 8 were on prednisolone. The median CDAI decreased from 19 at baseline to 7 after 12 weeks of treatment. No serious adverse events were reported during the 12-week treatment period. [Conclusion] OZR demonstrated clinical efficacy within a short period of time in elderly patients with RA. Given the high prevalence of comorbidities and difficult-to-treat RA in this population, OZR is a viable therapeutic option for elderly patients with RA.

W53-1

Consideration of switching to other molecular targeted drugs in cases of IL-6 inhibitor ineffectiveness

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Conflict of interest: None

[Objectives] We examined whether switching to a molecular target of another target is also effective when switching to an IL-6 inhibitor in the 1st. [Methods] Using a database of over 1600 cases of molecular-targeted agents at Osaka Public University, we selected patients who used IL-6 inhibitors as the first molecular-targeted agents in Phase 2 and entered Phase 3, and examined the continuation rate and efficacy of each target of the formulation used in Phase 3. [Results] The continuation rates at 52 weeks after transition from IL-6 inhibitors to Phase 3 were 91.7% (11/12) for TNF inhibitors, 16.7% (1/6) for IL-6 inhibitors, 75.0% (3/4) for CTLA4-Ig, and 37.5% (3/8) for JAK inhibitors. As for the change in CDAI from baseline to 52 weeks in patients who were able to continue up to 52 weeks, it was 18.7 to 7.7 for TNF inhibitors, 22.4 to 22.3 for IL-6 inhibitors, 20.0 to 9.9 for CTLA4-Ig, and 26.5 to 12.2 for JAK inhibitors. [Conclusion] In the case of IL-6 inhibitors, switching to a molecular target with a different target may be superior in terms of persistence rate and efficacy, but JAK inhibitors may also have low persistence rate and efficacy, and switching to a TNF inhibitor or CTLA4-Ig may be a better option.

W53-2

The relief of disproportionate pain with b/tsDMARDs in rheumatoid arthritis: ANSWER cohort study

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Conflict of interest: Yes

[Objective] In some patients with rheumatoid arthritis (RA), joint pain is more severe compared to joint swelling. This disproportionate pain (DP) is characterized as pain that is not aligned with the degree of joint swelling. This study aimed to evaluate the effects of various biological and targeted synthetic DMARDs (b/tsDMARDs) on DP. [Methods] From the ANSWER cohort, we identified 10,401 cases who started b/tsDMARDs between January 2020 and June 2024. Among them, 433 patients with DP (defined as seven or more painful joints than swollen joints at baseline) were analyzed. [Results] The three-month continuation rates for CTLA4-Ig, IL-6 inhibitors (IL-6i), JAK inhibitors (JAKi), and TNF inhibitors (TNFi) were 78.1%, 78.1%, 73.0%, and 68.2%, respectively. At three months, the proportions of patients with persistent DP were 30.0%, 38.4%, 25.9%, and 31.0%, respectively ($p = 0.38$). Among those continuing treatment for three months, factors improving DP included fewer painful joints at baseline and JAKi use compared to CTLA4-Ig (odds: 3.98, 95% CI: 1.18-13.4, $p = 0.03$) or IL-6i (odds: 3.6, 95% CI: 1.15-11.29, $p = 0.03$).

[Conclusion] The use of JAK inhibitors was a significant factor in improving DP compared to CTLA4-Ig and IL-6 inhibitors.

W53-3

Drug Retention Rates of Tocilizumab and Sarilumab in Rheumatoid Arthritis

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Conflict of interest: None

Objectives: We analyzed the drug retention rates of tocilizumab (TCZ) and sarilumab (SAR) in rheumatoid arthritis (RA). Methods: Patients who received subcutaneous injections of TCZ or SAR at our hospital between 2019 and 2024 were retrospectively identified. Results: There were 176 and 68 patients who received TCZ and SAR, respectively. For the TCZ and SAR groups, mean age was 65.3 and 61.6 years, female patients were 67.6 and 70.6%, mean disease duration was 107.6 and 125.6 months, the seropositivity rate was 68.2 and 75.0%, patients who were naïve to molecular targeted drugs were 43.2 and 27.9%, methotrexate (MTX) users were 50.6 and 52.9%, mean MTX dose was 7.3 and 8.3 mg/week, CDAI before treatment was 19.0 and 19.2, the 1-year retention rate was 59.2 and 60.7%, and the 3-year retention rate was 38.2 and 48.7% (Kaplan-Meier method), respectively. There were no significant differences in the continuation rates (log-rank test). In the TCZ group, the reasons for discontinuation were insufficient efficacy in 39 cases, adverse events in 32, and the other reasons in 23. In the SAR group, the reasons for discontinuation were insufficient efficacy in 15 cases and adverse events in 14. Conclusion: There was no clear difference in the drug retention rates between TCZ and SAR in RA.

W53-4

Risk Factor Analysis for Serious Infection (SI) and Herpes Zoster (HZ): 24-week, Post-Marketing Surveillance (PMS) Analysis of Upadacitinib (UPA) in Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: Yes

[Objectives] All patients (pts) treated UPA were included in this PMS started in Apr 2020. We examined risk factors for SI and HZ, AEs of special interest up to 24 week (24w). [Methods] Known and exploratory risk factors for SI and HZ were analyzed via univariate and multivariate Logistic regression models. A descriptive risk factor analysis has been performed to characterize the pts with pneumocystis pneumonia (PCP), a type of SI. [Results] The safety analysis included 2,771 pts with a mean age of 65.7 years, 80.6% female, and a mean RA duration of 11.9 years. Event rates of SI, HZ and PCP were 5.7, 8.0 and 0.9/100 PY up to 24w. Factors with odds ratio ≧2 (95% CI) by multivariate analysis were; SI: male [2.9 (1.1-7.4)], respiratory comorbidities or histories [3.6 (1.7-7.5)], hypertension comorbidities or histories [2.3 (1.1-4.9)], ≧10y RA duration [2.6 (1.2-5.6)], and glucocorticoid (GC) use (≧5 mg/day of prednisolone equivalent) [2.3 (1.1-4.9)]; for HZ: renal impairment [2.1 (1.1-4.0)]. None of the 11 pts with PCP received prophylaxis such as trimethoprim/sulfamethoxazole, and all had at least one known risk factor: age ≧65, GC use, or existing lung disease. [Conclusion] Some risk factors for SI and HZ in pts treated with UPA up to 24w have been identified.

W53-5

Ozoralizumab, a Next Generation TNF Inhibitor Not Cleaved by Serum MMP-3, Maintains Clinical Efficacy and Drug Levels in Patients with High MMP-3 Levels

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Conflict of interest: Yes

[Objectives] Matrix metalloproteinase-3 (MMP-3), a well-known marker of joint destruction, is reported to cleave not only collagen and proteoglycans, but also IgG. Although IgG has a Pro-Glu scissile bond near the hinge region that is susceptible to cleavage by MMP-3, ozoralizumab (OZR) does not have an IgG-type hinge region. Therefore, OZR is not expected to be cleaved by MMP-3. In this study, we investigated whether biologics including OZR are cleaved by MMP-3 and evaluated the effect of serum MMP-3 levels on the pharmacokinetics and the clinical score of OZR by performing a post hoc analysis of the OHZORA study. [Methods] Recombinant MMP-3 were co-incubated with Biologics. The effect of proteases on the integrity was assessed by SDS-PAGE. Patients enrolled in the OHZORA study were classified into 4 groups according to baseline serum MMP-3 quartiles. The plasma OZR concentration and DAS28-CRP score were evaluated in each MMP-3 titer group. [Results] In vitro study revealed that OZR was not cleaved by MMP-3. Post hoc analysis showed no decrease in plasma OZR concentration, even in the group with the highest MMP-3 levels, and OZR significantly improved disease activity in all groups. [Conclusion] These results suggest that OZR is a promising candidate for MMP-3 high level RA patient.

W53-6

The short-term efficacy and safety of switching to ozolarizumab in elderly patients with rheumatoid arthritis patients with secondary failure of TNF inhibitors

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Conflict of interest: None

TNF inhibitors reportedly cause secondary failure due to a neutralizing antibody production. Although methotrexate suppresses neutralizing antibody production and secondary failure, methotrexate may not be used in elderly patients due to renal impairment. Ozoralizumab is effective in a secondary failure mouse model expressing neutralizing antibody to adalimumab. However, the effect of ozoralizumab on secondary failure of TNF inhibitors in elderly rheumatoid arthritis patients has not been reported. In this study, ozoralizumab was administered to six patients who caused secondary failure of TNF inhibitors (Etanercept: n=4; Golimumab: n=2). The average age was 80.2 years. No patients used methotrexate. Two patients used steroids, and one used tacrolimus. As a result, the mean DAS28-CRP improved from 3.93 to 2.76, 1.90, and 1.89 before, 1, 3, and 6 months after the administration of ozoralizumab, respectively. CDAI improved from 18.42 to 8.08, 4.00, and 3.75. CRP improved from 0.9 to 0.2, 0.2, and 0.2 mg/dl. Patient global assessment pain scale also significantly improved in all patients. In conclusion, ozoralizumab could be effective and alternative treatment for elderly patients with rheumatoid arthritis with secondary failure of TNF inhibitors.

W54-1

Evaluation of risk of postoperative complications in elderly patients with rheumatoid arthritis after proximal femoral fracture using the DPC database

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) is an autoimmune disease characterized by polyarthritis and bone loss around joints, and RA patients are often complicated by osteoporosis. The purpose of this study was to evaluate postoperative complications and short-term life prognosis in patients with proximal femoral fractures compared to RA and non-RA patients. [Methods] We studied cases of proximal femur fracture from April 2016 to March 2023 using the Japanese National Administrative Diagnosis Procedure Combination (DPC) database. Propensity score matching was performed for age, gender, and complications, and the association with complications was investigated. [Results] Elderly RA patients with proximal femur fracture had significantly more complications of pneumonia and pulmonary embolism than elderly non-RA patients. Multivariate logistic regression analysis showed that RA was an independent risk factor for complications. [Conclusion] A large study based on the DPC database revealed that RA is an independent risk factor for complications such as pneumonia and pulmonary embolism in elderly patients with proximal femur fractures. Implementation of preventive strategies may be important to minimize complications in the treatment of proximal femur fractures in elderly RA patients.

W54-2

Analysis of Bone Mineral Density Using AI-assisted Osteoporosis Diagnostic System in Patients with Childhood-onset Systemic Lupus Erythematosus

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Conflict of interest: None

[Objectives] In patients with childhood-onset systemic lupus erythematosus (SLE), bone mineral density (BMD) loss has been reported to occur at a young age. We herein used an AI-assisted osteoporosis diagnostic system developed at our hospital to assess BMD in cSLE patients. [Methods] Patients who visited our hospital between November 2022 and April 2023 and were diagnosed with SLE before the age of 18, 24 patients who had chest X-rays (CXR) taken in their 20s were included in the study. and BMD of the proximal femur were assessed using the AI-assisted osteoporosis diagnostic system, which estimates BMD with high precision solely from CXR images. [Results] Although none of the patients had osteoporosis in their 20s, 7/24 (29.1%) of the patients had osteopenia (YAM 70-80%). There was no significant difference between the osteopenia group compared to the normal BMD group in the age at the diagnosis of SLE, but SLICC/ACR damage index (SDI) tended to be higher in the osteopenia group (1.1±1.3 vs 0.4±0.7, p = 0.09). [Conclusion] Among patients with cSLE, a substantial number of patients had osteopenia in their 20s. These patients tended to have higher SDI indicating a need for better treatment strategy to prevent accrual of damage in patients with cSLE.

W54-3

A Study of Arteriosclerosis in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Purpose: In chronic inflammatory conditions such as RA, arteriosclerosis is likely to occur, and intima-media thickness (IMT) correlates with inflammation. We retrospectively examined arteriosclerosis in RA patients using IMT. Methods: We analyzed echo findings of arteriosclerosis in 235 RA patients in relation to blood test, disease activity, and medications. Results: Age 68.8 years, male/female: 63/172, RF positivity 56% (113.9 mg/dl), LDLc 111.8 mg/dl, HbA1c 5.8%, DAS28-CRP 1.69, SDAI 3.08, CDAI 2.59, mHAQ 0.21, MTX administration 49%, mean dosage 8.3 mg/week, glucocorticoid (GC) dose 22%, mean dose 3.3 mg, statin dose 29%, and IMT averaged 1.7 mm. Univariate regression showed that IMT was positively correlated with age, MMP3, CDAI, SDAI, DAS28CRP, mHAQ, and GC dose, and negatively correlated with LDLc and MTX dose (including patients taking statins). Multiple regression analysis revealed that age, MMP3, CDAI, SDAI, MTX administration, and statin administration were significant explanatory factors. Conclusion: Prevention of atherosclerosis in RA patients is important to improve prognosis, especially in the elderly, and it is important to control disease activity, actively use MTX as a therapeutic agent, and pay attention to lifestyle-related diseases such as lipid abnormalities.

W54-4

Study on stratification of high-risk patients for developing adult T-cell leukemia (ATL) in human T cell leukemia virus type 1 (HTLV-1)-positive patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objectives] The aim of this study to attempt to stratify high-risk patients with for developing ATL in HTLV-1-positive patients with RA. [Methods] Fifty-seven HTLV-1-positive RA patients who were participated in a multicenter registry study of HTLV-1-positive RA (RADDAR-J [0-2]) were enrolled. Serial HTLV-1 proviral load (PVL) measurements and flow cytometric analysis of HTLV-1-infected cells (HAS-Flow) were performed in these patients. In addition, the clonality of HTLV-1-infected cells were analyzed by next-generation sequencing (NGS) (RAISING method) to identify major HTLV-infected clones. [Results] During the observation period from 2019 to 2022, 18 patients showed a trend toward increased PVL. The proportion of HTLV-1-infected cells determined by HAS-Flow showed a positive correlation with PVL ($R=0.44$, $P<0.01$). In 8 of 57 patients, HTLV-1-infected cells accounted for 25% or more of the CD4 T cell population. In 1 of these 8 patients, a major clone was identified by the RAISING method and an increase in the ATL progenitor cell population was confirmed using HAS-Flow. [Conclusion] Among HTLV-1-positive RA patients undergoing antirheumatic therapy, there may be patients at high risk of developing ATL, and it is necessary to develop an identification stratification algorithm.

W54-5

A review of six cases of immune checkpoint inhibitor-associated myositis in our hospital

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Conflict of interest: None

[Objective] Usefulness of ICI in cancer therapy, indications have been extended to many types of cancer, and prolonging life. irAE occur fre-

quency, are problematic and require appropriate measures. We report ICI-associated myositis experienced at our hospital. [Methods] We retrospectively investigated patients newly treated with ICI between January 2021 and September 2024, and evaluated the clinical and imaging characteristics of six myositis cases. [Results] Among 396 patients newly treated with ICI, irAE was identified in 226 and myositis in 6 (2.7%). The median age was 76 years (62-79), PS 0-1: 4, 4 lung cancer, 1 uterine cancer and carcinoma of unknown primary each, CK 2570±1919 U/L, aldolase 37± 23.6 IU/L, and troponin T 211±270.2 ng/ mL. PD-L1<1% was 2. Symptom was weakness of lower limbs in 5. Mean time from first ICI was 37± 16 day, and 4 were treated anti-PD-1 and anti-CTLA4 antibodies. All were treated glucocorticoids, and one relapse. MRI showed five of diffuse foggy pattern, five of spreading to the fascia, and two of atrophy and fatty degeneration. [Conclusion] ICI-associated myositis develops early in initiation and is characterized by symmetrical gluteal, adductor muscle and closed muscle center detects on imaging fascia and inflammation in the superficial muscle layers.

W54-6

The upper gastrointestinal (UGI) drug prescription rate in patients with rheumatic and musculoskeletal diseases (RMD): a single-center retrospective observational study

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Conflict of interest: None

[Objectives] Prescription for UGI symptoms is usual in RMD patients. However, not all prescriptions are reasonable. We conducted a survey to find out the UGI drug prescription rate in RMD patients in the real world. [Method] UGI medications prescription data of our department were extracted from electronic medical records from April 1, 2023 to March 31, 2024. Age, sex, underlying disease, glucocorticoid (GC) and NSAID use were collected. [Results] 1,490 patients were recruited. 316 (21.2%) were prescribed gastric acid suppressors (GASs), and 66 (4.4%) were prescribed Rebamipide. Proton-pump inhibitors (PPI) in 240 patients (16.1%), and vonoprazan in 52 patients (3.5%). By disease, the use of GASs was the highest in vasculitis syndromes (59.3%), followed by idiopathic inflammatory myopathy (56.8%). The use of GASs in SSc was 14.1%, with vonoprazan being the most common (12.5%). The use of GASs in RA was 15%, and Rebamipide was 6.2%. Rebamipide was used in 17% of patients using NSAIDs and a correlation coefficient of 0.23. The use of GASs was high in patients using GCs (48.2%). The correlation coefficient between GCs and GASs was 0.41. [Conclusion] The use of GASs was higher in patients with GC use, and the association with NSAID use was unclear.

W55-1

Evaluation of activity and safety before and after vaccination with a recombinant herpes zoster vaccine in 125 patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] To evaluate the change in activity within 2 months before and after vaccination with the recombinant zoster vaccine (RZV) and the safety after vaccination in 125 patients with rheumatoid arthritis (RA) undergoing treatment at our hospital. [Methods] The subjects were 125 RA patients who received RZV between May 2021 and August 2024. The impact of RZV on RA activity was evaluated using DAS28-CRP and CDAI within 2 months before and after the first and second RZV injections. Detailed safety was investigated using an adverse event diary. [Results] For the first vaccination, DAS28-CRP/CDAI showed significant improvement in activity, with pre-vaccination averages of 2.63/9.23 and post-vaccination averages of 2.20/6.82 ($p<0.001$, respectively). For the second vaccination, the average score before vaccination was 1.98/5.03 and the average score after vaccination was 1.94/4.81, showing no significant difference regardless of whether or not treatment was enhanced. One case of serious adverse event was observed (femoral neck fracture due to a fall). Three cases of herpes zoster were observed after RZV vaccination. [Conclusion] Although there was no worsening of RA activity or any notable side effects following RZV vaccination, some cases of herpes zoster were observed.

W55-2

The Impact of the Japanese Diet on Achievement of Clinical Remission in Patients with Rheumatoid Arthritis: An Analysis Using the IORRA Cohort

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Conflict of interest: None

[Objectives] We investigated the impact of the modified Japanese Diet Index (mJDI) on remission in elderly patients with rheumatoid arthritis (RA). [Methods] From April to June 2021, patients with RA in the IORRA survey completed the Brief Self-administered Diet History Questionnaire. The study focused on patients aged 75+ without DAS28 remission. Based on baseline mJDI scores, participants were grouped into three groups. Over 2.5 years, the proportion of DAS28 remission and composite clinical events (mortality, hospitalization, infections, malignancy, cardiovascular disease) were assessed, adjusting for sex, age, BMI, smoking, and medication use (methotrexate, b/tsDMARDs, steroids) in Cox analysis. [Results] Of 2,926 participants, 237 patients without DAS28 remission were analyzed. Patients were divided by mJDI score: Group 1 (low, n=88), Group 2 (moderate, n=79), and Group 3 (high, n=70). The proportion of DAS28 remission was 27.3% in Group 1, 35.4% in Group 2, and 44.2% in Group 3. Group 3 had higher remission than Group 1 (adjusted HR: 1.75, 95% CI: 1.02-2.99, $p=0.042$). No significant difference in composite clinical events was found between groups. [Conclusion] Higher mJDI was associated with early remission achievement in patients aged 75+ without DAS28 remission.

W55-3

Analysis of treatment response in rheumatoid arthritis patients with hypergammaglobulinemia: ANSWER cohort study

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Conflict of interest: None

[Objectives] This study aimed to investigate the effects of hypergammaglobulinemia on response to treatment and use of b/tsDMARDs in patients with rheumatoid arthritis (RA) within six months of onset. [Meth-

ods] The data in this study were extracted from 856 RA patients within six months of onset who were enrolled in ANSWER cohort after May 2011 and did not use b/tsDMARDs at the time of enrollment. We assessed the effect of elevated serum IgG levels at enrollment on the achievement of CDAI low disease activity or less (CDAI<10) after 1 year by logistic regression analysis, and on the use of b/tsDMARDs after 1 year by log-rank test. [Results] There were 115 patients in the increased IgG group and 741 patients in the non-increased IgG group. The prevalence of RF, anti-CCP and anti-SS-A antibodies was significantly higher in the increased IgG group, and CRP, MMP-3 and CDAI were also significantly elevated at the time of registration. Increased IgG levels showed no effect on CDAI<10 achievement at 1 year or the use of b/tsDMARDs at 1 year. [Conclusion] In RA patients within six months of onset, seropositivity and disease activity were significantly higher in patients with increased serum IgG, but CDAI LDA or use of b/tsDMARDs after 1 year was not affected by increased serum IgG.

W55-4

The significance of using an injectable MTX drug "Metoject" as an initial treatment for RA

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Conflict of interest: None

[Purpose] Methods: Examined the timing and effects of the MTX injectable drug Metjujt (MTJ) in 73 of the 92 patients who were able to continue MTJ (50 patients from the start of treatment, 23 patients changed in the middle of treatment). Results: The mean age was 62 years, the average duration of the disease was about 1.6 years, and 10 patients were treated with a combination of Bio and JAK inhibitors. Before introduction, mean DAS28-CRP 4.14, and HAQ 0.88, 2 month later, they were changed to 2.2, and 0.43. In the switching case, the mean oral MTX dose of 7.1 could be increased to 10.3 mg/week after 2 months. Induction rate of remission with MTJ 1 mo. use was 45% (DAS28CRP), and 58% (low disease activity). While, the one of oral MTX was 38%. The continuation rate of more than 6 mo. was around 80% in all age categories, which was higher than around 60% for oral agents [Conclusion] MTJ had fewer gastrointestinal symptoms than oral MTX, and the proportion of long-chain MTX-PG, correlated with improved disease activity, was higher than that of oral MTX. It was thought that RA could be controlled at an early stage if MTJ was used as early as possible and in sufficient doses.

W55-5

Longitudinal analysis on renal function after initiation of methotrexate in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] This study aimed to examine the relationship between methotrexate (MTX) doses and changes in renal function in rheumatoid arthritis (RA) patients after starting MTX. [Methods] RA patients, whose MTX was started between 2010 and 2023, were categorized based on their weekly MTX dose: less than 8 mg, 8 to 12 mg, and 12 mg or more per week. The analysis examined the relationship between the rate of decline in eGFR and MTX dose, during the entire observation period, during the induction phase (up to three years after initiation), and during the maintenance phase (from the third to fifth year). A linear mixed-effects model was used to analyze the repeated measurements of eGFR over time, adjusting for covariates. [Results] The study analyzed data from 430 RA patients. In the induction phase, patients on 8 to 12 mg per week showed a slower eGFR decline compared to those receiving less than 8 mg per week. In the maintenance phase, patients receiving 12 mg or more per week had a significantly faster annual decline in eGFR compared to those receiving less than 8 mg per week. [Conclusion] Decline in eGFR was associated with lower MTX doses during the MTX induction phase and higher MTX doses during the maintenance phase.

W55-6

A multicenter study investigating the efficacy of low-temperature warmers for morning stiffness in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] Despite advances in rheumatoid arthritis (RA) treatment, many patients still suffer from morning stiffness (MS) of their fingers. We reported at the 67th JCR that heating hands with low-temperature warmers at bedtime alleviates MS. A multicenter study was conducted to examine the effectiveness of hand warming using low-temperature warmers. [Methods] RA patients with MS at eight facilities were included. After a two-week observation period, patients used holders with low-temperature warmers on their hands at bedtime for two weeks. They recorded the severity and duration of MS in a diary. The primary endpoint was the change in the MS score (0-10 scale) between the warmer application and observation periods. [Results] Of 34 enrolled patients, 32 were included in the full analysis set. The mean MS scores during the observation and warmer application periods were 4.12 and 3.22, respectively, with paired t-tests indicating significantly lower scores during the warmer application period ($p<0.001$). Adverse events included temporary skin redness in one patient and worsening of finger joint symptoms in another, both resolving without treatment. [Conclusion] Heating hands with low-temperature warmers at bedtime alleviates morning stiffness in patients with rheumatoid arthritis.

W56-1

Case report of 10 cases of anti-PL-7 antibody-positive interstitial pneumonia

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Conflict of interest: None

[Objectives] Since reports of PL-7 antibodies are limited, we will examine its clinical characteristics. [Methods] We conducted a retrospective review of the clinical findings, treatment details, and prognosis of 10 cases diagnosed with anti-PL-7 antibody-positive interstitial pneumonia at our hospital between 2017 and 2024. [Results] Of the 10 cases, 9 cases (90%) were female, median age was 73.5 years, 9 cases had characteristic skin symptoms such as mechanic's hand and Gottron's sign, 7 cases had muscular symptoms, and 7 cases had muscle symptoms. Three of these cases were diagnosed as complications of rheumatoid arthritis. Interstitial pneumonia with an NSIP pattern was observed in nine cases, of which four were acutely progressive. Treatment included: High-dose steroid therapy was administered to 9 patients, of which steroid pulse therapy was also used in 6 patients. Cyclophosphamide therapy was administered to 7 patients as immunosuppressants, Tacrolimus was used concomitantly in all

cases. As for prognosis, clinical symptoms improved in all cases, but symptoms relapsed in 5 cases during follow-up. [Conclusion] Anti-PL-7 antibodies appear to have similar clinical characteristics to other anti-ARS antibodies. Relapses are still common, and further treatment is considered necessary.

W56-2

Three dermatomyositis (DM) cases with double positivity with anti-TIF-1alpha/gamma and anti-Mi-2 antibodies

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Conflict of interest: None

<Background> We experienced 3 cases with anti-TIF-1 α/γ and anti-Mi-2 double-positive DM. <Case 1> A 75-year-old woman had erythema on her face and limbs. Elevated CK, positive anti-Mi-2 and TIF-1γ and MRI and biopsy results led to a diagnosis of DM. Regardless of starting high-dose GC, muscle weakness and dysphagia worsened. Addition of intravenous immunoglobulin (IVIg) and tacrolimus resulted in disease stabilization. <Case 2> A 66-year-old woman visited with Gottron's sign and muscle weakness. Elevated CK, positive Mi-2 and TIF-1γ and MRI and muscle biopsy results led to the diagnosis. After starting high-dose GC, cecum cancer was accidentally found. Addition of IVIg led to a decrease of CK. <Case 3> A 57-year-old man presented with Gottron's sign. He had elevated CK, positive Mi-2 and TIF-1α. DM was strongly suspected and GC was started. Prostate cancer was detected afterward. GC were tapered off after the initiation of cancer treatment. <Discussion> Previous reports showed that clinical feature of double-positive cases were influenced by anti-Mi-2 when the titer of anti-TIF-1α/γ was low. However, our patients showed a clinical course similar to cases with TIF-1γ. Even with double-positive cases, the caution for cancer complication and rebellant course of DM may be necessary.

W56-3

Three Cases of Severe Rapidly Progressive Interstitial Lung Disease (RP-ILD) Associated with Anti-MDA5 Antibody-Positive Dermatomyositis Successfully Treated with Early Addition of Tofacitinib and Plasma Exchange to Triple Therapy

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Conflict of interest: None

Background: In rapidly progressive interstitial lung disease (RP-ILD) associated with anti-MDA5 antibody-positive dermatomyositis, some patients are resistant to traditional triple therapy. We report three cases where tofacitinib (TOF) and plasma exchange (PE) were added to treatment. Cases: (1) A 72-year-old male with myasthenia gravis developed RP-ILD. After no improvement with triple therapy, he received TOF and five sessions of PE from day 4, resulting in recovery and discontinuation of oxygen at discharge. He developed a lung abscess but was cured with antibiotics. (2) A 69-year-old female required intubation and mechanical ventilation for RP-ILD. After starting triple therapy, she received TOF and four sessions of PE from day 9, allowing her to discontinue oxygen. She developed invasive pulmonary aspergillosis, which improved with antifungal treatment. (3) A 74-year-old female was intubated for RP-ILD. She had TOF and six sessions of PE from day 8, enabling her to discontinue oxygen. She required treatment for hemorrhagic cystitis and CMV antigenemia during her course. Conclusion: Adding TOF and PE to standard therapy can lead to favourable outcomes in critically ill RP-ILD patients resistant to conventional treatment. Infection monitoring is essential during therapy.

W56-4

Two cases of anti-MDA5 antibody-positive dermatomyositis treated with plasma exchange and tofacitinib in addition to standard triple therapy

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Conflict of interest: None

[Case] A 72-year-old woman was referred to our hospital with inverse Gottron's sign and a heliotrope rash. She was positive for anti-MDA5 antibody (2200 index), and had interstitial pneumonia, leading to a diagnosis of anti-MDA5 antibody-positive dermatomyositis (anti-MDA5 DM). She was treated with prednisolone, tacrolimus, and cyclophosphamide, followed by plasma exchange (PE) and tofacitinib (TOF). She suffered a series of various infections, including cytomegalovirus (CMV) infection, and BK virus infection. She died on day 83 due to sepsis caused by catheter-related urinary tract infection. [Discussion] Besides the case mentioned above, we have treated another case of anti-MDA5 DM with PE and TOF in addition to the conventional triple therapy, who also experienced multiple episodes of different infections. Although the efficacy of PE and TOF in treating anti-MDA5 DM has been reported, high risk of infection due to immunocompromised condition needs to be recognized. [Conclusion] The addition of PE and TOF may be effective in the treatment of anti-MDA5 DM refractory to standard triple therapy, but close monitoring for infection is crucial.

W56-5

A case of anti-SAE antibody-positive dermatomyositis with severe dysphagia successfully treated by multidisciplinary treatment

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Conflict of interest: None

A 72-year-old woman was admitted to our hospital because of erythema all over her body and severe dysphagia. Blood test revealed marked eosinophilia, and CT scan showed multiple lung mass lesions. She was once diagnosed as hypereosinophilic syndrome. After starting prednisolone 25 mg/day, eosinophilia and lung abnormal shadows in CT immediately subsided. Then, intravenous methylprednisolone pulse therapy and cyclosporine were added due to remaining skin lesions. Skin lesions were improved after the additional therapies, but she almost lost the ability to swallow. Additional blood tests revealed positive anti-SAE antibody, so we revised her diagnosis to anti-SAE antibody-positive dermatomyositis. She continued dysphagia rehabilitation and received total of three times high-dose intravenous immunoglobulin therapy and cricopharyngeal myectomy., Her swallowing function was significantly improved shortly after the surgery, and finally she became to be able to eat foods orally. Anti-SAE antibody-positive dermatomyositis is a rare disease characterized by preceding skin symptoms, severe swallowing disorders, and a high incidence of interstitial pneumonia and malignant tumors. Our case that was successfully treated by multidisciplinary treatments will be discussed with literature review.

W56-6

A case of progressive multifocal leukoencephalopathy during treatment anti-MDA5 antibody-positive rapidly progressive interstitial lung disease with repeated relapses

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Conflict of interest: None

[Case] The patient was a 61-year-old woman. In June of X-6, she was diagnosed with rapidly progressive interstitial lung disease (RP-ILD) associated with anti-MDA5 antibody-positive asymptomatic dermatomyositis. She was treated with triple therapy of high-dose steroids, cyclosporine (CyA), intravenous cyclophosphamide (IVCY), resulting in remission. However, in June of X-5, the skin rash worsened and the ILD relapsed. IVCY has been administered and the calcineurin inhibitor has been changed from CyA to tacrolimus (TAC), and Mycophenolate mofetil (MMF) has also been added. But in February of X-1, PML was diagnosed, and treated with mirtazapine and mefloquine. However, in March of year X, the skin rash worsened again and the ILD relapsed. High-dose steroids and plasma exchange (PE), IVCY was added five times and was successful. Since then, there has been no recurrence of PML and the ILD has been maintained in remission. [Significance] This is a rare case of anti-MDA5 antibody-positive RP-ILD with repeated relapses after achieving remission. Furthermore, this is a suggestive case in which PML developed under immunosuppression that could not be discontinued and in which mirtazapine and mefloquine were effective. We report this case together with a literature review.

W57-1

Characteristics of Japanese systemic scleroderma (systemic sclerosis; SSc) by age of onset

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Conflict of interest: None

[Objectives] This study explores the relationship between age at onset and clinical features of systemic sclerosis (SSc) in Japanese patients. SSc, an autoimmune disease marked by fibrosis and circulatory failure, typically begins between ages 30 and 50 but can occur at other ages. [Methods] We categorized 346 patients from our hospital's SSc database into three groups based on age at onset: under 30 years (young-onset group), 30-50 years (middle-age group), and 60 years and older (elderly-onset group). We compared backgrounds, complications, autoantibodies, and treatments across the groups. [Results] Findings showed that 10.1% of patients were young-onset, 64.6% middle-age, and 24.3% elderly-onset. As age increased, the proportion of males and limited cutaneous SSc cases rose. Young-onset patients had more interstitial lung disease and digital ulcers, while elderly-onset patients had more anti-centromere antibodies and received less immunosuppressive therapy. [Conclusion] Poor prognostic factors were interstitial lung disease in young-onset patients and male gender in elderly-onset cases. Monitoring is crucial for elderly patients due to the challenges of immunosuppressive treatment and potential for severe progression. These patterns were similar to those seen in Western populations.

W57-2

The Usefulness of Eating assessment tool-10 (EAT-10) in patients with systemic sclerosis

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Conflict of interest: None

[Objective] Our aim was to evaluate the usefulness of patient-reported outcomes (PROs) in patients with SSc with dysphagia. [Methods] Patients with SSc who visited our department between 2021 and 2024 and underwent videofluorography (VF) and EAT-10, which is, a simple PRO for evaluating swallowing, were included. Dysphagia was evaluated as "unsafe swallowing (US)" when the Penetration Aspiration Scale in VF was 3 or more. Association between the EAT-10 score and dysphagic symptom, and between the EAT-10 score and each item and unsafe swallowing. [Results] Fifty-two SSc patients were included. The age was 64±13 years, 77% was female, and 38% withdcSSc. The total EAT-10 score was 3.7± 4.9. Dysphagic symptom was found in 31 (60%), and was associated with the total EAT-10 score ($p<0.001$). The total EAT-10 score and dysphagic symptom were analysed by ROC curve, the AUC was highest at the EAT-10 score of 2 points or more ($p=0.03$, sensitivity 77%, specificity 95%). US was detected in 15 (29%) by VF. US was not associated with dysphagic symptom, but was associated with a score of 2 or more on the EAT-10 ($p=0.047$). The presence of US was associated with the scores for Q2 and Q10 ($p=0.006$ and $p=0.029$, respectively). [Conclusion] EAT-10 might be an useful PRO for detecting dysphagia.

W57-3

Clinical relevance of anti-SMN complex antibodies in mixed connective tissue disease

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Conflict of interest: Yes

[Objectives] This study investigates the clinical consequences of anti-SMN complex antibodies (anti-SMN Ab) in patients with MCTD. [Methods] Anti-SMN Ab were detected via immunoprecipitation in patients diagnosed with MCTD (78 cases), SLE (74 cases), and SSc (17 cases), all positive for anti-U1 RNP antibodies. [Results] Anti-SMN Ab prevalence was 35% in MCTD patients, higher than 8% in SLE and 12% in SSc. MCTD patients with anti-SMN Ab showed no differences in polyarthritis, skin hardening, or hematological issues compared to those without. However, pulmonary arterial hypertension (PAH) was more common at 56% versus 6%, and interstitial lung disease (ILD) was present in 89% versus 45% of antibody-positive versus antibody-negative cases, respectively. Severity assessment classified 82% of positive cases as 'severe' and nearly all as 'moderate' or higher, making them eligible for healthcare benefits. In contrast, 51% of antibody-negative cases were classified as 'mild'. The one-year mortality rate was 12% in positive cases, due to PAH or infections, with no deaths reported in negative cases. [Conclusion] The presence of anti-SMN antibodies in MCTD patients correlates with PAH and ILD, highlighting their importance in assessing disease severity and prognosis.

W57-4

Effects of an S100 protein-based hybrid protein on macrophage phenotypes and its efficacy in a systemic sclerosis mouse model

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Conflict of interest: Yes

[Objectives] Based on the primary structure of human S100 proteins, we developed a novel hybrid protein, hMIKO-1, which regulates macrophage function via CD68. This study evaluated the effects of hMIKO-1 on murine macrophage polarization and its therapeutic efficacy in a bleomycin-induced systemic sclerosis (BLM-SSc) mouse model. [Methods] hMIKO-1 was co-cultured with murine macrophages to assess phenotypic changes. *In vivo*, mice were divided into a normal group, disease control (BLM only), and hMIKO-1 intervention (BLM + hMIKO-1) groups. hMIKO-1 (0.1 mg/mouse) was administered intraperitoneally for four weeks, after which skin and lung tissues were harvested for analysis. [Results] *In vitro*, hMIKO-1 significantly inhibited M2 macrophage polarization. Lung fibrosis scores

in the BLM + hMIKO-1 group were significantly lower than in the BLM-only group, with no differences in skin pathology. F4/80-positive cells in skin and lung lesions were significantly reduced in the BLM + hMIKO-1 group. Differential hMIKO-1 accumulation was observed between skin and lung lesions. [Conclusion] hMIKO-1 reduced inflammation and fibrosis in lung lesions of BLM-SSc mice but had limited effects on skin lesions, possibly due to differential organ accumulation.

W57-5

A real-world prospective observational registry of patients with systemic sclerosis (SSc) in Japan: Baseline characteristics

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Conflict of interest: Yes

[Objectives] We have launched a multicenter, prospective registry of SSc patients in specialized centers in Japan (J-STAR). [Methods] SSc patients who fulfilled 2013 ACR/EULAR classification criteria were enrolled between January 2022 and September 2023. Physical, laboratory, functional and imaging data were collected for each patient at baseline using the electric data capture system. Various patient-reported outcomes (PROs) and serum samples were also collected. [Results] Of 844 patients enrolled, 835 were eligible for analysis. At baseline, the mean age was 64 years, 85% were female, and 39% were classified as diffuse cutaneous SSc. Prevalence of interstitial lung disease was 56% and was higher than pulmonary arterial hypertension (1.9%), heart involvement (5.3%), and renal crisis (1.9%). Anticentromere (ACA), anti-topoisomerase I (ATA), and anti-RNA polymerase III (ARA) were detected in 32%, 30%, and 9%, respectively. Both functional abilities as reflected by SHAQ-DI and scleroderma skin PRO were worse in diffuse than limited cutaneous SSc, and were worst in the order of ARA, ATA, and ACA-positive patients. [Conclusion] We successfully enrolled SSc patients for the real-world registry in Japan.

W57-6

Prognostic value of circulating biomarkers in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) (encore presentation)

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Conflict of interest: Yes

Objective: To evaluate the prognostic potential of circulating biomarkers of epithelial injury (KL-6) and inflammation (CRP, CCL2) for FVC decline and change in mRSS over 52 weeks in the placebo group of the SENSCIS trial. **Methods:** Associations between baseline biomarker levels and i) rate of decline in FVC (mL/year) over 52 weeks, ii) absolute change from baseline in mRSS at Week 52 were assessed in the placebo group. **Results:** In 288 patients receiving placebo, higher baseline levels of selected biomarkers were associated ($p<0.05$) with a greater rate of FVC decline over 52 weeks (KL-6) and a worsening in mRSS at Week 52 (CRP, CCL2). These biomarkers were not significantly correlated with one another. In analyses wherein the baseline biomarkers were dichotomised by quantile-based cut-offs (Q1, median, Q3), we identified a cut-off for KL-6 that best predicted FVC decline over 52 weeks (960.0 U/mL) and cut-offs for CRP (2.5 ng/L) and CCL2 (198.0 pg/mL) that best predicted change in mRSS at Week 52. **Conclusions:** Biomarkers prognostic for progression of SSc/SSc-ILD based on worsening of mRSS and FVC decline have been identified in the placebo group of the SENSCIS trial. These biomarkers have the potential to be utilised for patient selection in future trials in SSc/SSc-ILD.

W58-1

Impact of disease activity in rheumatoid arthritis on physical function and body composition

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Conflict of interest: None

Purpose: Disease activity in rheumatoid arthritis (RA) is a factor in sarcopenia. The aim of this study was to compare the amount of change in body composition and physical function after one year in both medium/high disease activity RA (MHRA) and remission/low disease activity RA (RLRA) groups and to determine the impact of disease activity. Methods: Of the 329 patients, 17 MHRA and 169 RLRA were included. Patient background, body composition [BMI, skeletal muscle index (SMI), Phase-Angle (PhA)] and physical function [grip strength, walking speed, Time Up & Go Test (TUG)] were investigated. Results: Patient background (MHRA/RLRA) at study entry (age 63/63 years, 77/85% female) was not significantly different and DAS28-CRP 3.52/1.59 was significantly different ($p<0.001$). 1-year changes in ΔPhA -0. 22/0.05° ($p=0.006$) and ΔTUG 0.67 / -0.71s ($p=0.029$) were the only significant differences. Discussion: The results showed that PhA as an indicator of muscle quality and TUG as a gait function worsen in MHRA. This study shows that despite a short duration of one year, persistence of high disease activity has an impact on muscle quality and physical function. Conclusion: It is suggested that persistence of high disease activity may reduce muscle quality and affect gait function.

W58-2

Association Between Disease Activity, Muscle Quality, and Physical Function in RheumatoidArthritis: A Comparative Study with Healthy Controls

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Conflict of interest: None

[Objectives] This study aimed to compare RA patients, classified by disease activity, with healthy controls to understand the effects of chronic inflammation on muscle and motor function. [Methods] A total of 328 RA patients from our frailty cohort were classified into three groups based on disease activity. A control group of 440 healthy women aged 65-80 years was selected. Body composition was assessed using bioelectrical impedance analysis (BIA), and physical function was measured by grip strength and the 5-times sit-to-stand test. [Results] A total of 92 subjects from each group (healthy, remission, LDA, MDA+HDA), matched by age and BMI, were extracted. The average age was 72 years, and BMI was 22 kg/m^2 across groups. Grip strength was 24.3/18.3/17.3/14.6 kg, and the 5-times sit-to-stand test was 8.9/11.2/11.0/12.1 seconds ($p<0.05$), showing lower physical function with higher disease activity. Total muscle mass differed significantly between groups (33.5/32.5/32.2/32.2 kg, $p<0.05$). Phase angle (PhA) was 5.26/5.10/5.01/4.98 (upper limb) and 4.43/3.91/3.71/3.59 (lower limb), with lower PhA in higher disease activity groups ($p<0.05$). [Conclusion] In RA patients, muscle quality (PhA) and physical function declined as disease activity increased.

W58-3

The impact of rehabilitation intervention at diagnosis on patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] At our institution, RA patients receive rehabilitation at diagnosis, aiming to improve physical function and provide joint protection education, regardless of disease activity. This study examined the effect of early rehabilitation on RA treatment outcomes. [Methods] Among RA patients diagnosed and treated from January to October 2023, 51 who continued care for a year as of October 2024 were included. Patients were divided into a Rehabilitation Group (39 patients, mean age 60.7±14.6) and a Non-Rehabilitation Group (12 patients, mean age 66.0±16.45). DAS28-CRP scores were assessed at diagnosis, 3, 6, and 12 months. [Results] The Rehabilitation Group showed significant improvement in DAS28-CRP, from 3.51 at diagnosis to 2.05 at 3 months, 2.06 at 6 months, and 1.75 at 1 year ($p<0.01$). The Non-Rehabilitation Group improved from 3.03 at diagnosis to 1.83 at 3 months ($p<0.01$) and 1.86 at 6 months ($p=0.023$), but not at 1 year (2.17, $p=0.182$). The 1-year remission rate was 85% (33 patients) in the Rehabilitation Group and 50% (6 patients) in the Non-Rehabilitation Group ($p=0.037$). [Conclusion] These findings suggest early rehabilitation may improve RA remission and treatment continuity, indicating its essential role in RA care.

W58-4

Characteristics of late elderly rheumatoid arthritis patients by years of exercise habit

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Conflict of interest: None

[Objective] This study clarified the characteristics of late elderly RA patients grouped according to the number of years of exercise habit. [Methods] The subjects were 235 late elderly RA patients (mean age 81.1±4.6 years), who were divided into 4 groups according to the number of years of exercise habit: (1) no exercise habit, (2) exercise habit <5 years, (3) exercise habit 5 to 10 years, and (4) exercise habit >10 years. The following items were evaluated: age, gender, height, weight, BMI, disease duration, medications (MTX, PSL, biologics, JAK, osteoporosis drugs), blood samples (anti-CCP antibody, CRP, ESR, MMP-3), disease activity (DAS28-CRP, DAS28-ESR), femur bone density (T-score), functional disability index (HAQ), and lumbar spine compression fracture incidence were investigated. [Results] DAS28-CRP and DAS28-ESR were significantly different between (1) and (2), with (2) being better. T-score and HAQ were significantly different between (1) and (3) and (1) and (4), with (3) and (4) being better than (1). No significant differences were observed in other items. [Conclusion] Maintaining good disease activity, femur bone mineral density, and ability to perform activities of daily living were considered important for the continuation of exercise habits in late elderly RA patients.

W58-5

Changes in the rate and risk factor of sarcopenia in female patients with rheumatoid arthritis - a comparison with 16 years ago

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Conflict of interest: None

[Purpose] To study the proportion of sarcopenia (SP) of current RA pasients and its characteristics, and to study the differences from the same study conducted in 2006. [Methods] Among RA patients who visited our outpatient clinic from January to July 2022, 124 female patients aged 50 years and older, 68.9±9.8 years, were included. Based on AWGS 2019 sarcopenia diagnostic criteria, patients were divided into non-SP and SP groups and compared on background, disease activity, physical disability assessment (HAQ), and motor function. There were compared with the results of a study conducted in 2006. [Results] Of the 124 subjects, 104 (83.9%, 68.0±9.0 years) were non-SP and 20 (16.1%, 73.1±12.1 years) were SP. Differences between groups (non-SP vs. SP) were glucocorticoid (GC) intake (rate, dose), Class, Stage, DAS28-ESR, mHAQ, and motor function ($p<0.05$). Compared to 2006, the SP rate was halved from 32.5%, Class, Stage, GC, mHAQ was decreased, and the motor function was preserved ($p<0.05$), despite the average age was 3.6 years higher. [Conclusion] Although the RA patients were getting older, it was suggested that the reduction of GC and the control of disease activity prevented motor dysfunction associated with joint destruction and muscle weakness, and reduced the SP rate.

W58-6

A Report on Thumb Deformity in Patients with Rheumatoid Arthritis and Its Influence on Makeup Movement

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Conflict of interest: None

[Introduction] The thumb plays an important role in the hand, and is said to be involved in 40% of hand functions. In this study, we investigated the influence of thumb deformity on cosmetic activities in RA patients at home. [Methods] A questionnaire survey was conducted on 23 RA patients attending our hospital. Makeup operation was subdivided into 39 processes, and the subjective difficulty level of each process was surveyed in 4 levels. Patient background (age, years of disease) and disease factors (DAS28CRP, HAQ) were evaluated. In addition, the frequency of makeup application, makeup history, and use of self-help aids were also examined. [Results] Differences were observed in the number of years of illness ($P<0.01$) and in the subjective difficulty level of 7 of the makeup processes ($P<0.05$). In particular, opening and closing tools, grasping, and contacting the face with the palm surface tended to be more difficult. only one patient (4%) used a self-help tool. [Discussion] The deformity of the thumb makes it difficult to manipulate makeup tools, suggesting that some processes may not be carried out. OT should contribute to improving the quality of life of RA patients through movement analysis and guidance.

W59-1

Effect of Intra-articular Glucocorticoid Injections on Oral Glucocorticoid Reduction and Relapse Prevention in Polymyalgia Rheumatica

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Conflict of interest: None

Objective: To evaluate the clinical significance of intra-articular glucocorticoid injections in polymyalgia rheumatica (PMR). **Methods:** We studied 69 PMR patients treated from 2018 to 2024, with over 6 months follow-up. Outcomes at 6 months were assessed based on the use of injections at treatment start. Statistical comparisons were made using Student's t-test or Mann-Whitney U test. **Results:** Of 69 cases, 13 received injections initially. Three cases in the injection group improved with one injection, maintaining remission without oral glucocorticoids. No significant differences were found in background, inflammatory response, or relapse rates between groups. Univariate analysis showed benefits in the injection group in terms of initial PSL dose (12.5 vs. 15.0 mg/day, P<0.001), daily PSL dose at 6 months (4.00 vs. 6.87 mg/day, P<0.001), and cumulative glucocorticoid dose at 6 months (PSL equivalent 1424.0 mg vs. 1640.6 mg; P=0.005). **Conclusion:** Intra-articular glucocorticoid injections in PMR may help reduce PSL dosage initially and at 6 months, with some cases achieving remission through injections alone.

W59-2

Identification of predictive factors for glucocorticoid-resistant in polymyalgia rheumatica

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Conflict of interest: None

[Objectives] To clarify factors predicting glucocorticoid (GC) resistance in polymyalgia rheumatica (PMR). [Methods] PMR patients admitted to our hospital between January 2013 and December 2022 were included in this study. Patients with giant cell arteritis were excluded. Clinical findings of the patients were collected from medical records, and clinical characteristics, laboratory findings, and joint ultrasound findings were analyzed. [Results] Thirty-four patients (13 men, 21 women, median age 70.0 years) were enrolled. There were 20 GC-resistant cases (8 men, 12 women) and 14 non-resistant cases (5 men, 9 women). There was no significant difference in serum CRP levels, but 18 GC-resistant cases (90.0%) had high MMP-3 levels (median 219.8 ng/mL) compared with 7 non-resistant cases (50.0%, median 93.95 ng/mL) (p=0.0048). Power Doppler signals in shoulder ultrasound were significantly higher in GC-resistant cases (87.5%; 14 cases) than in non-resistant cases (23.1%; 3 cases) (p=0.0003). Logistic regression analysis revealed that power Doppler signals in shoulder ultrasound were an independent predictor of GC resistance (p=0.0104). [Conclusion] These results suggest that power Doppler signals in shoulder ultrasound may be an indicator of GC resistance in PMR.

W59-3

Exercise rehabilitation therapy to adjust the circadian rhythm may enable pain control with low-dose SNRI administration

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Conflict of interest: None

[Objectives] We examined whether exercise rehabilitation therapy to adjust circadian rhythms would improve pain in 10 patients diagnosed with fibromyalgia, and whether the SNRI dosage could be reduced. [Methods] We compared the progress of evaluation of the WPI and SS in five cases that received only high-dose (30 mg/day) SNRI (duloxetine hydrochloride) and five cases that received exercise rehabilitation therapy to adjust circadian rhythms + low-dose SNRI (10 mg/day) were compared for the evaluation of the progression of the WPI and SS. [Results] In the five cases where exercise rehabilitation therapy was used to adjust circadian rhythms, and low-dose SNRI was administered, the scores for the progression of the values for the evaluation of the WPI and SS improved significantly. In the five cases where high-dose SNRI (30 mg/day) was required, We focused on the circadian rhythm and carried out exercise rehabilitation therapy for one to two months to adjust the rhythm, it was possible to improve pain and reduce the dosage of SNRI, and the evaluation values of the WPI+ SS significantly improved. [Conclusion] Adjusting the circadian rhythm may improve the quality of life of patients with fibromyalgia and reduce the amount of SNRI and other oral medications required.

W59-4

A case of refractory TAFRO syndrome with pulmonary involvement and response to baricitinib

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Conflict of interest: None

A 63-year-old woman was diagnosed with TAFRO syndrome due to fever, thrombocytopenia, ascites, lymphadenopathy, adrenal enlargement, and bone marrow fibrosis. mPSL 60 mg and tocilizumab (TCZ) 500 mg were administered, reducing her fever and CRP. On the 23rd day, she developed cytomegalovirus pneumonia, treated with ganciclovir. TCZ was resumed on the 44th day. However, the fever reappeared with worsening CRP levels, pulmonary opacities, and pleural effusion. TCZ was administered on days 51 and 53 as an exacerbation of TAFRO syndrome. However, CRP and thrombocytopenia continued to worsen. We switched to sarilumab on the 57th day, which improved CRP and pulmonary opacities. However, due to persistent fever and pleural effusion, baricitinib (BAR) 4 mg was initiated on the 64th day. The fever resolved, CRP normalized, platelet counts began to increase, and the pulmonary opacities improved. TAFRO syndrome pathogenesis involves JAK-STAT and mTOR pathways downstream of IL-6 signaling, with mTOR playing a crucial role. Type I interferons, which also activate mTOR in a JAK-dependent manner, may explain the efficacy of BAR. Pulmonary involvement in TAFRO syndrome is rare, and this is the first reported case of successful treatment with BAR, suggesting a potential therapeutic option.

W59-5

A case of TAFRO syndrome during the course of juvenile idiopathic arthritis and refractory to treatment

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Conflict of interest: None

[Introduction] TAFRO syndrome is rare in juvenile onset and has no established treatment. We report a case of TAFRO syndrome during treatment of juvenile idiopathic arthritis (JIA), which was difficult to treat after overcoming initial treatment and leading to outpatient treatment. [Case] A 20-year-old female was diagnosed with JIA at the age of 6 years. She had fever and pancytopenia at the age of 17 years during treatment with methotrexate. Because of worsening renal function and pleural effusion, she was diagnosed with TAFRO syndrome and underwent steroid pulse (IVMP) and hemodialysis. After tocilizumab (TCZ) was introduced, the disease gradually improved. She continues to receive TCZ every 2 weeks in addition to PSL and tacrolimus. Although the clinical symptoms have calmed down to some extent, the IL-6 levels fluctuate between 30 and 300 ng/mL, and when IL-6 levels become high around 100 ng/mL, TCZ is administered every week. [Discussion] This is a rare case of JIA complicated by TAFRO syndrome and it is difficult to improve pathological condition. The treatment of TAFRO syndrome has not yet been established, but there are reports of treatment with rituximab or JAK inhibitors. We consider

whether she needs additional treatment or not based on literature review.

W59-6

Serum soluble interleukin-2 receptor as a potential marker for assessing disease activity in TAFRO syndrome

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Conflict of interest: None

[Objectives] To study the utility of serum soluble interleukin-2 receptor (sIL-2R) in the assessment of disease activity in TAFRO syndrome. [Methods] We retrospectively explored seven cases of TAFRO syndrome in which sIL-2R levels were measured over time. [Results] The median age of seven cases (all male) was 60 years. All cases were treated with a combination of glucocorticoids and immunosuppressive agents or biologics, including cyclosporine, rituximab, and tocilizumab. sIL-2R levels were elevated in all cases at diagnosis (median 3485 U/ml). Following initial remission induction therapy, sIL-2R levels decreased to normal range in five cases (Case 1-5) in correlation with improvement of clinical findings, whereas sIL-2R levels remained elevated in two cases (Cases 6, 7). In Case 6, TAFRO syndrome did not achieve remission, resulting in death due to complications of sepsis. Although Case 7 was initially discharged after the normalization of the inflammatory response and renal function, sIL-2R levels remained elevated, necessitating readmission two months later due to a flare-up. In Case 1, two relapses occurred over 52 months; both involved elevated sIL-2R levels. [Conclusion] Serum sIL-2R levels can serve as a useful marker of disease activity during TAFRO syndrome treatment.

W60-1

Application of metatarsal offset osteotomy of lesser toe to treat hallux valgus with metatarsus adductus

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Conflict of interest: None

Metatarsus adductus (MA) was observed in 45% of bunion cases. It was suggested that varus hindfoot, lateral forefoot loading, and MA are related. However, no correlation was found between cases of MA and postoperative HVA angle, Even in MA cases, dorsal-lateral/abductor offset metatarsal osteotomy of the lateral toes is not always required, but adapt when it is difficult to lateralize the first metatarsal head, and/or when the MAA is abnormally large.

W60-2

Abduction overcorrection of the metatarsophalangeal joint surface is a risk factor for degenerative articular changes in hallux valgus surgery using modified scarf osteotomy

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Conflict of interest: None

[Objective] There are rare cases of pain associated with degenerative changes in the MTPj requiring revision surgery after hallux valgus surgery. We evaluated the X-ray, suspecting postoperative MTPj conformity was the cause of the problem. [Methods] The study included 116 patients underwent hallux valgus surgery (modified scarf osteotomy) between 2020 and 2023 at our institution. The patients were divided into "no change group" and "change group" according to the presence or absence of degenerative changes in the MTPj at the last observation, and the X-ray parameters (HVA, M1M2A, M1M5A, DMAA, DMAA-M1M2A) before and after the operation were evaluated. [Results] There were 87 patients in the "no change group" (71 years, RA: 49) and 29 patients in the "change group" (74 years, RA: 18), and no significant differences in age, BMI and X-ray parameters between the two groups. In the postoperative DMAA-M1M2A (abduction angle of the articular surface of the metatarsal head of the greater toe to the second metatarsal axis), the "no change group" showed -0.5° and the "change group" 3.8°, P value=0.04, but no significant difference in other parameters was found. [Conclusions] In modified scarf osteotomy, abduction overcorrection of the MTPj may be a risk factor for degenerative changes.

W60-3

Comparison of the incidence of early postoperative periprosthetic femoral fractures between collared full HA stems and tapered wedge stems

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Conflict of interest: None

[Objectives] To compare early postoperative periprosthetic femoral fracture rates between tapered wedge (TW) and fully hydroxyapatite-coated (HA) stems, which rank highly in joint registries. [Methods] This single-center, single-surgeon, single-approach retrospective study examined 4,699 primary THAs performed between August 2004 and June 2023. Propensity score matching yielded 1,883 TW stems and 1,883 fully HA-coated stems. The TW group included Accolade and J-Taper stems, while the fully HA group consisted of collared Corail and Universia stems. All surgeries used a supine direct anterior approach. Periprosthetic fractures within 3 months postoperatively were analyzed. [Results] Overall, 15 periprosthetic fractures (0.4%) occurred. The TW group had 13 fractures (0.7%), while the collared fully HA group had 2 fractures (0.1%) (P= 0.007). Both fractures in the fully HA group occurred with Corail stems (1,410 hips) and were greater trochanter fractures. No fractures occurred with Universia stems (1,372 hips). [Conclusion] Collared fully HA-coated stems demonstrated a lower early periprosthetic fracture rate, showing superior fracture prevention compared to TW stems.

W60-4

How long should we withhold JAKi perioperatively in patient with rheumatoid arthritis?

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Conflict of interest: None

[Objectives] The purpose of the current study was to clarify any possible postoperative complications and flares when withholding Janus kinase inhibitors (JAKi) only on the day of surgery for rheumatoid arthritis (RA) cases. [Methods] 96 patients were divided into two groups: Group A (24 patients) stopped JAKi for less than one day during the perioperative period and Group B (72 patients) stopped JAKi for more than two days. [Results] There were no significant difference in demographic and medication data in the two groups. Preoperative ESR values were significantly lower in group A (32 v.s. 54 mm, $p<0.01$), but DAS28-ESR showed no significant difference (3.16 v.s. 3.45). Postoperative wound complications were not significantly different (8.3 vs 12.5%). No flare of joint symptoms was observed in Group A, while 20 patients (28%) in Group B ($p<0.01$). [Conclusion] While a short withholding period raises concerns about postoperative wound complications, a prolonged withholding period raises concerns about joint flaring. However, we observed no change in the degree of complications regardless of the withholding period. Although the

number of patients is small, it demonsctarted the possibility of reducing the perioperative withholding period of JAKi to only the day of surgery.

W60-5

Mid-term outcome of distal tibial oblique osteotomy (DTOO) in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Although advances in drug therapy have made it possible to control the progression of joint destruction in rheumatoid arthritis (RA), there are still some RA patients who require surgery. In RA patients, osteotomy for joint preservation has been contraindicated and joint fusion or joint replacement is commonly performed. We evaluated four cases of distal tibial oblique osteotomy (DTOO) for ankle arthropathy in RA patients. [Methods] Four patients with RA underwent DTOO were included. The mean follow-up period was 47.5 months. We examined pre and postoperative ankle radiographic parameters (TAS, TTS, TCA), ROM of ankle joint, JSSF scale (ankle and hindfoot), SAFEQ, and complications. [Results] The TAS and TTS improved postoperatively, and the TCA improved from 3° of varus to 3.8° of valgus. The average of JSSF scale improved 46.0 to 81.8, and all SAFEQ items showed significant improvement. Two patients developed skin ulcers directly above the implants less than one year after surgery and required implant removal. [Conclusion] In RA patients, joint replacement and joint fusion have been the treatment of choice. However, the fact that joint-sparing DTOO has achieved good mid-term results even in RA patients suggests the possibility of options for ankle arthropathy.

W60-6

Relation between the size of the gap inclination angle in extension and clinical outcoms in MA TKA using the modified gap technique

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Conflict of interest: None

[Objectives] To investigate relation between the size of the gap inclination angle (GA) in extension and clinical outcomes in MA TKA using the modified gap (MG) technique. [Methods] We investigated 72knees of a follow-up of more than 6 months among patients who have undergone MA TKA at our hospital. They were divided to two groups (group A-GA in extension > in flexion: 12 knees, group B-GA in extension < in flexion: 60 knees) and were examined component gap, radiological evaluation, clinical outcomes. [Results] GA in extension in group A showed statistically significant greater than one in group B. Preoperative FTA in group A was more varus angle than one in group B significantly. Both groups showed statistically significant improvement of ROM, JOA score, KOOS, KSS and OKS compared to those before surgery. Postoperative KOOS (symptoms, pain, ADL) in group A was higher than one in group B. But no significant difference was found to increase the amount of KOOS between the two groups. [Conclusion] The size of GA in extension was suggested to have no effect on clinical outcomes in MA TKA using the MG technique.

W61-1

Interim Report of the Avacopan Special Drug Use-results Survey (Post-Marketing Surveillance; PMS) -1st Report-

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Conflict of interest: Yes

[Objectives] We report the interim results of a PMS being conducted to investigate the safety of the selective C5a receptor antagonist avacopan. [Methods] Patients with MPA or GPA who received avacopan were followed for 2 years, and patients' background and the incidence of adverse events (AEs) and adverse drug reactions (ADRs) during the first 6 months of treatment were evaluated as of August 2024. [Results] A safety analysis was performed on 332 cases: female 184 cases (55.4%), 70.2 ± 13.9 years old, MPA 264 cases, and GPA 68 cases. AEs and serious AEs were observed in 148 cases (44.6%) and 65 cases (19.6%), while ADRs and serious ADRs were observed in 117 cases (35.2%) and 48 cases (14.5%), respectively. ADRs related to "Hepatic function disorder", which is set as an important identified risk in the risk management plan, was reported from 64 cases (19.3%) including 25 serious cases, and the timing of onset was from the start of avacopan to day 28 in 6 cases, from day 29 to 56 in 30 cases, from day 57 to 84 in 17 cases, and from day 85 onward in 11 cases. Serious infections (ADR) occurred in 19 cases (5.7%). [Conclusion] It is necessary to conduct laboratory tests for hepatobiliary system and monitor patients' condition closely.

W61-2

Analysis of clinical features in ANCA-associated vasculitis treated with Avacopan: a single center experience

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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] Thirty-two patients [15 (47%) females)] followed since 2022 (up to Aug 2023) were analyzed. [Results] AVA was used in 32 patients with AAV (20 MPO-MPA, 9 MPO-GPA, 3 PR3-GPA), 19 newly diagnosed, 5 relapsing disease and 8 maintenance phases. The mean age was 70.7±11.7 years-old, At the start of AVA, BVAS 13.9±5.1, and 59% of patients had rapidly progressive glomerulonephritis, and 72% had pulmonary disease. Patients who achieved remission, AVA was administrated 11.3±7.9 days after the start of remission treatment. At week 12, 24 and 48, percentages of patients who could discontinue PSL were19%, 23%, 24% and remission rates were 74%, 70%, 60%, respectively. AVA was discontinued in 10 patients (1 death, 4 liver disorder, 4 abdominal symptoms and 1 hospital transfer). In addition, four of the five cases in which more than two years had passed since AVA-administration were still continuing. [Conclusion] These results showed that AVA may be effective and have acceptable safety profiles in relatively elder AAV patients in daily practice.

W61-3

Analysis of ANCA-Associated Vasculitis cases treated with avacopan

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Conflict of interest: None

[Objectives] To investigate the efficacy and safety of avacopan in clinical practice. [Methods] We investigated the clinical course of patients who were started on avacopan for ANCA-associated vasculitis (AAV) by September 2024 at our hospital. [Results] There were 16 patients (7 males) with a median age of 74.0 years: 13 MPA, 4 GPA, 13 MPO-ANCA (+), and 4 PR3-ANCA (+). Combination medications for remission induction therapy included GC and RTX in 14 patients, CY and GC in 1 patient, and

GC only in 1 patient. The timing of initiation of avacopan was during induction therapy in 12 cases and after induction remission in 4 cases. The median duration of medication for avacopan was 198 days. The 6-month continuation rate was 77%, and the relapse-free continuation rate was 69%. Two patients discontinued due to abnormal liver function, and one discontinued due to acute exacerbation of interstitial pneumonia. The median PSL at the start of avacopan was 30 mg (n=6) during induction therapy, which was reduced to 5.5 mg (n=6) at 3 months and 5 mg (n=5) at 6 months. [Conclusion] In this study, GC reduction was achieved faster than in the RemIT- JAV study. Whether the combination of avacopan will allow for more aggressive GC reduction or treatment without GC is an issue for future study.

W61-4

Experience with ANCA-associated vasculitis (AAV) treated with Avacopan without rituximab or cyclophosphamide

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of Avacopan in AAV patients treated with Avacopan without rituximab (RTX) or cyclophosphamide (CY). [Methods] We conducted a retrospective analysis of 9 AAV patients newly introduced with Avacopan in our department from June 2022 to June 2024. The mean age was 76±9.3 year-old, two male and seven female. All patients were microscopic polyangiitis, and positive for MPO-ANCA alone. Two cases were complicated with NTM. The duration of treatment with Avacopan ranged from 1 to 24 months (median 12 months). The concomitant immunosuppressive drug used was azathioprine in one case. Glucocorticoids (GC) were used in all cases, and methylprednisolone pulses treatment were given before Avacopan use in 8 cases. [Results] The BVAS changed from 13±4.7 to 2±2.4 after Avacopan use. None of the patients had relapse after initiation of Avacopan. The GC dose at the start of Abacopan was PSL 30±9.9 mg. The GC dose after Avacopan use was PSL 6.3±1.3 mg at 24 weeks. There were two cases of liver dysfunction due to Avacopan, both of which improved with the use of ursodeoxycholic acid, and the drug could be continued. No case was discontinued due to side effects. [Conclusion] Avacopan may contribute to GC reduction in the treatment of AAV without RTX or CY.

W61-5

Safety of Avacopan in Remission Induction Therapy: A Retrospective Multicenter Cohort Study (J-CANVAS)

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Conflict of interest: None

[Objectives] Avacopan is a novel therapeutic agent that may replace glucocorticoids (GC) in remission induction for ANCA-associated vasculitis. However, real-world safety data from Japan are limited. This retrospective multicenter cohort study evaluated the safety of avacopan during remission induction. [Methods] Patients with new-onset or relapsing microscopic polyangiitis or granulomatosis with polyangiitis between January 2017 and March 2023 were included. We compared serious infection incidence between patients treated with avacopan and those who didn't receive it. Discontinuation cases were analyzed for causes. [Results] A total of 774 patients were included, including those treated before avacopan's approval. The avacopan group (n=16) had a younger median age (72 vs. 75 years, p=0.024), lower GC use (88% vs. 99%, p=0.027), and higher rituximab use (81% vs. 38%, p<0.01). No significant difference in serious infections was found (6% vs. 19%, p=0.33). Univariate Cox regression found no significant link between avacopan and infections. Avacopan was discontinued in 6 cases, with liver dysfunction as the most common reason (4 cases). [Conclusion] Avacopan wasn't significantly linked to serious infections. Liver dysfunction was the most frequent reason for discontinuation.

W61-6

A Study of the Efficacy of Avacopan in 23 Japanese Patients Aged 75 Years or Older with ANCA-Associated Vasculitis: Real World Data from a Single Center

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Conflict of interest: None

[Objectives] To assess the efficacy and safety profile of Avacopan (AVA) in elderly patients diagnosed with ANCA-associated vasculitis (AAV). [Methods] Patients who were initiated AVA for AAV as of May 2024 were selected from electronic medical record data, and those with onset of 75 years of age or older who could be followed for 26 weeks were included. [Results] Twenty-three patients (22 MPA, 1 GPA) were included, with a mean age of 81 years. The median time from onset or recent relapse to AVA initiation was 223 days. At 26 weeks, clinical remission was achieved in 17% of patients, with an AVA continuation rate of 83%. Glucocorticoid use significantly decreased, with 50% of patients reducing their prednisolone dose to 1 mg/day (P=0.03). ANCA levels decreased significantly at 12 weeks. Three patients discontinued due to adverse events. [Conclusion] AVA enabled glucocorticoid reduction or discontinuation in elderly AAV patients, with a continuation rate comparable to the ADVOCATE trial. The lower clinical remission rate may be attributed to delayed treatment initiation and inclusion of maintenance therapy patients. Further investigation into optimal administration timing is warranted.

W62-1

A parent-child case of cryopyrin-associated periodic syndrome that was diagnosed after adulthood

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Conflict of interest: None

[Case 1] 65-year-old female. She came our hospital becouse of chronic diarrhea. She have a history of juvenile idiopathic arthritis (JIA). 13 years ago, She had multiple enlarged lymph nodes and was followed up. She had diarrhea symptoms three months before. cryopyrin-associated periodic syndrome (CAPS) was suspected from the findings of the above. Genetic testing revealed a mutation in the NLRP3 gene, and the diagnosis was confirmed. [Case 2] A 28-year-old female (daughter of case 1) came our hospital complain with repeated fever and skin rash at the recommendation of her mother. Symptoms worsened by cold stimuli. Genetic testing revealed a mutation in the NLRP3 gene, which confirmed the diagnosis of CAPS. [Clinical Significance] Our Department of Rheumatology primarily treats adult patients, resulting in rare encounters with undiagnosed autoinflammatory diseases, particularly those originating in infancy. Nonetheless, there are instances, such as this one, where patients reach adulthood without a diagnosis. The lack of early diagnosis led to a distrust in medical care, necessitating a more meticulous interview process. We recognize the substantial clinical importance of this issue and hereby report it.

W62-2

A case of Schnitzler's syndrome maintaining remission after switching to sarilumab from tocilizumab due to skin rash

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Conflict of interest: None

A 72-year-old man was admitted to the hospital for intermittent fever. He had chronic urticaria, bone pain, multiple lymphadenopathy, high serum CRP, monoclonal immunoglobulinemia, and gallium scintigraphy showed abnormal accumulation in the bones. After excluding malignancy, a diagnosis of Schnitzler's syndrome was made. Forty mg / day of prednisolone (PSL) was started and he went into remission. The patient relapsed with generalized pain and elevated CRP, so the dose of PSL was increased to 40 mg/day and tocilizumab (TCZ) 8 mg / kg IV every other week was added, again leading to remission. But a skin rash accompanied with eosinophilia developed, and TCZ was discontinued on suspicion of drug eruption. After the rash subsided, 200 mg of sarilumab (SAR) was started every other week. [Clinical Significance] Schnitzler's syndrome is an extremely rare disorder characterized by chronic urticaria and IgM monoclonal gammopathy. Although it has been suggested that biologics, especially IL-1 inhibitors, may be most effective, their indications are currently limited in Japan, In this case, TCZ could not be continued due to rash, and the patient was able to maintain remission with sarilumab.

W62-3

Elderly-onset familial Mediterranean fever carrying MEFV exon 10 variants in a Japanese

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Conflict of interest: None

[Background] Familial Mediterranean fever (FMF) is the most prevalent hereditary autoinflammatory disease caused by MEFV gene mutations. FMF in patients carrying MEFV exon 10 variants usually develops at an early age. This is the first case report of an elderly-onset Japanese patient with FMF in the 70s carrying the MEFV exon 10 variant. [Case] A 76-year-old Japanese male patient developed a periodic fever of >38°C lasting 2-3 days, chest pain, and abdominal pain. The fever peaked at 40°C but disappeared within 3 days. Periodic fever was recognized at the age of 71 years at 1-month intervals. He underwent laminoplasty at C4-5 and laminectomy at C6 for cervical spondylotic myelopathy at 75 years of age. Postoperatively, he experiences serositis symptoms, such as chest pain and abdominal pain, in addition to periodic fever. MEFV gene analysis detected compound-heterozygous M694I/E148Q/L110P. Colchicine treatment (0.5 mg/day) improved the patient's symptoms. [Discussion] Even older people aged >70 years develop typical FMF that carries MEFV exon 10 variants, and symptoms may become apparent due to external factors. Therefore, autoinflammatory diseases, such as FMF, should be considered as a differential diagnosis when periodic fever is observed in elderly patients.

W62-4

Nation-wide Prospective Registry of VEXAS Syndrome: Changes in Disease Activity and Incidence of Adverse Events Over a 6-Month Period After Registration

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Conflict of interest: Yes

Objective: To obtain real-world evidence on disease actvity and adverse events in Japanese patients with VEXAS syndrome. Methods: Patients suspected of having VEXAS syndrome across Japan were enrolled in a registry study. Sequencing of the *UBA1* gene was performed using next-generation sequencer. A novel disease activity score, the VEXAS Clinical Activity Index (VEXASCAF), was evaluated at baseline, 3 months, and 6 months. Additionally, AEs, survival rates, CRP levels, and treatment regimens were investigated. Results: Pathogenic variants in the *UBA1* gene were confirmed in 30 cases. All patients were male, with a median age of 73.5 years. VEXASCAF showed a significant decrease from baseline at both 3 and 6 months, although no significant changes were observed in oral prednisolone doses or CRP levels. Based on FRENVEX criteria, only two patients achieved complete remission at 3 months, and none at 6 months. Over the 6-month observation period, 21 AEs were recorded, including 3 deaths, 3 malignancies, 1 thrombosis, and 9 infections. Pulmonary lesions and cervical inflammation were the most common AEs. Conclusion: The current treatment strategies for patients with VEXAS syndrome result in few cases of remission and are associated with a high incidence of adverse events.

W62-5

VEXAS syndrome presenting with severe muscle weakness due to peripheral neuropathy: a case report

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Conflict of interest: None

Introduction: VEXAS syndrome develops various autoinflammatory manifestations and hematological disorders, but the involvement of peripheral nervous system is rare. Here we report a case with severe muscle weakness due to peripheral neuropathy. Case report: A 74-year-old man presented with fever, skin rash, subcutaneous nodules, polyarthralgia, scleritis, mesenteric panniculitis, sensory disturbance of distal extremities and muscle weakness of legs. Creatine kinase was elevated and HLA-A26 was positive. Skin biopsy revealed neutrophilic dermatosis. Autoinflammatory disorder was assumed, so he was treated with PSL 30 mg and colchicine, whose efficacy was limited. Oral aphthous ulcers and colitis newly occurred. Apremilast was cancelled for headache and adalimumab was ineffective. 1 year later, thrombocytopenia and liver injury newly occurred, and he could not walk due to muscle weakness. Nerve conduction study showed axonal polyneuropathy. Sural nerve biopsy showed no evidence of vasculitis. He was diagnosed as VEXAS syndrome because vac-

uoles in myeloid precursor cells and somatic mutation in UBA1 gene were positive. PSL 60 mg and IVIG did not improve muscle weakness. He presented with abdominal pain and died because asystole suddenly occurred. Pathological autopsy was performed.

W62-6

A case of VEXAS syndrome presenting with frequently relapsing polyarteritis nodosa

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Conflict of interest: None

Text: An 82-year-old man was referred to our department of internal medicine because of steroid-resistant panniculitis. Serum CRP was elevated to 19 mg/dl, while autoantibodies including ANCA were not detected. Although the inflammation improved with 30 mg of PSL, it relapsed with PSL less than 20 mg. At the fifth relapse, a skin biopsy was performed for a rash appeared in lower limbs, showing periarterial inflammatory cell infiltration, fulfilling the criteria of polyarteritis nodosa (J Autoimmun. 2014, 48, 84-89). 60 mg of PSL resulted in complete remission, however, there was some difficulty in reducing it. A mutation (p. Met41Val) in the UBA1 gene was detected by analysis at the department of hematology Kanazawa university, indicating that the patient was with VEXAS syndrome. The patient is now treated with combination of PSL, azathioprine, and colchicine. Clinical Significance: VEXAS syndrome is a newly reported syndrome in 2020 (N Engl J Med 2020; 383: 2628). The diagnostic criteria and optimal treatment are unknown. This case shows that patients with recurrent inflammatory symptoms of unknown cause are to be evaluated for VEXAS syndrome.

W63-1

Clinical features of juvenile onset systemic sclerosis with interstitial lung disease from nationwide survey in Japan

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Conflict of interest: None

[Objectives] To investigate the clinical features of juvenile onset systemic sclerosis (jSSc) with interstitial lung disease (ILD) in Japan. [Methods] We analyzed the clinical features of jSSc with ILD based on data from a national survey of jSSc developed before the age of 18 years with a history of medical visits from 2016 to 2020. [Results] Of the 130 patients, 53 (40.8%) cases had ILD, the proportion of female was 79.2%, and the median age at survey and SSc diagnosis (22 and 13 years) was similar to whole patients. The proportion of diffuse cutaneous subset (75.4%) and the frequency of pulmonary hypertension (15.1%) were higher than whole (65.4% and 7.7%, respectively). Autoantibodies were positive for anti-topoisomerase I antibody in 84.9%, anti-centromere antibody in 4.1%. Decreased %VC was observed in 64.1%, decreased DLco in 54.7%, and increased serum KL-6 in 69.8%. Mycophenolate mofetil was the most commonly used immunosuppressant (41.5%) and the most frequently continued (86.3%). Biologics were used in 15 patients (28.3%), with tocilizumab being the most common (7 patients). Antifibrotic agents were used in 15 cases with nintedanib. [Conclusion] The frequency and clinical feature of jSSc with ILD in Japan were similar to adults, and tended to be treated more aggressively.

W63-2

Human Leukocyte Antigen May Influence the Clinical Presentation/ Clinical Course of Juvenile Dermatomyositis

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Conflict of interest: None

[Objectives] Juvenile dermatomyositis (JDM), like adults, has different clinical features depending on the myositis-specific antibodies (MSA), and there may be racial differences. Therefore, we investigated human leukocyte antigen (HLA) in JDM in Japan to identify HLA susceptibility compared to healthy subjects and to investigate the relationship between MSA and clinical features. [Methods] Information on JDM patients attending 6 facilities in Japan was collected and analyzed using SPSS ver 29. HLA testing was performed by GenoDive Pharma, and 11-locus analysis was performed using a next-generation sequencer. [Results] 39 JDM: male 16 (41%), female 23 (59%), age of onset 6.2 years, TIF1γ 12/35 (34.3%), MDA5 7/35 (20%), NXP2 6/28 (21.4%), MSA negative 3/35 (8.6%), MSA not measured 4 cases. Multiple HLA carriage was significantly higher in JDM (odds ratio (OR) 2.4-8.8), including DRB1 locus. In Caucasians, DQA1:05:01 is associated, but no one in this study possessed it. MSA-positive patients had both DPA1:02:02 and DPw5 in 88% of cases. Depending on the HLA, there were differences in the amount of treatment, the presence of relapse, and the frequency of skin symptoms. [Conclusion] HLA may influence the clinical presentation/progression of JDM, and the HLA may determine which MSAs are positive.

W63-3

Key clinical findings indicative of macrophage activation syndrome improvement in patients with systemic juvenile idiopathic arthritis

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Conflict of interest: Yes

[Objectives] To investigate the clinical findings associated with the improvement of macrophage activation syndrome (MAS) in patients with systemic juvenile idiopathic arthritis (sJIA). [Methods] This study included patients with sJIA who developed MAS between 2016 and 2023. Patient characteristics, clinical findings during MAS, and treatment details were obtained from medical records. Improvement of MAS was defined as the date when either glucocorticoid (GC) dose was reduced or biological agents (Bio) were administered. [Results] A total of 23 patients (57% female) experienced 31 MAS episodes. GC was used in 18 episodes, while Bio was used in 16 at the onset of MAS. For first-line treatment of MAS, dexamethasone palmitate was used in 22 episodes, methyl prednisolone pulse therapy in 8, with continuous intravenous CyA given in 18. The median duration from the MAS onset to improvement was 6 days (range: 3-20). On the day of improvement, fever was absent in 30/31 episodes (97%), Plt >181,000/uL in 25/31 (81%), AST <=48 IU/mL in 19/31 (61%), ferritin <=684 ng/mL in 18/31 (58%), and fibrinogen >360 mg/dL in 4/27 (15%). [Conclusion] The absence of systemic symptoms and an elevated platelet count were suggested as key clinical findings indicative of MAS improvement in patients with sJIA.

W63-4

Investigation on the Clinical Characteristics of Enthesitis-Related Arthritis and the Clinical Efficacy of Sulfasalazine

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Conflict of interest: None

[Objectives] Enthesitis-related arthritis (ERA) represents 1.4% of juvenile idiopathic arthritis (JIA) cases. Although treatment often aligns with adult spondyloarthritis protocols, ERA-specific efficacy remains unclear. This study examines Japanese ERA patients' characteristics and optimal treatment. [Methods] We reviewed clinical characteristics and treatment responses in 18 ERA patients treated from April 2015 to March 2023. [Results] The male-to-female ratio was 1.0, with a median onset age of 10 years and a median diagnosis delay of 11 months. Pain was reported in 78% of axial joints, 94% in peripheral joints, and 78% at entheses. HLA-B27 positivity was 9%, and 50% had psychological comorbidities. Salazosulfapyridine (SASP) was used in 89% of cases, with 81% showing response or partial response. Biologic agents (bDMARDs) were used in 78% of cases, with half requiring two or more drugs. [Conclusion] The study found a higher female incidence, lower HLA-B27 positivity, and more psychological comorbidities compared to European data. SASP was effective and often combined with bDMARDs, suggesting it as a viable option for patients needing multiple bDMARDs. Some pain relief was linked to psychological improvement, underscoring the importance of early intervention.

W63-5

Clinical course of childhood-onset Takayasu arteritis

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Conflict of interest: None

[Objectives] To clarify the clinical course of childhood-onset Takayasu arteritis (cTAK). [Methods] Using medical records, we retrospectively reviewed the clinical course of cTAK treated in our hospital from April 2003 to March 2024. [Results] Eighteen patients were included (15 girls, 3 boys). The median age at onset was 9.4 (range: 0.5-13.3) and median observation period 5.2 (range: 1.4-13.9) yrs. Initial symptoms were fever in 14 (78%) cases and abdominal symptoms in five (28%). Initial lesion sites were thoracic aorta in 13 cases, abdominal aorta in nine, branches of the aortic arch in 14, and pulmonary arteries in five. Eleven cases (61%) were HLA-B52 positive. Initial treatment involved glucocorticoids in 17 cases (methylprednisolone pulse therapy in nine), azathioprine in 14 cases, methotrexate in two and cyclophosphamide in one. Three cases required surgical intervention, including initial treatment. Biological agents were used in 10 cases (tocilizumab in seven, infliximab in four). Ten relapses occurred (eight relapses without biologics, and two with biologics). The mean latest dose of prednisolone was 3.75 mg/d (0.097 mg/kg/d). [Conclusion] The use of biologics was more frequent than previously reported. Prednisolone dose could be reduced in many cases.

W63-6

Hydroxychloroquine sulfate therapy for Pediatric Rheumatic Diseases

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Conflict of interest: None

[Objectives] Efficacy of Hydroxychloroquine sulfate (HCQ) therapy for various rheumatic diseases has been reported in other countries. However, HCQ has been approved for only SLE patients in Japan. Here, we report efficacy and safety of HCQ in patients with pediatric rheumatic diseases except for SLE. [Methods] We treated 6 cases with HCQ: 2 of steroid dependent histiocytic necrotizing lymphadenitis (HNL) with recurrences, 3 of juvenile dermatomyositis (JDM) with refractory skin rash, 1 of Sjögren syndrome (SS) with refractory annular erythema on the cheeks. Treatment of HCQ was administrated after obtaining approval from the hospital ethics committee for off-label use in Japan. [Results] Both of 2 HNL patients had no recurrence after starting HCQ therapy. In all three cases of JDM, skin symptoms improved after starting HCQ. In one patient, the rash relapsed after exposure to sunlight, but improved with topical medication alone. In a SS case, the annular erythema on the cheeks disappeared quickly. No side effects such as rash or alopecia were observed in any of the cases. Retinopathy was not observed even in cases of long-term HCQ therapy. [Conclusion] HCQ might be effective and safe for pediatric rheumatic diseases other than SLE. Expansion of insurance coverage for HCQ is desired.

W64-1

Evaluation of Bone Mineral Density and Bone Geometry in Romosozumab-Treated Patients Using HR-pQCT

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Conflict of interest: None

[Objectives] This study investigated changes in BMD and structure in patients treated with Romosozumab (Romo) using HR-pQCT. [Methods] HR-pQCT measurements of the distal radius were analyzed in 74 patients with severe osteoporosis who received monthly treatment with Romo for 12 consecutive months and underwent DXA measurements of bone density at the lumbar spine and proximal femur. Changes in cortical and trabecular bone volume densities and bone structural parameters over time were compared. [Results] The lumbar spine BMD by DXA significantly increased by +10.6% at 6 months and +14.1% at 12 months, and the proximal femur BMD by +1.9% at 6 months and +2.6% at 12 months. HR-pQCT showed that the volumetric BMD of the distal radius tended to decrease in both cortical and trabecular bone, and the trabecular BMD significantly decreased to -1.4% at 6 months and -1.8% at 12 months after the start of treatment. Cortical bone porosity increased by +3.9% at 12 months, trabecular bone BV/TV decreased by -1.2% at 6 months, and trabecular meshwork heterogeneity worsened by +1.9%. [Conclusion] During the first 12 months of treatment, BMD at the lumbar spine and proximal femur measured by DXA significantly increased, while volumetric BMD at the distal radius measured by HR-pQCT decreased.

W64-2

Treatment outcome of one year of romosozumab plus denosumab (two years in total) for women with glucocorticoid-induced osteoporosis

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Conflict of interest: None

[Objective] A retrospective study of the treatment outcomes over a total of 2 years of ROMO + DMB for female GIO. [Methods] The subjects were 12 female GIO patients who started ROMO after July 2019 and completed 2 years of treatment. Patient background, rate of change in BMD, rate of change in BTMs, and new fractures over 2 years were investigated. [Results] Patient background at the start of ROMO: mean age 69.4 years, mean PSL dose 5.3 mg/day, all patients had a history of fragility fractures. The BMD change rate (%) [at 6/12/18/24 months] was lumbar BMD

[3.8/5.8/8.0/10.1] and proximal femur BMD [1.6/2.1/3.0/3.1], with statistically significant increases observed in the lumbar spine from 6 months onwards and in the proximal femur from 12 months onwards. The change rate (%) of BTMs [at 1/6/12/18/24 months] was P1NP [168.4/65.2/21.9/-37.8/-31.0], TRACP5b [-23.7/-15.8/-16.0/-31.6/-32.1]. There was one case of new fracture. [Conclusion] Compared to the FRAME study targeting postmenopausal osteoporosis, the BMD increase rate in this study targeting women with GIO was lower. However, although the number of cases was small, the efficacy of 1 year of ROMO + 1 year of DMB was confirmed in female GIO patients.

W64-3

Incidence of Vertebral Fractures and Spinal Sagittal Alignment in Elderly Rheumatoid Arthritis with and without Denosumab Use

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Conflict of interest: None

[Objective] This study aims to investigate the effect of denosumab use on the incidence of vertebral fractures and sagittal spinal alignment. [Methods] The subjects were 100 rheumatoid arthritis (RA) patients aged 65 years or older. They were divided into three groups: a non-osteoporotic group with femoral neck young adult mean (YAM) values of 80% or higher (31 cases, mean age 72.8 years), a denosumab group with YAM values of 79% or lower using denosumab (31 cases, mean age 74.3 years), and a non-denosumab group with YAM values of 79% or lower not using denosumab (38 cases, mean age 72.9 years). [Results] The number of vertebral fractures at baseline and after three years was 16/34 vertebrae in the non-osteoporotic group (new fracture rate 212%), 51/80 vertebrae in the denosumab group (151%), and 39/96 vertebrae in the non-denosumab group (246%). The SVA change from baseline to three years was 29.0 mm to 34.0 mm (p=0.35) in the non-osteoporotic group, 46.3 mm to 49.1 mm (p=0.82) in the denosumab group, and 42.4 mm to 52.0 mm (p=0.02) in the non-denosumab group, with significant progression in the non-denosumab group. [Conclusion] In elderly RA patients, the use of denosumab may reduce the incidence of new vertebral fractures and the progression of SVA.

W64-4

Relationship between bone mineral density, bisphosphonate treatment, and trabecular bone structure index (Trabecular Bone Score: TBS) in female patients with osteoporosis

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Conflict of interest: None

[Objectives] We conducted a cross-sectional study to determine the relationship between trabecular bone score (TBS), BMD, and bisphosphonate treatment (BP). [Methods] The subjects were 84 female OP patients who underwent measurements of lumbar spine BMD and TBS, of which 31 patients (N) were not receiving OP drug treatment or were receiving active vitamin D, and 52 patients (BP) were receiving BP. We compared patient backgrounds between the N group and the BP group, compared lumbar spine BMD and lumbar TBS, and investigated the correlation between BMD and TBS. [Results] Comparison of patient backgrounds [N/BP]: mean age (years) [72.1/73.9], mean BMD [21.1/21.3], GC administration [7/12]. Mean lumbar BMD (g/cm^2) was 0.810 in the N and 0.958 in the BP, and mean TBS was 1.263 in the N and 1.320 in the BP, with both being statistically significantly higher in the BP. The Pearson correlation coefficient between BMD and TBS was 0.371 in the N and 0.454 in the BP, indicating a statistically significant correlation in both. [Conclusion] Compared to the N, BMD and TBS increased in the BP. Although BMD and TBS have a statistically significant positive correlation, the correlation coefficient was not strong, suggesting the existence of cases in which the evaluations of BMD and TBS diverge.

W64-5

Association of bone mineral density with patient characteristics and treatment in rheumatoid arthritis: analysis of 5-year longitudinal data

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Conflict of interest: None

[Objective] To identify rheumatoid arthritis (RA) patients with rapid declines in bone mineral density (BMD) and explore their characteristics. [Methods] We analyzed RA patients in our hospital over 2 BMD measurements between 2010 and 2023. Based on five-year BMD data, we classified the patients into groups using group-based trajectory models and compared patient characteristics and treatments. [Results] The study included 337 patients with a mean age of 60 years, of which 253 (75%) were female. Lumbar spine BMD trajectories identified three groups with different patterns of BMD: improved/stable (n=53), slow decline (n=197), and rapid decline (n=82). The percentages of patients with denosumab were associated with the groups (47% in improvement/stability, 12% in slow decline, and 6% in rapid decline respectively ($p<0.01$)). The use of other osteoporosis/RA medications was comparable between the three groups. A similar trend regarding osteoporosis medication was observed in the femoral BMD, but the rapid decline group had a higher percentage of patients with glucocorticoid ($p<0.01$). [Conclusion] Denosumab use conversely associated with BMD decline. Future studies should investigate the long-term effects of medication on BMD of each bone, considering various clinical factors.

W64-6

Impact of a Clinical Decision Support System on Osteoporosis Management in Patients on Long-Term Glucocorticoid Therapy

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Conflict of interest: None

[Objectives] Long-term glucocorticoid (GC) use increases fracture risk due to glucocorticoid-induced osteoporosis (GIOP), a preventable and treatable condition. This study aims to evaluate the effect of a Clinical Decision Support System (CDSS) on the prescription rates of osteoporosis medication for GIOP. [Methods] A retrospective cohort study targeting long-term GC users was conducted. The intervention group included CDSS-eligible patients, while the control group comprised rheumatoid arthritis (RA) patients not subject to CDSS. The primary outcome was the osteoporosis medication prescription rate. [Results] After CDSS implementation in July 2017, the prescription rate in the intervention group rose from under 80% to 85%, with a temporary dip between May and September 2018. During the CDSS suspension (2019-2022), the rate continued to rise, reaching 88% after reactivation in November 2022. The control group showed a gradual increase over time. [Conclusion] CDSS implementation led to a temporary increase in osteoporosis medication prescription rates but was not sustained. QI improvement during the suspension may reflect ongoing education, and further enhancement post-reactivation may be due to multifaceted strategies.

W65-1

Glucocorticoid prescribing in patients with lupus nephritis in actual clinical practice: Real World Evidence Using Medical Claims Database (Encore)

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Conflict of interest: Yes

Purpose: Oral glucocorticoids (GC) improve the prognosis of lupus nephritis (LN), but a dose reduction to 5 mg/day (prednisolone equivalent) or less is recommended due to the risk of complications from high doses and prolonged administration. **Methods:** We investigated the actual status of GC prescriptions after initial therapy in Japanese LN patients using the JMDC Claims Database. Patients who received at least two LN diagnoses and oral GC or methylprednisolone pulse therapy of 20 mg/day or more (initial prescription date = Day 1) between June 2016 and March 2023 and who also met a prespecified algorithm were included. **Results:** The median GC prescription dose at baseline was 35 mg/day for 295 eligible patients, and 26.8% of patients had received steroid pulse therapy prior to GC prescription. The percentages of patients with GC prescriptions of 5 mg/day or less were 1.0% at Day 1 and 48.1% at Day 540 (median GC prescription dose: 6 mg/day). The top percentages of concomitant immunomodulators/suppressants prescribed were hydroxychloroquine 46.8%, MMF 41.7%, and tacrolimus 16.9%. On the other hand, flares occurred in 24.7% of patients between Day 181 and 540. **Conclusion:** We described the actual situation of GC prescriptions after initial therapy.

W65-2

Association Between Treatment Patterns and Outcomes in Elderly SLE Patients: An Analysis Using DPC Data

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Conflict of interest: None

[Objective] This study investigates inpatient treatment patterns and outcomes for SLE patients using DPC (Diagnosis Procedure Combination) data, focusing on differences by age and hospital facility case volume, with emphasis on outcomes in elderly patients. [Methods] Using the DPC database, we analyzed 6,174 SLE cases from 571 hospitals in Japan from April 2019 to March 2021. Treatment patterns, length of stay, and readmission rates were assessed by age and facility volume. Patients were grouped as elderly (65+) or non-elderly (18-64), with specific analysis of the frequency and impact of intensive treatments such as GC pulse therapy, intravenous cyclophosphamide (IVCY), rituximab administration, and plasma exchange. [Results] In elderly SLE patients, antimalarial (AM) and immunosuppressive (IM) therapies were limited, with lower use of guideline-recommended triple therapy. Glucocorticoid (GC) monotherapy was frequent, particularly in low-volume facilities. The readmission rate was 21.0%, with elderly patients at higher risk for intensive treatment and readmission. [Conclusion] Our findings highlight distinct treatment patterns in elderly vs. non-elderly SLE patients and suggest the need for standardizing treatment across facilities with different case volumes.

W65-3

Incidence of Serious Infections (SI), Herpes Zoster (HZ), Hepatitis B Virus (HBV) Reactivation, and Malignancy in Japanese Patients with Systemic Lupus Erythematosus (SLE) -A Cohort Study Using a Health Claims Database

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Conflict of interest: Yes

Objective: To investigate the incidence of SI, HZ, HBV reactivation, and malignancy in SLE patients. **Methods:** Using data from Health Claims database in Japan (IQVIA Integrated Claims Data), we selected patients who were diagnosed as having SLE (ICD-10 codes), received SLE medication, and underwent anti-double stranded DNA antibody test during 1 Apr 2017-31 Mar 2021. We calculated the incidence rates (IR), including recurrence, and the 1-year cumulative incidence rates (CIR), and identified risk factors in subgroup analyses. **Results:** Among 10,865 SLE patients (female 83.1%, median age 53.0), the IRs (100 person-years) with/without history of individual complications were 4.80/3.67 for SI, 0.52/0.48 for HZ, 0.37/0.25 for HBV reactivation, 6.98/2.17 for malignancy, respectively. The 1-year CIRs with/without the corresponding history were 7.72%/5.39% for SI, 0.74%/0.70% for HZ, 0.87%/0.58% for HBV reactivation, and 13.29%/2.78% for malignancy. The subgroups with the higher incidence of individual complications were its medical history, severe SLE disease activity at baseline or during follow-up, and glucocorticoid pulse therapy during follow-up. **Conclusion:** Real-world data of the incidence and risk factors for infections of special interest and malignancy are useful for safety management in SLE patients.

W65-4

Association between disease activity and financial toxicity in RA patients using biologics and JAK inhibitors: a cross-sectional study using the NinJa2020 registry

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Conflict of interest: None

[Objective] Biologic and JAK inhibitors (b/tsDMARDs) reduce disease activity and improve quality of life (QOL) in RA patients but increase financial burden. Financial toxicity, the economic strain of treatment, is well-studied in oncology but not in RA. This study examines the link between RA disease activity and financial toxicity in b/tsDMARD users. [Methods] RA patients in NinJa2020 using b/tsDMARDs with available data on out-of-pocket costs and financial toxicity were analyzed. RA disease activity (DAS28-CRP) was the exposure, and financial toxicity (COST) was the outcome. Linear regression adjusted for age, sex, treatment duration, and out-of-pocket costs; missing data were imputed. [Results] Among 618 patients, the median age was 70 years [IQR 57-77], 83.3% were female, and median out-of-pocket expenses were ¥13,395 [IQR 3,176.8-24,613.9]. Median DAS28-CRP was 1.98 [IQR 1.39-2.71] and COST was 25 [IQR 20-28]. Financial toxicity increased with disease activity (1-point DAS28-CRP increase led to 1.81-point COST increase [95% CI 0.28-2.04]). In remission, COST was lower by 2.84 points [95% CI 1.74-3.93]. [Conclusion] In RA patients using b/tsDMARDs, higher disease activity correlates with increased financial toxicity, highlighting the need to consider financial impact in care.

W65-5

Sustained remission in rheumatoid arthritis patients from NinJa database

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Conflict of interest: None

Objective: To analyze the sustainability of remission in clinical settings and clarify the predictors for sustained remission. Methods: Among the patients registered in NinJa, the data of patients who were in remission in 2003 (group A), 2010 (group B), and 2017 (group C) were analyzed. The Kaplan-Meier curves were used to assess the survival rate of remission. Results: Number of patients were 427 (12.8%) in group A and 1568 (28.1%) in group B, and 3758 (39.9%) in group C. The average remission time was 2.93, 3.18, and 3.45 years respectively. Survival rate was significantly higher when patients were male, disease duration < 5 years or without NSAIDs in group A. In group B and C, survival rate was significantly higher when patients were male or under 65 years, those without NSAIDs or glucocorticoids, and mHAQ ≦ 0.5. Especially, the survival rate in the patients treated with MTX, biologics or Jak inhibitors in the group C was significantly longer. The survival rate decreased as Steinbrocker stage and

class advanced. Conclusion: The average duration of remission was around 3 years and recently induced remission tended to sustain longer. MTX and Biologics/Jak inhibitors prolonged the survival rate of remission period.

W65-6

ACPA as a hospitalization risk factor of patients with RA

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Conflict of interest: None

[Background and Objectives] The role of ACPA as a predictor of hospitalization remains ambiguous, prompting the conduction of this study. [Subhects and Methods] This cross-sectional study utilized data from NinJa 2022. Participants were categorized into three groups based on ACPA status. The primary outcome measured was overall hospitalization, while the secondary outcome focused on cause-specific hospitalizations. Analyses were adjusted for variables including patients' backgrounds and medications, employing logistic regression analysis. [Results] 6,384 had available data on ACPA and hospitalization. The median age was 70.5 years. All hospitalizations were 829 (13%). The main reasons for hospitalization were infection (143), management of RA (112), and joint surgery (84). Logistic regression analysis revealed no significant association between positive ACPA and overall hospitalizations. However, in secondary outcomes, ACPA positivity exhibited a significant correlation with hospitalizations due to infections. [Discussion and Conclusion] While no correlation was found between ACPA and overall hospitalizations, this investigation explored the relationship between ACPA positivity and hospitalization. ACPA positivity suggests the need to pay attention to serious infections.

W66-1

The relationship between B cell-related cytokine profiles and anti-TRIM21 antibody positivity in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] This study investigated the serum cytokine profile of anti-TRIM21 antibody-positive SLE patients to clarify mechanisms of increased B cell activation. [Methods] Serum samples from the LUNA SLE patient registry were analyzed. Anti-TRIM21 antibody titers were measured by ELISA, and B cell-related cytokines were assessed via multiplex immunoassay. [Results] Of 238 samples, 133 (56%) were anti-TRIM21 antibody-positive. No significant differences were found in age, sex, disease duration, or SLEDAI scores. The antibody-positive group showed higher IgG levels (1,530±519 vs. 1,270±478 mg/dL, p<0.001), higher pleuritis frequency (17.1% vs. 6.25%, p=0.016), and lower anti-DNA antibody frequency (66.7% vs. 82.2%, p=0.013). sCD40L levels were higher in the anti-TRIM21 antibody-positive group compared to the negative group (15.2 ±29.9 vs. 14.1±18.7 pg/mL). Multivariate analysis adjusting for age, sex, disease duration, immunosuppressant use, steroid dosage, and SLEDAI confirmed a significant association with antibody positivity (p=0.042). [Conclusion] Anti-TRIM21 antibody positivity in SLE was linked with elevated sCD40L and IgG, suggesting a role for sCD40L in the link between anti-TRIM21 positivity and B cell activation.

W66-2

Predicting the interferon signature in SLE from routine clinical test items

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Conflict of interest: None

[Objectives] To develop an easy method for estimating the IFN signature on the basis of routine clinical test items. [Methods] Gene expression was analyzed via next-generation sequencing of 36 peripheral blood samples from 21 SLE patients. Genes related to Type-1, Type-2, and Type-3 IFNs were selected, and the IFN score was calculated by summing the Z scores of these genes. A total of 129 clinical tests were evaluated, and multiple regression analysis was employed to identify the tests that best predicted the IFN score. [Results] Compared with those of healthy controls, all IFN scores were significantly elevated in SLE. A positive correlation was observed between the IFN score and neutrophil count, whereas a negative correlation was found with the lymphocyte count. The neutrophil/lymphocyte ratio (NLR) showed the strongest correlation, with the correlation coefficients for the Log_2NLR being significant for Type 1 IFN (R^2=0.57, P=1.74e-07), Type 2 IFN (R^2=0.36, P=1.74e-07), and Type 3 IFN (R^2=0.57, P=1.32e-07). [Conclusion] ANI has demonstrated effectiveness in SLE patients with high IFN signatures. The NLR is strongly correlated with all types of IFN signatures. NLR is easily calculated in clinical practice and a valuable tool for estimating IFN signatures.

W66-3

The Investigation of the Correlation Between Soluble Immune Checkpoint Molecules and SLEDAI

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Conflict of interest: Yes

[Objectives] To evaluate the utility of soluble immune checkpoint molecules (CM) as objective markers for disease activity in systemic lupus erythematosus (SLE). [Methods] Plasma and blood samples from healthy controls (HC) and SLE patients were used. Plasma levels (pg/mL) of sPD-1, sPD-L1, and sCTLA4 were measured. 1. CM levels in HC and SLE patients were compared (Mann-Whitney U test). 2. Correlations between

CM, clinical parameters, and SLEDAI were analyzed (Spearman's rank correlation). 3. Multiple regression was used to develop a predictive model for SLEDAI. [Results] Fourteen HC samples (7 females; median age: 48) and 28 SLE samples (26 females; median age: 44) were included. The median SLEDAI was 3 (min: 0, max: 36), with 75% receiving PSL and 86% testing positive for anti-DNA antibodies. 1. In HC vs SLE, sPD-1 was 117 vs 281 (p=0.0007), sPD-L1 was 148 vs 217 ($p < 0.0001$), and sCTLA4 was 1.3 vs 1.7 (p=0.07). 2. Correlation with SLEDAI: sPD-1 (0.744, <0.0001), sPD-L1 (0.7863, <0.0001), sCTLA4 (0.5705, <0.0001); 3. A predictive model for SLEDAI was developed using sPD-1 and sPD-L1 (independent of each other) (R^2: 0.74, $p < 0.0001$). [Conclusion] CMs showed strong correlations with SLEDAI, confirming their potential as objective activity markers.

W66-5

Clinical characteristics and treatment patterns of systemic lupus erythematosus patients with serologically active but clinically quiescent disease: the multicenter ANSWER-SLE cohort study

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Conflict of interest: None

[Objective] Compare the clinical characteristics and treatment patterns between serologically active, clinically quiescent (SACQ) and serologically quiescent, clinically quiescent (SQCQ) states in SLE patients. [Methods] We extracted cases meeting SACQ and SQCQ criteria from the ANSWER-SLE cohort, including patients registered since 2019. SACQ was defined as low complement levels and/or positive anti-dsDNA antibodies, cSLEDAI=0, prednisolone ≦7.5 mg/day, with persistence of these criteria for ≧3 months. [Results] Of the 1,344 SLE patients, 132 were SACQ and 319 SQCQ. Compared to the SACQ group, the SQCQ group had a significantly higher proportion of anti-Sm antibody positivity, tacrolimus (TAC) use, along with lower PGA scores (p=0.04, 0.0002, <0.0001). Multivariable analysis showed absence of TAC and mycophenolate mofetil (MMF) was significantly associated with SACQ (OR: 2.89, p=0.0001; OR: 1.98, p=0.03). At 1 year, 66% SACQ group and 77% SQCQ group achieved CQ. The SACQ patients who CA at 1 yeat had higher baseline SDI scores (p=0.0405). The optimal SDI cutoff predicting CQ at 1 year was 2 (AUC 0.64, sensitivity 58%, specificity 64%). [Conclusion] The absence of TAC and MMF use is a risk factor for SACQ. SDI score ≦2 at baseline may predict CQ at 1 year even in SACQ patients.

W66-6

Factors Associated with Achieving Remission from LLDAS to DORIS: The ANSWER-SLE cohort

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Conflict of interest: Yes

[Objective] This study aimed to identify the factors leading to DORIS remission from LLDAS. [Method] Among patients enrolled in the ANSWER-SLE cohort, 780 patients who achieved LLDAS for the first time in the cohort were included. The primary outcome was whether or not DORIS remission was achieved 12 months after achieving LLDAS. We compared patient characteristics between those who achieved remission and those who did not, using univariate and multivariate analyses. [Results] 180 eligible patients remained. Of these, 27 patients achieved DORIS remission, while 153 did not. Univariate analysis revealed that lupus nephritis (LN) at diagnosis was associated with failure to achieve DORIS remission. In logistic regression analysis adjusted for sex and disease duration, a lower SLEDAI-2K score at LLDAS achievement (median 2 vs. 3, OR 0.74, p=0.0393) and absence of LN (OR 0.34, p=0.0333) were associated with DORIS remission at 12 months. Additionally, maintaining LLDAS for at least 9 months was associated with DORIS remission at 12 months (p=0.0394). [Conclusion] Achieving a lower SLEDAI-2K score at LLDAS, absence of lupus nephritis, and sustaining LLDAS for 9 months were significant factors associated with achieving DORIS remission 12 months after the initial LLDAS achievement.

W67-1

Relationship Between Achievement of LLDAS After Remission Induction Therapy and Long-Term Prognosis at 7 Years in Systemic Lupus Erythematosus

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Conflict of interest: Yes

[Objectives] Achieving low disease activity state (LLDAS) within 12 months after remission induction therapy for systemic lupus erythematosus (SLE) is linked to reduced flare risk. This study aimed to investigate the impact of LLDAS on the long-term outcomes. [Methods] We analyzed 41 active SLE patients who began remission induction therapy between 2015 and 2017, classified with a BILAG 1A or 2B. Patients were followed for 7 years to examine the relationship between achieving LLDAS within 12 months and flare, DORIS remission, and the SLICC/ACR damage index (SDI). [Results] The mean age was 41.6 years, with a disease duration of 8.2 years and the mean SLEDAI was 17.5. LLDAS within 12 months was achieved by 51.2%, with flare rates of 48.8% over 7 years. The DORIS remission at 7 years was 73.2%, with a 24.4% of increase in the SDI. The group achieving LLDAS exhibited a higher DORIS remission rate compared to those without LLDAS (p=0.086). Patients experiencing flares had a lower DORIS achievement rate at 7 years (p=0.015), particularly those with severe flares after achieving LLDAS, who showed a higher SDI increase (p=0.060). [Conclusion] Patients with SLE achieving LLDAS within 12 months after remission induction therapy and without flares have a higher DORIS remission rate at 7 years.

W67-2

Do SLE patients continue to experience symptoms even during LLDAS achievement?: The SLE-PROCTCAE Study

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Conflict of interest: None

[Objective] While achieving LLDAS is considered one of the treatment goals, there are few reports on symptoms during LLDAS achievement. Using our developed PRO-CTCAE app for SLE patients, we investigated the prevalence of symptoms while achieving LLDAS. [Methods] This was a prospective observational study. SLE outpatients from 5 facilities used a smartphone app to complete 54 PRO-CTCAE items every two weeks for 6 months. We calculated composite grades and defined symptoms as present when Grade 2 or higher appeared during the course. For analysis, we calculated the prevalence of each symptom, divided patients into LLDAS achieved/non-achieved groups, calculated the proportion of each symptom. [Results] The study included 170 patients with a mean age of 46.2 years, 91.7% female, and mean SLEDAI of 3.9. LLDAS was achieved in 98 cases (57.7%). The top three symptoms with Grade 2 or higher were headache (58.8%), irregular bleeding (53.5%), and pain (52.4%). Nightmares, hand tremors, skin fragility, constipation, diarrhea, acne, mood depression, and sadness were significantly lower in the LLDAS achievement group. [Conclusion] The most common symptoms during treatment were headache, irregular bleeding, and pain.

W67-3

A study of factors related to Definitions of Remission in SLE (DORIS) remission in patients with systemic lupus erythematosus at our hospital

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Conflict of interest: None

Purpose: DORIS remission is one of the methods to evaluate disease activity in SLE. The purpose of this study was to investigate whether there are differences in patient backgrounds and medications used between patients who achieved DORIS remission and those who did not, and to identify factors associated with DORIS remission. Methods: Among 280 patients with SLE who visited our hospital between April and September 2024, 280 patients on maintenance remission therapy with glucocorticoids below 0.2 mg/kg/day were divided into two groups: patients who achieved DORIS remission and patients who did not achieve remission. Patient background (n=280) was as follows: mean age: 52.0±15.0 years, females: 252. The odds ratio (95% CI) between the two groups was 0.22 (0.08-0.60 P=0.003) for men and 0.46 (0.25-0.82 P=0.009) for HCQ use, while the odds ratio (95% CI) between the two groups was 4.57 (1.67-12.50 P=0.003) for men and 2.19 (1.22-3.95 P=0.009) for HCQ use. The results showed that the use of HCQ was associated with the achievement of DORIS remission in patients with SLE. Conclusion: The use of HCQ and male patients with SLE were considered to contribute to the achievement of DORIS remission.

W67-4

Association of dietary factors, physical function, and subjective fatigue with health-related quality of life in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] This study aims to investigate the contribution of dietary factors to health-related quality of life (HRQOL) in patients with SLE, including their association with physical function and subjective fatigue. [Methods] We conducted a cross-sectional survey of SLE patients. Dietary intake was assessed by brief-type self-administered diet history questionnaire, physical function by the five times sit to stand test (FTSST), fatigue by the FACIT-F Scale, and HRQOL by the EQ-5D-5L, respectively. The contribution of dietary factors to these factors was tested by multiple regression analysis adjusting for some basic patient demographics, and path analysis. [Results] A total of 110 patients (mean age 48 years, 84% female) were included in the analysis. In multiple regression analysis, the intake of beans contributed to the FTSST (β=-0.30, p=0.002) and to the FACIT-F Scale score (β=0.18, p=0.07), but did not contribute significantly to the EQ-5D-5L score (β=0.11, p=0.22). In the path analysis, the standardized direct effect of beans on the EQ-5D-5L score was 0.02, and the standardized indirect effect of beans → FTSST → Facit-F Scale score → EQ-5D-5L score was 0.18. [Conclusion] Bean consumption may contribute to HRQOL via physical function and subjective fatigue in SLE patients.

W67-5

Is Fatigue During SLE Treatment Associated with Disease Flares?: The SLE-PROCTCAE Stud

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Conflict of interest: None

[Objective] Using our newly developed PRO-CTCAE collection app for SLE patients, we investigated the relationship between fatigue and disease flares. [Methods] The study included outpatients from five institutions between October 2021 and May 2023, using consecutive sampling. The exposure was fatigue. Using the application, PRO-CTCAE data was collected for six months, and “presence of fatigue” was defined as a composite Grade 2 or higher on the fatigue item. The outcome was defined as SLE flare, characterized by clinical organ damage deterioration requiring consideration of treatment modification or addition. Analysis was performed using logistic regression, adjusting for age, sex, PSL dose, and immunosuppressant use. [Results] The study included 164 patients with a mean age of 46.4 years, mean disease duration of 15.4 years, and mean SLEDAI of 3.9. Grade 2 or higher fatigue was observed in 62 patients (37.8 %), and disease flares occurred in 19 patients (11.6%). Logistic regression analysis showed no significant association between fatigue and disease flares (odds ratio 0.54, 95% confidence interval [0.17, 1.63]). [Conclusion] While fatigue was observed in nearly 40% of SLE patients, it showed no significant association with disease flares. We plan to conduct a longitudinal study.

W67-6

Glucocorticoid Dose and Risk of Organ Damage in Young Systemic Lupus Erythematosus Patients: From the PLEASURE-J Study

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Conflict of interest: None

[Objectives] Lupus Low Disease Activity State (LLDAS) for systemic lupus erythematosus (SLE) defines a prednisolone (PSL) dose ≦7.5 mg/day as one criterion. However, organ damage has been reported at fewer dose. This study aimed to investigate the relationship between GC dose, organ damage and remission in SLE patients. [Methods] SLE patients aged 18-40 years from the PLEASURE-J were included. Patients were divided into two groups based on their PSL dose one year after treatment initiation: a low-dose group (≦7.5 mg/day) and a high-dose group (>7.5 mg/day). The primary outcome was SLICC/ACR Damage Index (SDI) increase, and secondary outcomes were SLEDAI ≦4 and PGA ≦1. [Results] A total of 153 patients were included, with 40.5% in the high-dose group. PSL dose decreased in recent years (p-trend=0.006). Propensity score matching showed no significant difference in SDI increase (high-dose 22.0%, low-dose 12.6%; HR 1.75, 95% CI 0.73 to 4.22; p=0.21). Although not statistically significant, lower dose of PSL had consistently lower SDI increase risk. No significant differences were found in secondary outcomes. [Conclusion] While no significant differences were observed, there may be a trend toward a reduced risk of SDI increase with lower PSL dose, warranting further studies.

W68-1

Elucidation of Factors Influencing Spinal Ankylosis in Patients with Axial Spondyloarthritis (Encore presentation)

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Conflict of interest: None

[Objectives] Spondyloarthritis includes conditions such as ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Recent therapeutic agents have enhanced the control of inflammation, yet they do not consistently stop the axial progression. This study aimed to identify factors influencing the progression of axial lesions over a two-year period in Japanese patients. [Methods] This retrospective and cross-sectional study included 47 axial spondyloarthritis patients. Spinal lesions were assessed using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Patients were categorized into progressive and non-progressive groups based on changes in their mSASSS scores. Various clinical parameters were analyzed for correlation with ankylosis progression. [Results] The study found that modified Health Assessment Questionnaire (mHAQ) scores were associated with disease progression. The baseline mSASSS was another significant factor, underscoring the importance of early detection and management. [Conclusion] This study showed that patient-reported outcomes and baseline mSASSS scores are crucial for assessing axial spondyloarthritis progression. This underscores the need for a comprehensive treatment strategy that addresses both clinical indicators and patient-reported outcomes.

W68-2

Differences in Clinical Characteristics between HLA-B27 Positive and Negative Patients with Ankylosing Spondylitis: Insights from the Tsurumai Axial Spondyloarthritis in Musculoskeletal Study (T-ASK Study)

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Conflict of interest: None

Objective: HLA-B27 is a genetic factor for ankylosing spondylitis (AS), but its prevalence is lower in Japan. Studies report clinical differences between HLA-B27 positive and negative AS patients. This study compares clinical features between HLA-B27 positive and negative Japanese AS patients. **Methods:** We analyzed 53 Japanese AS patients diagnosed from 2005 to 2023 who underwent HLA-B27 testing from 81 patients in the T-ASK study. **Results:** Of the patients, 34 (64%) were HLA-B27 positive. The mean age was 41.5±12.4 years for the positive group and 42.1±19.2 years for the negative group, with 76% and 68% males, respectively. Disease duration was 19.4±12.1 years for the positive group and 10±8.9 years for the negative group. Onset age was younger in the positive group (21.9±9.9 vs. 31.5±17.3 years, P<0.05), and uveitis was more common (32% vs. 11%, P<0.05). Family history and peripheral joint symptoms were more frequent in the positive group. No differences were found in psoriasis or inflammatory bowel disease. **Conclusion:** HLA-B27 positive AS patients had a younger onset age, higher uveitis prevalence, and trends of higher family history and peripheral joint symptoms. Clinical differences between HLA-B27 positive and negative AS patients were observed in the Japanese population.

W68-3

Characteristics of ankylosing spondylitis with ankylosis of head-vertebral joints

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Conflict of interest: None

[Objective] To examine the characteristics of patients with ankylosing spondylitis (AS) who have ankylosis in the head-vertebral joints (HVJ). [Methods] This study included in 26 patients who were available to assess 24 joints on both sides of the 1st-12th HVJ using CT. Ankylosis was considered to be present if partial or complete bony bridging was in HVJ. [Results] 19 patients (73%) had ankylosis in one or more of the 24 HVJ. Patients with HVJ ankylosis had a longer disease duration than those without (with vs. without=15.2±10.3 years vs. 6.2±1.9 years, p=0.032). Patients with HVJ ankylosis tended to be more positive for HLA-B27 than those without (with vs. without=66.6% vs. 8.3%, p=0.061). All 14 patients with sacroiliac joint ankylosis had one or more HVJ ankylosis. In addition, four patients of 12 patients without sacroiliac joint ankylosis had one or more HVJ ankylosis. [Conclusion] AS patients had frequently HVJ ankylosis. AS patients with HVJ ankylosis had a longer disease duration and tended to be a higher prevalence of HLA-B27 positivity. HVJ ankylosis occurred even in patients without sacroiliac joint ankylosis. Imaging evaluation of the HVJ as well as the sacroiliac joint should be performed in AS patients.

W68-4

Association of sacroiliitis findings on MRI with clinical features in patients with low back pain

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Conflict of interest: None

[Objectives] To clarify the association between MRI findings of sacroiliitis (MRI positive) and clinical features in patients with low back pain (LBP). [Methods] The patients who underwent MRI for LBP, were enrolled. 1) For MRI positive cases, the fulfillment rate of diagnostic guidance for nr-axSpA in Japan (nr-axSpA criteria) was analyzed. 2) We divided into 2 groups according to MRI positive or not, and compared symptoms and blood findings. 3) We analyzed the relationship between MRI findings and scores of questionnaire methods (VAS method, JOABPEQ, ODI, EQ-5D). [Results] 32 cases (male: 12/female: 20), age: 46.2±15.6 years, clinical diagnoses were axSpA: 11 (nr-axSpA: 6, AS: 3, PsA: 2), PAO: 3, and others: 18. 1) The rate of MRI positive: 53.1% (17/32 cases), fulfillment rate of nr-axSpA criteria in MRI positive: 47.1% (8/17 cases). 2) Fulfillment rate of IBP criteria was not significantly different between the 2 groups. CRP was significantly higher in MRI positive (0.16±0.24 vs 0.80±1.29, P=0.02). 3) MRI positive was weakly correlated with standing LBP-VAS (rs= -0.4, P=0.02), and similar trends were observed in other items related to pain during movement. [Conclusion] MRI positive significantly increase CRP, and may affect the score of pain during movement by questionnaire method.

W68-5

Safety and effectiveness of ixekizumab in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: postmarketing safety study in clinical use in Japan

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Conflict of interest: Yes

[Objectives] We assessed the safety and effectiveness of ixekizumab in Japanese patients with ankylosing spondylitis (AS) or non-radiographic axial spondyloarthritis (nr-axSpA). [Methods] In this multicenter postmarketing safety study for ixekizumab (June 2020-May 2024), demographics, adverse events (AEs), and overall improvement (physician-assessed) were collected for 96 weeks. [Results] A total of 39 patients were registered and, of these, 29 gave consent for publication (21 with AS; 8 with nr-axSpA). Mean age was 53.7 (SD: 11.8) years, 16 patients were male, mean disease duration was 8.7 (SD: 8.9) years. HLA-B27 was tested in 17 patients; 5 were positive. Fifteen (51.7%) patients discontinued ixekizumab treatment (7 due to insufficient effect, 2 due to AEs of injection site pain/reaction). AEs and adverse drug reactions (ADRs) occurred in 14 (48.3%) and 4 (13.8%) patients, respectively; inflammatory bowel disease was not observed. No serious AEs/ADRs were reported. At Week 96, 8.3% (1/12) and 75.0% (9/12) of patients were assessed as remarkably improved or improved, respectively. [Conclusion] Up to 96-weeks of treatment, the safety profile of ixekizumab was consistent with prior reports and the findings based on overall improvement suggested the effectiveness of ixekizumab.

W68-6

Efficacy and Safety of Upadacitinib Through 2 Year in Patients with Active Non-Radiographic Axial Spondyloarthritis: Post-hoc Analysis of Sub-group Similar to the Diagnostic Guidance in Japan

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Conflict of interest: Yes

[Objectives] 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] In the SELECT-AXIS 2 nr-axSpA study, pts who completed the 52-week (wk) placebo (PBO)-controlled period received open-label UPA 15 mg for up to a further 52 wks. 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, 212 pts met the Japan nr-axSpA diagnostic guidance-like criteria. In this sub-group, ASAS40 response rates were maintained from wk52 to wk104 in the continuous UPA group (As observed with non-responder imputation [AO-NRI] analyses; 61.9% at wk104) and improved through wk104 in the group those who switched from PBO to UPA at wk52 (AO-NRI; 51.0% at wk104). Rate of treatment-emergent adverse events was 207.3 events/100 pt-years in pts who received ≧1 dose of UPA and consistent with overall population. [Conclusion] UPA showed consistent efficacy and similar safety profile in sub-group who met the Japan nr-axSpA diagnostic guidance-like criteria.

W69-1

Factors affecting the discordance between the patient's and physician's global assessment in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] To investigate the factors influencing discordance between patient global assessment (PtGA) and physician global assessment (PhGA) in patients with rheumatoid arthritis (RA). [Methods] Questionnaires were obtained from 817 consenting cases, PtGA and PhGA were available in 788 cases and included in the analysis. Discordance and accordance were defined as a difference of 30 point or more and a difference of less than 10 points between PtGA and PhGA, respectively. [Results] Discordance group were 108 patients (13.7%) and accordance group were 509 patients (64.6%). Discordance group tended to be older, more female, have a longer disease duration, higher PtGA, PhGA and tender joints. Multivariate analysis showed significant associations with HAQ (OR: 2.30, 95%CI: 1.21-4.38), patient satisfaction (OR: 2.69, 95%CI: 1.60-4.52), and total RAID score (OR: 1.75, 95%CI: 1.35-2.28). Within the RAID items, significant associations were found for pain and sleep. [Discussion] Significant associations with discordance were found with HAQ, patient satisfaction, and RAID scores, particularly for pain and sleep. The findings suggest that difficulties in daily living due to such symptoms may influence discordance, those might be difficult for healthcare providers to fully understand in a clinical setting.

W69-2

Characteristics of rheumatoid arthritis patients with discrepant patient reported outcomes

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Conflict of interest: None

[Background] In the treatment of rheumatoid arthritis (RA), there is often a discrepancy between patient-reported outcomes and physician assessment. [Objectives] To investigate the factors in RA patients with normal CRP and ESR and no swollen joints who have poor patient VAS. [Methods] 2159 RA patients were registered in the Akita Orthopedic Rheumatology Group (AORA registry) in 2019, and 295 cases with normal CRP and ESR and no swollen joints were selected. The patients were divided into two groups: VAS>30 (high VAS group) and VAS≦30 (low VAS group). [Results] The mean age was 63.8 years. There were 81 patients (27.5%) in the high VAS group and 214 patients (72.5%) in the low VAS group. When the two groups were compared, disease duration (p=0.002), stage (p=0.001), class (p=0.001), MMP-3 (p=0.005), HAQ (p<0.0001), and number of tender joints (p=0.002) were all higher in the high VAS group. [Discussion] The factors of this discrepancy are advanced joint destruction, functional impairment and high MMP-3 levels. In such cases, orthopedic approaches such as surgery should be considered. [Conclusion] In RA patients with normal CRP and ESR and no swollen joints, those with poor patient VAS had long disease duration, advanced joint destruction and high MMP-3 levels.

W69-3

Association of Early Remission on Clinical and Patient-reported Outcomes in Patients with Rheumatoid Arthritis: Post-hoc Analysis of Data from the SELECT-COMPARE Study (ENCORE)

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Conflict of interest: Yes

Objectives This study assessed the association of early remission (DAS28-CRP<2.6 at week (wk) 12) with outcomes in RA patient (pts) with inadequate response to methotrexate, treated with upadacitinib or adalimumab. Methods Post-hoc analysis used SELECT-COMPARE data. Mean change from baseline and the proportion of pts who reached MCID and normative cut-off scores were evaluated for pain VAS, HAQ-DI, SF-36 PCS and MCS, FACIT-F, PtGA, PhGA, swollen and tender joint counts. Outcomes in early remission vs non-remission pts were compared at wk26, 48, 156 and 252. Differences in mean change from baseline and adjusted odds ratios (aOR) were compared. Results 28% (247/885) reached early remission at wk12. Significantly greater improvements from baseline were observed for all outcomes at wk26 in pts who achieved early remission. Early remission was associated with significantly greater odds (aOR range: 2.9-5.1) of achieving meaningful improvements in HAQ-DI, FACTI-F, pain, PtGA, and SF-36 PCS for at least 48 wks. Early remission pts had significantly greater odds (2.4-3.5) of achieving meaningful improvements in HAQ-DI, pain and PtGA for a minimum of 252 wks. Normative values showed similar trends. Conclusion Achieving remission early was associated with better health outcomes in patients with RA.

W69-4

Cluster analysis identifies the differential impact of disease activity and severity on functional status and patient satisfaction in rheumatoid arthritis: FRANK registry

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Conflict of interest: None

Objective: This study aimed to investigate the impact of disease activity and severity on functional status and patient satisfaction in rheumatoid arthritis (RA) using cluster analysis on FRANK registry data. Methods: 3,619 RA patients were grouped using hierarchical and k-means cluster analyses based on age, physician's global assessment (PhGA), patient's pain assessment (PtPA), and Steinbrocker stage. Clusters were evaluated for differences in functional status (mHAQ), quality of life (EQ5D), and patient satisfaction. Results: Five distinct patient clusters were identified. Clusters 1 and 2, with lower disease activity and severity, showed better functional outcomes and higher satisfaction. Cluster 3, with less activity and more severity, had significant joint damage despite controlled inflammation. Cluster 4, with patient-physician discordance in disease activity, had a more pronounced negative effect on satisfaction. Cluster 5, with more activity and moderate severity, had the poorest outcomes in functional status, quality of life, and satisfaction. k-Means clustering produced similar results to hierarchical clustering. Conclusion: Identifying distinct patient phenotypes may guide tailored interventions to improve treatment satisfaction and long-term outcomes.

W69-5

Wrist-worn Wearable Device Data Associated with Rheumatoid Arthritis Disease Activity: AMED RA IoT prospective study for digital biomarkers

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Conflict of interest: Yes

[Objectives] To clarify the relationship between wearable device data and rheumatoid arthritis (RA) disease activity. [Methods] RA Patients wore a Fitbit wristwatch-type wearable device for 3 months, and RA-related PRO was recorded daily on a smartphone. Physicians examined participants every month for 3 months. Data on number of steps, METs, heart rate, and sleep were obtained from the Fitbit. Relationship between Fitbit data and CDAI were evaluated. [Results] A total of 129 subjects completed the 3-month study. The mean age was 55±13 years, mean disease duration was 8.5±10.3 years, CDAI was 13.5±10.7. Higher number of steps was associated with lower CDAI (r=-0.28). Higher heart rate during sleep (r=0.23), sympathetic nerve hyperactivity (r=0.33), and a tendency to increase heart rate (r=0.32) were associated with higher CDAI. Associated with CDAI were CRP (r=0.33; P<0.001) and ESR (r=0.32). [Conclusion] Steps and heart rate-related data acquired by wearable devices correlated with RA disease activity, providing a new digital biomarker (dBM) for estimating RA activity from wearable device-only data. The correlation coefficients between CDAI and CRP and ESR, which are blood collection indices conventionally used in daily practice, were equivalent to the dBM obtained in this study.

W69-6

External validation study of AI for modified Total Sharp Score: A KURAMA cohort study

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Conflict of interest: Yes

[Objectives] To validate the accuracy of the AI for van der Heijde's modified total Sharp score (mTSS) measurement in the hand (AI) developed by Honda et al. using external data. [Methods] A total of 174 rheumatoid arthritis (RA) patients who were enrolled in the KURAMA cohort and had hand X-rays taken at least twice at intervals of at least 1 year were evaluated. mTSS evaluations were performed by several rheumatologists, and the same patient was read by two of them. The mTSS was also assessed by an AI at the same time. Intraclass correlation was used to analyze the concordance of mTSS between the primary rater 1, the other rater 2, and AI. [Results] 174 RA patients and 696 radiographs were evaluated. A very high concordance rate was found between rater 1, rater 2, and AI for the baseline bone erosion (JE) score (ICC=0.908). Accuracy worsened for the joint space narrowing (JSN) score, ICC=0.782. For JSN, rater 1 and rater 2 showed high agreement, while lower agreement was observed between AI and Rater 1 and 2. For mTSS change, ICC was 0.346. While Rater 1 and Rater 2 showed moderate concordance, lower concordance was observed between AI and Rater 1 and 2. [Conclusion] AI showed high mTSS agreement with rheumatologists for JE, but lower agreement for JSN and mTSS change.

W70-1

Comparative Effectiveness of Upadacitinib (UPA) Versus Other JAK Inhibitors in Patients With Rheumatoid Arthritis in a Global Real-World Setting (Encore)

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Conflict of interest: Yes

Objectives: This study assessed the effectiveness of UPA vs other JAKis (tofacitinib, baricitinib, and peficitinib) using real-world data. **Methods:** Data were extracted from the Adelphi RA Disease-Specific Programme. Patients (Pts) receiving UPA 15 mg or other JAKis for ≧6 months were included. Physician-reported clinical outcomes included disease activity (physician-reported DAS28 remission, LDA, MDA, and HDA), pain, fatigue and medication adherence. Unadjusted physician-reported outcomes are descriptively reported; adjusted outcomes for UPA vs other JAKis were compared using inverse probability weighted regression adjustment (IPWRA). **Results:** 1440 pts were included (UPA 15 mg, n= 1205; other JAKis, n=235). At treatment initiation, 63% of UPA were in MDA/HDA, while 51% of other JAKi were in MDA/HDA. At the latest follow-up, 85% of UPA and 88% of other JAKi pts were in LDA/remission. IPWRA showed that UPA pts were significantly more likely to achieve physician-reported DAS28 remission (54% vs 44%, P=.03), no pain (43% vs 33%, P=.02), and complete adherence (60% vs 49%, P=.03) vs other JAKis. No significant difference in fatigue was observed. **Conclusions:** In this real-world study, UPA led to higher rates of remission, pain absence, and medication adherence compared to other JAKis.

W70-2

The clinical efficacy of Baricitinib in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To investigate the clinical efficacy of Baricitinib (BAR) and TNF inhibitors (TNFi) (Infliximab (IFX), Etanercept (ETN), Adalimumab (ADA), Golimumab (GLM)), IL-6 receptor inhibitors (IL-6i) (Tocilizumab (TCZ), Sarilumab (SAR)) at 1st line, and BAR and Upadacitinib/ Filgotinib (UPA/FIL) at 1st or more line in the patients with rheumatoid arthritis (RA). [Methods] We evaluated disease activities in RA patients for 52 weeks (W) after administrations of BAR (N=12) and IFX (N=99), ETN (N=57), ADA (N=63), GLM (N=32), TCZ (N=63), SAR (N=18) at 1st line, and BAR (N=58) and UPA/FIL (N=97) at 1st or more line. [Results] There were no significant differences in the mean CDAI during 52W between BAR and TNFi, IL-6i groups at 1st line. The mean tender joint count (TJC) of BAR group was significantly lower at 12W than TNFi, IL-6i groups (TJC at 12W: BAR 1.2 vs IFX 4.6, ETN 4.0, ADA 4.0, GLM 3.2, TCZ 4.8, SAR 4.6; P<0.05). The mean CDAI after 24W and TJC after 4W of BAR group were significantly lower than UPA/FIL group at 1st or more line (CDAI, TJC at 52W: BAR 10.6, 3.6, UPA/FIL 14.3, 5.9; P<0.05). [Conclusion] BAR and TNFi, IL-6i at 1st line and BAR and UPA/FIL at 1st or more line had good clinical efficacy, however, BAR had better efficacy to improve pain of joints than other drugs.

W70-3

Effect of autoantibodies on long-term efficacy and retention rates of JAK inhibitors: Findings from a comparison of five formulations

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Conflict of interest: None

Purpose: In the treatment of rheumatoid arthritis (RA), five JAK inhibitors are available in Japan. However, the long-term retention rate of JAK inhibitors including rheumatoid factor (RF)/anti-CCP antibody (CCP) positivity/negative was not evaluated. Methods: 251 patients treated with JAK inhibitor, tofacitinib (TOFA): 57, baricitinib (BARI): 64, upadacitinib (UPA): 73, pefitinib (PEFI): 28, filgotinib (FIL): 29, were included in this analysis. The retention rates up to 52 weeks and long-term retention rates including the reasons for discontinuation were compared. Moreover, retention rate and reasons for discontinuation were also investigated in the

RF+/CCP+ and other groups. Results: The retention rates at 52 weeks were TOFA: 56.2%, BARI: 64.1%, UPA: 68.5%, PEFI: 42.9%, and FIL: 48.3%, indicating a high continuation rate for BARI and UPA. The percentage of patients with CDAI <10 at 52 weeks were TOFA 28.1%, BARI: 48.4%, UPA: 42.5%, PEFI: 32.1%, and FIL: 13.8%. UPA had the lowest rate of inadequate response at 52 weeks and the highest rate of long-term retention in the non-RF+/CCP+ group. Conclusions: The selection of JAK inhibitors should take into account autoantibodies.

W70-4

Survival rate of secondary bDMARDs or JAK inhibitor after used JAK inhibitor: From the NOSRAD registry

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Conflict of interest: None

[Objective] To examine the survival rate of secondary bDMARDs or JAK inhibitor (JAKi) after used JAKi with using the NOSRAD registry. [Methods] 276 patients of rheumatoid arthritis who introduced secondaly bDMARDs or JAKi before August 2022 were included in this study. The examination items consist of Cumulative survival rate of Kaplan-Meier method. [Results] 2 years survival rate of JAKi changed from TNF-α inhibitor (TNFi) was 68%, from anti IL-6 receptor antibody (aIL-6R) was 80.2%, from abatacept (CTLA4-Ig) was 38.1%. After used JAKi, 2 years survival rate of aIL-6R was 68.6%, of CTLA4-Ig was 66.7%, of JAKi was 83.9%, of TNFi was no data because most long case was 1.3 years. 2 years survival rate of treatment after used JAKi was no significant difference. [Conclusions] If JAK inhibitor was used to rheumatoid arthritis patients in phase 2, survival rate of treatments in phase 3 was good and no difference in each treatments.

W70-5

Efficacy of JAK inhibitors switch and its predictive factors -Investigation in rheumatoid arthritis cohort FIT-RA-

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Conflict of interest: None

[Objectives] This study aimed to clarify the therapeutic effectiveness of JAK inhibitors (JAKi) switch in rheumatoid arthritis (RA) and the factors related to its effectiveness. [Methods] Among the 450 JAKi-treated patients with RA registered in the FIT-RA (Fukui Ishikawa Toyama Database of Rheumatoid Arthritis), 74 with JAKi switch were analyzed. Age-, sex-, and disease duration-adjusted logistic regression analyses were performed to explore factors related to low disease activity (LDA) and remission (R) at 6 and 24 months, respectively. [Results] Six months after JAKi switch, LDA and R was achieved in 67% and 27% of the patients, respectively. The number of past molecular target drug use (OR 0.74), high SDAI value at the time of switch (OR 0.94), and satisfaction of D2TRA definition (OR 0.07) were related to non-achievement of LDA at 6 months. The number of past molecular target drug use (OR 0.62) and high SDAI value at the time of switch (OR 0.93) were also related to non-achievement of LDA at 24 months. [Conclusions] Although the JAKi-to-JAKi switch is effective, it is suggested that the efficacy is reduced in patients who experienced multiple molecular target drugs failures. Early initiation of JAKi may be preferable.

W70-6

Effectiveness of JAK inhibitors for patients with difficult-to-treat rheumatoid arthritis (D2TRA)

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Conflict of interest: None

[Objectives] This study utilized the Tsurumai Biologics Communication Registry (TBCR) to investigate the efficacy of Janus kinase inhibitors (JAKi) for patients with difficult-to-treat rheumatoid arthritis (D2TRA). [Methods] We examined 690 cases that had received JAKi treatment for a minimum of 52 weeks. We defined patients with a history of more than two b/tsDMARDs with different mechanisms of action and moderate or high disease activity as D2TRA cases (D group: 158 cases) and compared them with non-D2TRA cases (N group: 532 cases). [Results] D group had a longer duration of disease, lower eGFR values, lower rate of MTX use, higher rate of glucocorticoid use, and higher titer of CDAI than N group. There were no significant differences in the rates of JAKi use. The mean CDAI at 52 weeks was 8.5 ± 6.5 and 5.9 ± 5.4, with significantly higher values observed in group D. The change in CDAI at 52 weeks was 13.7 in D group and 10.5 in N group, showing a significantly greater improvement in D group. The remission and the continuation rate at 52 weeks was 16.5 %, 68.3% in D group and 34.6% 67.4% in N group. [Conclusion] Although the CDAI was higher in the D2TRA group than in the non-D2TRA group at 52 weeks, the findings demonstrated the efficacy of JAK inhibitors in patients with D2TRA.

W71-1

Predictors of Glucocorticoid Discontinuation Following Initiation of Janus Kinase Inhibitors in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Objective: Glucocorticoid (GC) use in rheumatoid arthritis (RA) treatment is ideally short-term, but in practice, many RA patients continue GC. This study aimed to identify predictors for GC discontinuation following Janus kinase (JAK) inhibitor initiation. Methods: From a multicenter registry, 180 of 681 RA patients who began JAK inhibitors between September 2017 and August 2024 and were using GC at JAK inhibitor initiation were included. Logistic regression evaluated the impact of baseline factors on GC discontinuation at 24 and 52 weeks. Results: Patient characteristics at JAK initiation were: age 67, female 78%, disease duration 13 years, ACPA/RF positive 87%, SDAI 22.5, prior b/ts DMARDs use 67%, maximum JAK inhibitor dose 66%, GC dose 4.1 mg, and MTX use 47%. GC discontinuation rates were 4% at 4 weeks, 12% at 12 weeks, 24% at 24 weeks, and 34% at 52 weeks. Multivariate analysis showed that no prior use of b/ts DMARDs (OR: 2.94) and maximum JAK dose (OR: 4.89) were predictors for GC discontinuation at 24 weeks. At 52 weeks, no prior use of b/ts DMARDs (OR: 2.66) and maximum JAK dose (OR: 3.13) remained significant predictors. Conclusion: RA patients on JAK inhibitors are more likely to discontinue GC if they have no prior use of b/ts DMARDs and are on the maximum JAK dose.

W71-2

Body composition changes in RA due to different mode of action of the b/tsDMARDs from PRESENT study

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Conflict of interest: None

[Object] We examined whether the mode of action of the b/ts DMARDs makes differences in improving body composition in RA patients. [Methods] Data from weeks 0 and 52 of the prospective observational study, (PRESENT study) were analyzed. RA patients were divided into TNF inhibitor (TNFi) (n=30), non-TNF inhibitor (nTNFi) (n=23), and JAK inhibitor (JAKi) (n=27) groups. Changes in disease activity, body composition, muscle function, and the status of sarcopenia and frailty were compared. [Results] The median age and disease duration was 70 years and 4.4 years. The mean DAS28ESR was 5.07 and the median mHAQ was 0.5. MTX usage rate was significantly lower in nTNFi group at 38.5% (p=0.001). After 52 weeks, DAS28ESR was significantly improved in all groups. Creatine kinase was significantly higher in JAKi group. The mean change in body weight was 0.44 kg in TNFi group, 1.12 kg in nTNFi group, and 1.11 kg in JAKi group, not significantly different (p=0.535). Muscle mass increased in all groups, while fat mass decreased only in TNFi group. There were no significant differences in changes in muscle function and the status. [Conclusions] The b/tsDMARDs increased body weight and muscle mass, but there was no significant difference in body composition improvement between the modes of action.

W71-3

Clinical Efficacy of JAK Inhibitors in Poor Prognostic Factors for Rheumatoid Arthritis: An Analysis from the ANSWER Cohort

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Conflict of interest: Yes

[Objectives] Several poor prognostic factors (PPFs) for joint destruction in rheumatoid arthritis (RA) have been identified, but studies comparing JAK inhibitors and biologics are limited. This study defines PPFs as seropositivity, CDAI ≧22, CRP ≧0.6 mg/dL, and HAQ-DI ≧0.5, and aims to compare treatment continuation rates and outcomes, focusing on patients with all four PPFs (4PPF). [Methods] From the ANSWER cohort, 1,235 JAK inhibitor cases and 559 TNF inhibitor cases (from 2013 onwards) were analyzed. After matching patient backgrounds, 544 cases from each group were statistically compared. Continuation rates for each PPF and stratified 4PPF and non-4PPF groups were evaluated, alongside CDAI improvement. [Results] At 24 months, no significant difference was found in continuation rates between JAK and TNF inhibitors. While TNF inhibitors showed no differences across PPFs, JAK inhibitors had significantly higher continuation rates in RF-positive patients. Furthermore, JAK inhibitors showed a significant reduction in CDAI in 4PPF patients compared to non-4PPF. [Conclusion] Both TNF and JAK inhibitors showed clinical efficacy in PPF patients. However, JAK inhibitors may be more effective in patients with multiple PPFs.

W71-4

Comparison of the clinical effects of JAK inhibitors and IL-6 inhibitors in the patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] JAK inhibitors (JAKi) and IL-6 inhibitors (IL6i) are effective medications for treatment of the patients with rheumatoid arthritis (RA). In this study, we investigated the clinical effects of JAKi and IL-6i in RA patients. [Methods] We analyzed RA patients treated with JAKi (JAKi group) and IL6i (IL-6i group). We evaluated disease activity at 0, 4, 12, 24, 36, 52 weeks (w). We investigated the relationship between type of medications and changes of disease activity in RA patients by using repeated ANOVA. [Results] In JAKi group (N=291; First: 69, Second: 70, Third or more: 152) and IL6i group (N=326; First: 126, Second: 126, Third or more: 74), there were 167 (57.4%) and 193 (59.2%) patients treated with MTX, respectively. At 0w, there were no significant differences in CDAI (JAKi 20.6±11.7, IL6i 22.2±13.9; P=0.12) and Pain VAS (51.6±28.4, 54.9±25.4; P=0.13). In the analysis of interaction, significant interactions between changes in CDAI and Pain VAS and type of medication were observed. There were significant improvements of CDAI and Pain VAS at 4w in JAKi group than IL6i group. In the patients treated with or without MTX, similar results were observed. [Conclusion] We found that JAKi may improve disease activity and pain at earlier stage than IL-6i in the real-world data.

W71-5

Comparison of Efficacy and Retention Rates of IL-6 and JAK Inhibitors in Refractory Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] While biologics and JAK inhibitors have improved remission rates in RA, some patients with difficult-to-treat (D2T) RA struggle with disease control. This study compared the efficacy and retention rates of IL-6 inhibitors and JAK inhibitors in D2T RA. [Methods] We analyzed 41 patients who switched to IL-6 inhibitors (Group I) and 94 who switched to JAK inhibitors (Group J) at our institution by September 2024. Efficacy and retention rates were followed for 24 weeks. [Results] At baseline, patients had a mean age of 65.4 years, disease duration of 20.3 years, MTX use in 34% at 7.5 mg, and glucocorticoid use in 37% at 5.7 mg. At 24 weeks, retention rates were 59% in Group I and 67% in Group J. DAS28-ESR improved from 5.45 to 4.18 in Group I and from 4.57 to 4.11 in Group J; CDAI from 24.6 to 21.2 (I) and 19.5 to 12.8 (J); CRP from 3.07 to 0.32 mg/L (I) and 0.95 to 0.67 mg/L (J); MMP-3 from 332.3 to 185.8 ng/mL (I) and 189.5 to 100.9 ng/mL (J); pain VAS from 57.0 to 56.7 (I) and 50.2 to 34.0 (J). [Conclusion] IL-6 inhibitors reduced inflammatory markers, while JAK inhibitors were more effective in reducing pain, showing beneficial effects on disease activity in D2T RA.

W71-6

Comparing the efficacy of the bDMARD switcher group and JAK cycler group in patients with rheumatoid arthritis fail to the JAK inhibitors

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Conflict of interest: None

[Objectives] We analyzed the efficacy of bDMARD switchers who selected biological agents and JAK cyclers who switched to JAK inhibitors in patients who discontinued JAK inhibitors due to ineffectiveness. [Methods] Of 4,516 patients registered in SHARE (SHin-yokohama Arthritis REgistry), 406 patients who met the ACR/EULAR RA classification criteria and started JAK inhibitor treatment were included. Efficacy was evaluated by continuation rate and CDAI improvement rate. [Results] 406 patients (53 men and 353 women) received JAK inhibitors. 84 patients (20.7%) discontinued JAK inhibitors due to ineffectiveness. Of the 84 patients who discontinued JAK inhibitors due to ineffectiveness, 55 (65.5%) were bDMARD switchers, 22 (26.2%) were JAK cyclers, and 7 (8.3%) switched to csDMARDs only. The continuation rates for the next treatment in the bDMARD switcher group and JAK cycler group were 63.3% and 78.6%, respectively, at 12 weeks, showing a significant difference (Log-rank p=0.0006). The CDAI improvement rates for the next treatment in the bDMARD switcher group and JAK cycler group were 53.7% and 57.3%, respectively, at 12 weeks, showing no significant difference. [Conclusion] JAK cycler, as well as bDMARD switcher, may be useful as the next treatment for patients who discontinue JAKi.

W72-1

Evaluating the effectiveness of a new treatment framework for the management of rheumatoid arthritis

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Conflict of interest: None

[Objectives] We evaluated the effectiveness of the framework for management in RA. [Methods] We formulated a medical care system (framework) that can be used in outpatient care. The framework was used for the purpose of patient education, adverse events, and comorbidities. The effectiveness was evaluated using 1) the treatment continuation rate of JAK inhibitors and 2) a comparison of the incidence of adverse events (severe pneumonia), and 3) free-form responses from patients and medical staff. [Results] The disease management framework was put into practice in August 2015. Work was divided into five parts and redistributed across each profession. As a result, the 48-week continuation rate of JAK inhibitors was 63.4% in May 2018, but improved to 75.3% in October 2024. In addition, the number of severe pneumonia cases in the 5 years prior to August 2015 was 12, but in the 9 years since August 2015, it has decreased to 6 cases. In the free-form responses, patients gave high marks to the thorough interviews, detailed explanations of treatment drugs. Medical staff gave high marks to the easy extraction of problems the standardization of instructions for each patient. [Conclusion] This framework, which responds to changes in disease management due to advances in DMARDs, was effective.

W72-2

Survey on Rheumatologists' Perceptions of Social Insurance and Welfare Systems

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Conflict of interest: Yes

[Objectives] To investigate rheumatologists' understanding of social insurance and welfare systems for rheumatoid arthritis (RA) patients and identify related issues. [Methods] A survey was conducted via Google Forms among Japan College of Rheumatology members. [Results] Responses were obtained from 478 physicians, with an average age of 49.0 [11.7] years. Workplaces included university hospitals (31.2%), hospitals with over 400 beds (22.4%), hospitals with 200-399 beds (13.8%), hospitals with fewer than 200 beds (13.2%), and clinics (18.2%). Younger physicians were more likely to work in large hospitals. Over 80% had a good understanding of long-term care and high-cost medical systems, but only 69.7% knew about the Physical Disability Certificate. Knowledge of the disability pension system and care facility types was lower, at 54.6% and 54.0%. Younger physicians showed less knowledge and indicated a need for more education. A total of 73.0% reported difficulties supporting RA patients due to knowledge gaps. Additionally, 45.8% felt RA patients were often assessed at a lower care level than warranted. [Conclusion] Younger rheumatologists showed greater knowledge gaps, highlighting the need for improved education to better support RA patients.

W72-3

Survey on Rheumatologists' Perceptions of Home Medical Care for Rheumatoid Arthritis Patients

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Conflict of interest: Yes

[Objectives] To investigate the perceptions and challenges of home medical care for rheumatoid arthritis (RA) patients among rheumatologists. [Methods] A survey was conducted via Google Forms among Japan College of Rheumatology members. [Results] Responses were received from 478 physicians, with an average age of 49.0 years. Workplaces included university hospitals (31.2%), large hospitals (22.4%), mid-sized hospitals (13.8%), small hospitals (13.2%), and clinics (18.2%). When asked if the need for RA home care would increase, 71.5% "strongly agreed", and 23.8% "somewhat agreed". As for their own involvement, 20.3% "strongly agreed", and 36.0% "somewhat agreed", but only 24.5% had experience. Ideal primary physicians were themselves (7.7%) or rheumatologists (57.3%), but in practice, it was themselves (12.8%) or non-rheumatologists (59.8%). In transitioning to home care, 93.1% adjusted medications, citing patient issues (83.8%), facility needs (78.4%), and unfamiliarity with RA (76.0%). Major challenges were the lack of skilled home care physicians (70.9%) and concerns about drug monitoring (66.9%). [Conclusion] Rheumatologists are concerned about the shortage of skilled RA home care physicians and emphasize the need for further education and support.

W72-4

Initiatives to Improve Understanding in Outpatient Methotrexate Guidance for Elderly Rheumatoid Arthritis Patients

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Conflict of interest: None

[Objectives] At Tenri Hospital, we educate outpatients starting methotrexate and assess understanding through tests after consultation, pharmacist guidance, and follow-ups. Results showed higher correct answer rates after guidance, but patients aged 60 and above had lower rates, particularly at follow-ups. To improve this, we introduced illustrated leaflets, enhanced question clarity, and used all multiple-choice tests for older patients, while maintaining conventional methods for those under 60. This study aimed to evaluate the impact of these changes on follow-up answer rates. [Methods] We compared follow-up correct answer rates for patients aged 60 and above before and after changes in instructional methods, using median [interquartile range] for test results and the Mann-Whitney U test for group comparisons. [Results] Correct answer rates (%) at follow-ups before and after the changes were: 60s age group: 85.7 [78.6-100] vs. 100 [92.9-100] ($p<0.01$) 70s age group: 89.3 [78.6-92.9] vs. 100 [87.5-100] ($p<0.005$) Both age groups showed significant improvement after the changes. [Conclusion] The results show that adapting educational methods for elderly patients can improve their understanding, indicating this approach is beneficial.

W72-5

Approaches to Medication Guidance aiming for Therapeutic Effectiveness in Patients with Rheumatic Disease

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Conflict of interest: None

[Objectives] To evaluate the effectiveness of medication regimens of glucocorticoids (GCs), immunosuppressants (ICs), csDMARD, bDMARD, and JAK inhibitors, which are the mainstay of treatment for patients with collagen disease. [Methods] We retrospectively examined the frequency and content of adjusted prescriptions of GC, ICs, csDMARDs, and bDMARDs in patients with rheumatic disease who had been continuously visiting our clinic for one year from October 2023 to September 2024. [Results] Of the total of 2017 visits, 143 (7.1%) had residual medication at the time of visit, 109 patients were in the no residual group (N) and 88 patients were in the residual group (R). N was significantly less likely to use MTX (N 41.3% vs. R 55.7%; p=0.046), to use all immunomodulators (N 1.6 vs. R 2.0; p=0.029) and to visit the doctor (N 9.6 vs. R 11.0; p=0.013) than R, but not significantly different in age, gender, GC use, bDMARD or JAK inhibitor use. [Conclusion] Adherence was found to be higher the lower the number of drugs used. In rheumatoid arthritis, it has been reported that drug adherence declines by more than 20% after one year. In this study, less than 10% of the patients decreased in drug adherence, suggesting that our clinic's approach is effective.

W72-6

Evaluation of task-shifting to pharmacists in our rheumatology centre

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Conflict of interest: None

[Objectives] We conducted to analyse the task shift to pharmacists and assess their contribution to outpatient rheumatology care. [Methods] We conducted a survey of patients who received medication advice from pharmacists in 2023. We also looked at the number of patients seen in rheumatology centres in the same year, as well as the duration of consultations, and assessed the contribution of task shifting in terms of the impact of pharmacist medication advice on the duration of consultations. [Results] In FY2023, pharmacists gave 349 medication instructions, with an average instruction time of 8.5 minutes per patient. Medication instructions for biologics and JAK inhibitors were significantly longer than those for other drugs (p=0.00761, chi-squared test). A total of 7068 patients were seen at the rheumatology centre in the same year, with an average treatment time of 9.7 minutes per patient. These results suggest that pharmacist medication advice contributed to a reduction in clinic time equivalent to 305 patients per year. [Conclusion] Task-shifting to pharmacists in rheumatology centres can be useful. In particular, medication advice on biologics and JAK inhibitors can contribute to efficient outpatient rheumatology care.

W73-1

Investigation of the medical needs of telemedicine for juvenile idiopathic arthritis and childhood systemic lupus erythematosus

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Conflict of interest: None

[Objectives] This study aimed to identify the needs and issues of telemedicine for the treatment of juvenile idiopathic arthritis (JIA) and childhood systemic lupus erythematosus (cSLE). [Methods] A Google Forms survey was distributed to members of the JCR, the Pediatric Rheumatology Association of Japan, and pediatricians from core pediatric specialty training facilities. [Results] Responses were received from 128 physicians who had 77, 50, 27, and 21% of patients traveling over an hour, crossing prefectural borders, from areas with limited specialized care, and from remote islands and regions, respectively. The JCR board-certified rheumatologists reported higher experience with patients requiring telemedicine. Telemedicine was expected to reduce treatment time (92%) and travel time (92%). Concerns included patient preference for face-to-face treatment (90%) and quality differences between in-person and telemedicine consultation (87%). The use of telemedicine was supported by 80 and 79% of physicians for stable JIA and cSLE patients, respectively. [Conclusion] Many physicians support telemedicine for patients with JIA and cSLE who travel long distances. Further studies should explore the quality differences between telemedicine and in-person consultation.

W73-2

Investigation of the medical needs of telemedicine for patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and juvenile idiopathic arthritis (JIA)

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Conflict of interest: None

[Objective] To clarify the needs and issues regarding telemedicine for patients with RA, SLE, and JIA. [Method] A survey was conducted using Google Forms targeting members of the Japan College of Rheumatology. [Results] Questionnaires were collected from 351 internal medicine physicians, 155 orthopedic surgeons, and 144 patients or their families. 77.5% and 58.6% of physicians and orthopedic surgeons treat cases that require more than an hour's travel each way, respectively. 28.5% and 19.5% of physicians and orthopedic surgeons treat patients from remote islands and isolated areas, and 52.1% and 38.3% of physicians and orthopedic surgeons treat patients from areas with few specialized medical facilities. 32.8% of physicians and 45.1% of orthopedic surgeons, as well as 28.7% of patients or their families, expressed a negative view of telemedicine. Doctors expressed concerns about the quality of medical care and patients expressed concerns about reduced opportunities for communication. [Conclusion] In the current situation where many doctors who treat RA, SLE, and JIA are treating patients from far away, concerns from both doctors and patients were made clear. Concrete solutions need to be considered for the future.

W73-3

A case of primary erythromelalgia caused by an SCN9A variant, presenting with lower limb pain and livedo-like skin erythema that resembles SLE

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Conflict of interest: None

Background: Primary erythromelalgia (PEM) is a rare autosomal dominant disorder characterized by episodic redness, pain, and burning sensations in the extremities triggered by fatigue or exercise. PEM usually develops in childhood and is caused by gain-of-function variants in the sodium channel Nav1.7, coded in the SCN9A gene. The concept of the disease, however, is not well recognized. Case Report: A 20-year-old woman experienced burning sensations, redness, and pain in her extremities since around age 10. She had livedo-like rash and antinuclear antibodies. Nerve conduction studies showed abnormal findings, which are consistent with multifocal mononeuropathy. She was diagnosed with systemic lupus erythematosus and treated with 20 mg of prednisolone, but she did not respond. Given that her father had similar symptoms, PEM was suspected. The genetic test revealed a heterozygous SCN9A p. G856D variant, confirming the diagnosis of autosomal dominant PEM. Discussion: PEM caused by SCN9A variants can present with skin erythema resembling those of connective tissue diseases, in addition to characteristic episodic pain. Conclusion: Physicians should consider PEM due to SCN9A variants when they meet patients with painful erythema in the extremities.

W73-4

Effectiveness of enzyme replacement therapy on skeletal muscle pain in adult-onset hypophosphatasia: a case report

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Conflict of interest: None

A 44-year-old female who was diagnosed with adult-onset hypophosphatasia (HPP), due to tooth mobility, low serum alkaline phosphatase levels and Genetic tests detected *ALPL* gene heterozygous missense mutation, visited our hospital. She had no history of early loss of primary teeth nor family history of skeletal dysplasia. One year after our hospital visitation, she had suffered skeletal muscle pain and malaise, followed by her quality of life (QOL) impairment. In addition, because she had been indicated the tooth mobility deterioration, she began treatment with, enzyme replacement therapy, asfotase alfa. Consequently, her musculoskeletal subjective symptoms were subsided and her QOL was ameliorated. HPP is a rare inherited metabolic disease from deficient activity of the tissue-nonspecific isoenzyme of alkaline phosphatase and adult-onset HPP tend to be mimic rheumatologic diseases. Thus, adult-onset HPP should be considered as a possible diagnosis in patients presenting with musculoskeletal pain of unknown origin in rheumatologic medical examinations. We hope that this report will help many clinicians to better diagnose and report adding the current literature.

W73-5

Effective Early Combination Therapy with Tocilizumab, Cyclosporine, and TPO Receptor Agonist in a Case of iMCD-TAFRO

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Conflict of interest: None

A 77-year-old Asian woman was admitted to our hospital because of massive edema, progressive renal dysfunction, elevated CRP. On admission, lymphadenopathy, thrombocytopenia with increased megakaryocytes were observed, and the lymph node biopsy showed vascular proliferation with the feature of Castleman's disease. Based on the biopsy, we diagnosed this patient as having iMCD-TAFRO. On hospital day 5, renal dysfunction progressed rapidly, leading to anuria. we initiated treatment with PSL 1 mg/kg/day, TCZ 8 mg/kg, and CHDF. Subsequently, CyA was added. CRP levels gradually improved, weaned from dialysis in about 10 days, and on the 30th day of treatment, CRP <0.5 mg/dL and PSL was gradually decreased. Because of persistent thrombocytopenia and CMV reactivation, eltrombopag (EPAG) was introduced. Platelet count dropped to a low of 7,000/μL, requiring daily platelet transfusions, and HLA antibodies appeared. Gradually increasing EPAG to 37.5 mg resulted in improved platelet counts. We report a case with iMCD-TAFRO in which immunosuppressive therapy with TCZ and CyA led to early dialysis discontinuation and PSL tapering. Although thrombocytopenia was challenging to manage due to CMV activation. And in this case we represents a rare case of EPAG application in management.

W73-6

Clinical features of rituximab-induced acute thrombocytopenia (RIAT) in autoimmune diseases

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Conflict of interest: None

[Objectives] To assess clinical features of RIAT in patients with autoimmune diseases. [Methods] We assessed patients (pts) with autoimmune diseases who visited our department between January 2019 and September 2024 and received at least two doses of RTX. [Results] RTX was administered to 59 pts (37 AAV, 9 inflammatory myopathy (IM), 3 SLE, and 7 others). 5 pts who already had thrombocytopenia (≦75,000/μL) at the time of RTX administration were excluded, leaving 54 cases, 6 cases (AAV: 5, IM: 1) developed thrombocytopenia (≦75000/μL) after RTX administration, with a median age of 72 years (43-77). The median time from the first RTX administration to thrombocytopenia was 18 days (14-19), and it took a median of 9.5 days (5-29) for platelet counts to recover (>75000/μL). 3 pts discontinued RTX, and 3 were re-administered RTX after platelet recovery, but there was no recurrence of thrombocytopenia. 3 pts had chronic kidney disease as a comorbidity. In the two cases where complement was measured, C3 decreased to below the reference value. In cases without thrombocytopenia, C3 remained within the reference range. [Conclusion] RIAT requires caution, especially in patients with chronic kidney disease, but it may be possible to re-administer it by waiting for the platelet count to recover.

W74-1

The long-term efficacy of a rapid glucocorticoid tapering protocol in remission-induction therapy for ANCA-associated vasculitis: A retrospective cohort study using the J-CANVAS registry

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Conflict of interest: None

[Objectives] This study examined the long-term efficacy of rapid glucocorticoid (GC) tapering during remission induction for microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). [Methods] MPA/GPA patients with new onset or severe relapse from 2017 to 2023 in J-CANVAS registry were included. Cases using avacopan were excluded. Patients tapering GC faster than the PEXIVAS trial rapid tapering protocol during the eight weeks were classified as rapid taper (RT) group, and patients tapering GC slower as control group. Primary outcome was five-year remission maintenance rate, and secondary outcomes were cumulative GC dose and GC-related adverse events. [Results] Among 109 patients, 34 were assigned to RT group and 51 to control group. Cumulative-remission rates at three years were not significantly different between two groups (RT: 82.2%; control: 89.6%). The hazard ratio for severe relapse in RT group at three years was 1.29 (95% confidence Interval: 0.43, 3.86). The cumulative GC dose was significantly lower in RT group (9,262.5±1,568.3 mg vs. 11,686.9±3,715.7 mg), with comparable severe infection rates. [Conclusion] Rapid GC tapering during remission induction in MPA/GPA achieved comparable long-term remission rate with significant reduction in cumulative GC dose.

W74-2

Efficacy and safety of avacopan in patients with MPA/GPA receiving remission induction therapy with rituximab

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Conflict of interest: None

[Objective] To clarify the efficacy and safety of avacopan (AVA) in patients with MPA/GPA receiving rituximab (RTX). [Methods] MPA/GPA patients who received remission induction with RTX at our institution from January 2017 to June 2023 were included in this study. The remission rate (defined as BVAS=0), glucocorticoid (GC) dose (/day), and the incidence of adverse events (AEs) during 12 months were compared between the two groups (AVA group vs. non-AVA group). [Results] A total of 18/30 patients were included in the AVA/non-AVA. Patient's characteristics at baseline were as follows: mean age, 70.9/71.3 years; MPA, 88.9%/63.3%; mean BVAS, 12.4/13.2 points; mean GC dose, 34.3/37.8 mg/day. The remission rate at 6 and 12 months was 100% and 100% in the AVA, and 90.0% and 86.7% in the non-AVA. Mean GC doses (/day) at 6 and 12 months were 3.2 and 3.0 mg in the AVA, and 7.4 and 4.3 mg in the non-AVA. The incidence of GC-related AEs (hypertension, diabetes, severe infection, etc) during 12 months was 16.7% in the AVA and 53.3% in the non-AVA. [Conclusion] Our results showed that AVA significantly reduced GC dose and the incidence of GC-related AEs in a real-world clinical setting. Additionally, the effect of AVA on the renal function and serum biomarkers were also analyzed in this study.

W74-3

Remission induction therapies and their outcome with Microscopic polyangiitis (MPA) and Granulomatosis with polyangiitis (GPA) in our department

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Conflict of interest: None

[Objective] To clarify remission induction therapies and their outcome in patients with MPA and GPA in our department. [Methods] We retrospectively reviewed the medical records of patients who were diagnosed and treated for MPA and GPA in our department from January 2005 to October 2021 and were followed up to 156 weeks after the start of treatment. The criteria for relapse were defined as patients with elevated BVAS values over 2, and the addition or increase dose of GC and immunosuppressants. [Results] There were 28 patients with MPA and 19 patients with GPA, respectively. The median age of each patient was 72 and 65 years old, and males were 32 and 47%, respectively. The median score of BVAS before induction therapy was 14 and 10, respectively. The recurrence rate of the GC+IVCY group compared to the GC group in patients with MPA and

GPA was 50 vs. 15% and 50 vs. 50%, respectively. During 156 weeks, diabetes mellitus (DM) was detected in 53.6% of MPA and 52.6% of GPA. All patients with MPA and GPA of the GC+IVCY group were found to have diabetes after 52 weeks, focused on recurrent cases. [Conclusions] Patients with MPA and GPA complicated by DM had high relapse rates regardless of treatment, even during remission maintenance therapy.

W74-4

The Effects of Avacopan, C5a Receptor Antagonist, on Tapering of Glucocorticoid with Sustained Renal Function in ANCA-associated Vasculitis

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Conflict of interest: None

[Objectives] To investigate the capability of avacopan (AVA) to taper glucocorticoid (GC) with maintaining renal function during 52-week observation. [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 titers, and treatment were reviewed in their medical charts. [Results] Thirty-five patients with AAV treated in our hospital for over 12 months (19 females, 16 males, 26 MPA, nine GPA) were eligible for this study. Comparing patients with AVA and the standard of care (SOC) (AVA group) with those with SOC alone (SOC group), the age, CRP, and BVAS scores at the onset were similar between the two groups. Renal impairment was found in 43.8% of the AVA group and 63.2% of the SOC group at the onset, and renal function was maintained in 52-week observation in both groups. GC doses at three, six, and twelve months were tapered earlier in the AVA group than the SOC group. The AVA group showed significantly lower BVAS score than the SOC group. [Conclusion] The real-world data suggested the potential of concomitant AVA for early tapering GC with maintained renal function in AAV treatment for remission induction.

W74-5

Effects of IL-21 inhibition on the pathology in a rat model of MPO-ANCA-associated vasculitis

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Conflict of interest: Yes

[Objectives] Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by the production of ANCA and necrotizing small-vessel vasculitis, with an association with IL-21. Standard treatments for AAV include glucocorticoids and immunosuppressants; however, cases of resistance and relapse necessitate new therapeutic developments. This study aimed to demonstrate the effects of anti-rat IL-21 aptamer (Apt), an IL-21 inhibitor, on an AAV model. [Methods] 4-week-old WKY rats were immunized with human myeloperoxidase (MPO) to induce MPO-AAV. The rats were divided into 5 groups and treatment was started on day 21. On day 42, all rats were euthanized for evaluation. [Results] Anti-rat IL-21 Apt inhibited the differentiation from post-germinal center follicular B cells to non-switched early plasmablasts, but did not reduce MPO-ANCA titers. The rates of necrotic glomerular lesion, total glomerular lesion, and intraglomerular neutrophil extracellular trap (NET) formation were significantly reduced in the Apt-treated rats compared to the non-treated rats. There was a decreasing trend in peripheral blood NET-forming neutrophils and urinary NGAL. [Conclusion] Anti-rat IL-21 Apt has a potential to ameliorate renal injury in AAV by inhibiting NET formation.

W74-6

A novel therapeutic strategy for ANCA-associated vasculitis inhibiting the formation of degradation-resistant neutrophil extracellular traps

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Conflict of interest: Yes

[Objectives] In anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, DNase I-resistant neutrophil extracellular traps (NETs) deposit in tissues, contributing to disease pathogenesis. We have identified protein X as a factor that confers DNase I resistance to NETs and demonstrated that anti-protein X antibodies inhibit the formation of DNase I-resistant NETs in vitro and in vivo. This study aims to elucidate the therapeutic effects of anti-protein X antibodies in a mouse model of ANCA-associated vasculitis. [Methods] Female BALB/c mice were administered with 3% thioglycolate, phorbol myristate acetate, and propylthiouracil intraperitoneally and given subcutaneous Freund's complete adjuvant inoculation weekly. Anti-protein X antibodies were administered intraperitoneally every other week. Urine was collected on days 23-25, and blood and organs on day 28 for analyses. [Results] The elevated MPO-ANCA titers, urinary albumin levels, and affected glomerular rates in the model were significantly reduced by anti-protein X antibodies. Plasma protein X levels were not altered by antibody administration. [Conclusion] Anti-protein X antibodies improved disorders in ANCA-associated vasculitis model mice, suggesting their therapeutic potential.

W75-1

Evaluation of the Utility of Muscle Biopsy Combined with MRI for Improving the Diagnostic Accuracy of Vasculitis

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Conflict of interest: None

[Background] Muscle biopsy has been reported to be useful for the histological evaluation of vasculitis. Identifying biopsy sites using MRI may improve diagnostic accuracy. We retrospectively evaluated the diagnostic rate of using MRI before performing muscle biopsy for the diagnosis of vasculitis. [Methods] We analyzed 21 patients who underwent muscle biopsy between 2020 and 2024. 16 patients who met the classification criteria for vasculitis were selected. We analyzed their clinical characteristics, muscle pathology findings, MRI findings, and the sensitivity and specificity of muscle biopsy. [Results] Muscle tenderness was observed in 9 patients, but none of the patients showed elevated CK levels. MRI findings of myositis were diffuse in 11 patients and patchy in 1 patient. Vasculitis findings were observed in 12 patients. Comparing the vasculitis-positive and vasculitis-negative groups, no significant differences were observed in sex, muscle tenderness, CRP, MPO-ANCA, peripheral neuropathy, biopsy site, BVAS, or diagnosis. The sensitivity and specificity of muscle biopsy for vasculitis diagnosis were 75%. [Conclusion] Muscle biopsy is useful for the diagnosis of vasculitis, and performing biopsies from sites with MRI-confirmed myositis may improve diagnostic accuracy.

W75-2

Usefulness of contrast-enhanced magnetic resonance imaging in lower extremity for the diagnosis of polyarteritis nodosa

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Conflict of interest: None

Objective: Diagnosis of polyarteritis nodosa (PN) often relies on findings in angiography such as aneurysms, stenosis, or occlusion; however, many cases lack these findings, complicating its diagnosis. This study examines the clinical features and the utility of lower extremity contrast-enhanced MRI in PN. Methods: We reviewed 17 PN patients, diagnosed or suspected based on Ministry of Health, Labour and Welfare criteria, and hospitalized at Tsukuba University Hospital from January 2014 to October 2024. We retrospectively analyzed: (1) organ damage related to PN, (2) lower extremity MRI findings, and (3) change of MRI findings between before and after treatment. Results: (1) Organ damage included 13 cases of skin involvement such as skin ulcers, gangrene, or purpura; 8 with myalgia/myositis; 2 with fever; and 1 case each of hypertension, pericarditis, pleuritis, or gastrointestinal bleeding. (2) 9 cases with lower extremity symptoms underwent MRI, revealing 2 cases with contrast enhancement along vessel walls and 4 cases with STIR high signals in muscles. (3) After treatment, MRI improvement was noted in 1 of 3 cases. Conclusion: Contrast-enhanced MRI in lower extremity, though not part of the diagnostic criteria, may aid in diagnosis and treatment evaluation in PN.

W75-3

Characteristics and Diagnostic Utility of FDG-PET/CT Findings in Polyarteritis Nodosa

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Conflict of interest: None

[Objectives] This study evaluated the characteristics and diagnostic utility of FDG-PET/CT (PET) findings in polyarteritis nodosa (PAN). [Methods] Ten PAN cases diagnosed between 2003 and 2024 were analyzed. Seven underwent PET during examinations, while three had PET for unexplained fever or inflammation, suspected of medium-vessel vasculitis but not meeting PAN criteria and testing negative for other conditions. Blood test, PET, and histopathology results were compared. [Results] Of the PAN-diagnosed patients, four were PET-positive (Group A) and three were PET-negative (Group B). Three PET-positive cases not meeting PAN criteria were classified as Group C. Across groups, no significant differences in age, gender, or lab results were found. However, CRP was significantly higher in Group A than in Group B (P=0.04). Among Groups A and C, five showed high uptake in peripheral arteries, and four in muscle and soft tissue. Histopathology revealed leukocytoclastic vasculitis without immune complex deposition in two Group C skin biopsies. [Conclusion] Higher inflammation may increase the detectability of PAN findings on PET. PET may also serve as a aapplicable adjunctive diagnostic tool for PAN, especially in cases of leukocytoclastic vasculitis with negative serological markers.

W75-4

Validation of new ACR/EULAR 2022 classification criteria for ANCA-associated vasculitis in otitis media with ANCA-associated vasculitis (OMAAV)

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Conflict of interest: None

[Objectives] To compare the new ACR/EULAR 2022 criteria with the previous classification algorithm for ANCA-associated vasculitis in patients with OMAAV. [Methods] Fifty-six patients with OMAAV who attended our hospital between June 2013 and October 2024 were included. Each patient was classified as having EGPA, GPA, or MPA according to the ACR/EULAR 2022 criteria, Watts' algorithm, and MHLW diagnostic criteria. [Results] Using the new criteria, 3, 11, and 43 patients were classified as having EGPA, GPA and MPA, respectively. Two patients were unclassifiable, and three patients met both GPA and MPA criteria. Using Watts' algorithm, 3 and 52 patients were classified as EGPA and GPA, respectively. One patient was unclassifiable, while the new criteria reclassified 40 as MPA and 8 as GPA. Using MHLW diagnostic criteria, 20 probable GPA cases and 17 probable MPA cases met at least two criteria. However, the new criteria reclassified 31 probable GPA cases to 6 GPA cases and 19 MPA cases, and 26 probable MPA cases to 1 GPA case and 21 MPA cases. Additionally, only two probable GPA cases and one probable MPA case met both GPA and MPA criteria. [Conclusion] Using the new criteria in OMAAV patients, the majority of cases were classified as MPA and GPA, in that order, reducing duplicate cases.

W75-5

A Case of Epstein-Barr Virus Reactivation Accompanied by Vasculitis Mimicking Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: None

We describe Epstein-Barr virus (EBV) reactivation that mimicked eosinophilic granulomatosis with polyangiitis (EGPA). A 75-year-old man presented with a two-months history of myalgia and a one-month history of abnormal sensations in his limbs, along with left foot drop. He had no history of asthma. Laboratory tests revealed eosinophilia, elevated C-reactive protein and MPO-ANCA levels. MRI of the limb indicated abnormal signals in the fascia and muscle. A muscle biopsy showed small vessel occlusion and monocyte infiltration, suggestive of vasculitis. A nerve conduction study revealed axonopathy in the left tibial nerve. Urinalysis showed glomerulocystic hematuria and proteinura. Renal biopsy revealed crescentic glomerulonephritis and interstitial nephritis, with a predominance of plasmacytes. The patient's whole blood EBV-DNA levels were elevated to 4.55 Log IU/mL, and re-evaluation of the renal biopsy showed EBER-positive lymphocytes in interstitium. He was diagnosed with EBV reactivation accompanied by vasculitis. His myalgia and glomerulonephritis improved after initiating prednisolone. This case highlights that EBV reactivation can induce small vessel vasculitis and mimic EGPA. EBV reactivation should be considered in cases of atypical ANCA-associated vasculitis.

W75-6

A case of peripheral T-cell lymphoma (PTCL) presenting as eosinophilic polyangiitis granulomatosa (EGPA)

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Conflict of interest: None

[Case] A 51-year-old man with allergic rhinitis developed generalized erythema with pruritus in April, X year. Despite steroid treatment, fever persisted and CRP (12 mg/dl) and blood eosinophil (4929/μL) elevated. When he was referred to our hospital in August, enlarged cervical lymph nodes with LDH 1003 U/L and sIL-2R 2649 U/mL were noted, suggesting malignant lymphoma. While two needle biopsies showed no malignancy, the swollen lymph nodes were spontaneously resolved. Skin biopsy showed fibrinoid necrosis of microvessels with eosinophilic infiltration, which fulfilled "definite" items in the EGPA classification criteria of the Ministry of Health, Labour and Welfare, Japan. Employment of mepolizumab and 35 mg (0.5 mg/kg) of PSLresulted in improvement of CRP and blood eosinophil. However, cervical lymph nodes were enlarged again and sIL-2R increased to 6219 U/mL, with multiple enlarged lymph nodes and intraperitoneal mass. Finaly, cervical lymph node biopsy showed peripheral T-cell lymphoma (PTCL). He was transferred to the Department of Hematology in September. [Clinical Significance] It is known that monoclonal proliferation of IL5-producing T cells causes eosinophilia (NEJM 1999; 341: 1112-20), but this is the first case of PTCL patient presenting with EGPA.

W76-1

Long-term low dose Colchicine therapy for patients with difficult-treated acute Calcium Pyrophosphate crystal arthritis

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Conflict of interest: None

[Objectives] This study aimed to investigate the clinical outcomes of low-dose colchicine therapy in patients with difficult-treated acute calcium pyrophosphate crystal (CPP) arthritis. [Methods] The study included eight patients with refractory acute CPP arthritis, who frequently relapsed despite intra-articular glucocorticoid (GC) injections and NSAIDs during the acute phase. The cohort consisted of 3 men and 5 women, with a mean age of 77.9 years. Colchicine was administered according to the 2019 Japanese gout treatment guidelines, with 0.5 mg of colchicine taken daily. The only concurrent therapy was oral NSAIDs, and none of the patients received oral GC. [Results] After initiating 0.5 mg/day colchicine, six patients had no further acute arthritis and showed a positive response to the treatment, while two patients did not respond. The average duration of colchicine treatment was 14.3 months (range: 2-36 months). There were no cases of colchicine discontinuation due to side effects. Colchicine was more effective in patients with monoarthritis, whereas the two non-responders had polyarthritis. [Conclusion] Long-term low-dose colchicine therapy may be useful in preventing acute flares in CPP arthritis, especially in patients with monoarthritis.

W76-2

Clinical Features of Calcium Pyrophosphate Dihydrate Deposition in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To clarify the clinical background factors of rheumatoid arthritis (RA) patients in whom calcium pyrophosphate dihydrate (CPPD) deposition are detected in synovial fluid. [Methods] Patients with RA who underwent knee arthroplasty between March 2020 and September 2024 at our department were included. Patients were divided into two groups: those in whom CPPD deposition were detected in intraoperative synovial fluid via polarized light microscopy, and those in whom CPPD deposition were not detected, and their backgrounds were compared. [Results] Seventy-one patients with 84 knees were included, with a mean age of 73.6 years old, 84.5% were female, and the mean disease duration was 14.9 years. 17 knees (20.2%) were detected with CPPD deposition. The age, disease duration, and percentage of seropositive (anti-CCP antibody and/or rheumatoid factor positive) were 77.0 years old, 17.5 years, 29.4%, and 73.2 years old, 13.5 years, 23.9%, respectively, in the detected and non-detected groups. The percentage of female was significantly lower in detected group (64.7%) than in non-detected group (89.6%). [Conclusion] The prevalence of CPPD deposition in RA patients was 20.2%. The presence of CPPD deposition was associated with age.

W76-3

A case of an elderly patient with chronic kidney disease fatally treated with high doses of colchicine

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Conflict of interest: None

[Background] Low dose colchicine for gouty arthritis are recommended from the viewpoint of adverse events. Japanese package insert lists high dose of 3 to 4 mg/day. We report a case of an elderly patient with chronic kidney disease (CKD) who experienced fatal pancytopenia and multiple organ failure (MOF) due to high dose colchicine. [Case] 81-years-old man with microscopic polyangiitis and CKD. 6 days before transfer, gouty arthritis appeared during hospitalization at a previous hospital for colon colitis, and colchicine 4 mg/day was started. Serum creatinine level was 1.61 mg/dL. Diarrhea appeared, and colchicine was stopped 2 days before transfer. 1 day before transfer, hypoxemia and renal dysfunction progressed, and rapid pancytopenia appeared, the patient was transferred to our hospital. G-CSF were administered, but the pancytopenia and MOF did not progress any further, and the patient passed away on the third day after transfer. The colchicine blood levels was measured using serum at the time of transfer and was 5.716 ng/mL. [Conclusion] Although it is difficult to prove a causal relationship based solely on the measurement of colchicine blood levels at a single point in time, colchicine poisoning was strongly suspected based on the clinical course of diarrhea, pancytopenia, and AKI.

W76-4

Evaluation of bone lysis images using HR-pQCT after uric acid lowering therapy in a case where a gouty tophus penetrated the distal phalanx of the big toe

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Conflict of interest: None

[Case] A man in his 20s visited our hospital because of pain in his left big toe for 10 years. His serum uric acid level was 9.2 mg/dL, and X-ray images showed bone erosion in the left 1st MTP and a circular osteolysis in the center of the distal phalanx. US showed a tophus in contact with the extensor tendon attached to the distal phalanx, but there was no continuity with the IP joint. HR-pQCT images showed that the tophus penetrated the distal phalanx and was continuous with the tophus on the plantar side. Two years after starting uric acid-lowering therapy, X-ray images showed that the osteolysis of the left big toe distal phalanx had decreased, and US examination showed that the tophus had disappeared. Subtraction images were created using a 3D workstation from the HR-pQCT data, and the area of the cross section with the largest osteolysis at the initial visit was measured and compared. After two years of treatment, bone formation and remineralization were observed around the osteolysis, which had decreased by up to 57%. [Conclusion] After two years of continued uric acid lowering therapy, the urate crystals decreased and the tophus and inflammation disappeared, resulting in a marked improvement in the osteolysis of the distal phalanx of the left big toe due to bone formation.

W76-5

Study of US findings in cases of gout in the hand

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Conflict of interest: None

[Objectives and Methods] In this study, we examined the US findings of 30 men with gout in the hand. [Results] There were 18 cases of hand arthritis. There were 17 cases of tendonitis with one tophi in one case. In the MCP joint, there were 8 cases of arthritis (1.5±0.8 joints), with 1 tophus in 1 case, and 20 cases of tendonitis (3.0±2.5 tendons), with 13 tophi in 7 cases. Both inflammation ($p < 0.001$) and tophi ($p < 0.05$) were significantly more common in the tendons than in the joints. In the PIP joint, there were 4 cases of arthritis (1 joint each), with 1 tophi in 1 case, and 20 cases of tendonitis (2.1±1.5 tendons), with 5 tophi in 3 cases. Inflammation ($p=0.001$) was significantly more common in the tendons than in the joints. A comparison was made between 12 cases without wrist ar-

thritis (no group) and 18 cases with wrist arthritis (present group). The incidence of nail bed inflammation was significantly higher in the no group (3.5±3.2) than in the present group (1.1±1.9) ($p<0.05$). The double contour sign was present in 14 joints in the present group with and 0 joints in the no group. [Conclusion] These results suggest that gout in the hand may be a mixture of arthritis similar to that of the great toe and tendonitis accompanied by enthesitis.

W76-6

A case of gout with multiple inflammation and gouty tophi in the finger flexor tendons

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Conflict of interest: None

[Case] A man in his 50s with a history of gout in his big toe developed pain in his fingers and underwent US. Positive power Doppler signals (PD (+)) were observed in the nail bed, and the urate crystal depositions were observed in the right 5th extensor tendon (PD (+)), PIP joint (PD (+)), and left 3rd extensor tendon (PD (+)). On the flexor side, PD (+) was observed at the enthesis of the finger pad, and most flexor tendons showed inflammatory signs such as swelling, synovial fluid accumulation, and PD (+) from the wrist to the distal phalanx. The urate crystal depositions were observed in the tendons and in the subcutaneous tissue around the tendons. Many PD (+) gouty tophi were also observed in contact with the flexor tendons and spreading to the subcutaneous tissue. [Conclusion] It is said that The urate crystals are deposited in joints due to the high concentration of uric acid in the synovial fluid, but usually there is little fluid in the enthesis or tendon. On the other hand, US of cases with pain and stiffness of the fingers shows more enthesitis and itendonitis on the flexor side than on the extensor side. In this case, it is thought that urate crystals were formed due to the exudation of plasma caused by the enthesitis and tendonitis preceding gout.

W77-1

The long-term outcome of Swanson implant arthroplasty at the 1st metatarsophalangeal joint for the rheumatoid forefoot deformity

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Conflict of interest: None

Objectives: To investigate the long-term outcome of Swanson implant arthroplasty at the 1st metatarsophalangeal (MTP) joint in patients with rheumatoid arthritis (RA). Methods: A retrospective study was performed on 107 feet in 74 patients with RA (median age 60 years, 97.3% women) who underwent Swanson implant arthroplasty at the 1st MTP joint combined with shortening oblique osteotomy at the 2nd through 5th metatarsal necks. Radiological and clinical assessments were investigated more than 10 years after surgery. At the last follow-up, the range of motion (ROM) and pain visual analog scale (VAS) for the operated 1st MTP joint, and patient's VAS of satisfaction with surgery were investigated on 48 feet in 28 RA patients. Results: The median ROM was 32.5°, postoperative pain VAS was 17 mm, and satisfaction VAS was 85.5 mm. The median hallux valgus angle improved from 43.9° to 13.9°. The median implant subsidence was 4.0 mm, and complete implant fracture occurred in 6 feet There were delayed wound healing in14 feet, superficial and deep surgical site infection in two feet each Implant removal was done in two feet and re-osteotomy at the lessor toes was done in four feet. Conclusion: More than ten 10 years after surgery, the outcome of this procedure was generally good.

W77-2

Effect of foot length and width variations after surgical procedures for rheumatoid forefoot deformities

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Conflict of interest: None

[Objectives] The aim of this study was to evaluate the effect of variations in foot length and width after surgical procedures for rheumatoid forefoot deformities. [Methods] Fifty feet of 38 patients underwent joint preserving arthroplasty (n=20) and arthrodesis of the first metatarsophalangeal joint with shortening osteotomy of the lesser metatarsals or resection arthroplasty of the lesser metatarsal heads (n=30). Pre- and postoperative hallux valgus angle (HVA), intermetatarsal angle (IMA) of the first and second metatarsals (M1M2A), and IMA of the first and fifth metatarsals (M1M5A) were measured on weightbearing radiographs as well as foot length and width. We also evaluated the relationship between variations of radiographic parameters with Δ-foot length and Δ-foot width. [Results] Foot width changed significantly from 10.1 cm to 9.7 cm, while no significant difference was found between pre- and postoperative foot length. HVA, M1M2A, and M1M5A were significantly improved after the surgery. Significant positive correlation was found between the variation of food width with Δ-HVA, Δ-M1M2A, and Δ-M1M5A. [Conclusion] Surgical procedure for rheumatoid forefoot deformity improved radiographic parameters and reduced foot width while maintaining foot length.

W77-3

Comparative retrospective study of reverse shoulder arthroplasty in patients with rheumatoid shoulder and cuff tear arthropathy

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Conflict of interest: None

[Objectives] The purpose of this study is to compare the clinical outcomes of reverse shoulder arthroplasty (RSA) between rheumatoid arthritis (RA) group and rotator cuff tear arthropathy (CTA) group at 2 years postoperatively, limited to women. [Methods] Twenty-six shoulders in the RA group and 16 shoulders in the CTA group who underwent RSA from August 2016 to May 2022 were subjected. Trabecular metal reverse (TMR) was used for the glenoid and TMR or Comprehensive system were used for the humeral side. [Results] The Const ant score of CTA group (67 points) was significantly higher than that of RA group (57 points) at 2 years postoperatively (P=0.04). Intraoperative and postoperative fractures were significantly higher in the RA group (9/26 shoulders, 34.6%) than in the CTA group (0 shoulders) (P=0.02). The RA group was subdivided into a non-fracture group (17 shoulders) and a fracture group (9 shoulders). The postoperative external rotation in the fracture group was lower than that in the non-fracture group (P=0.01). [Conclusion] The short-term clinical outcome of RSA in the female RA and CTA groups was better in the CTA group, with more fractures in the RA group and decreased postoperative external rotation in the group with concomitant fractures.

W77-4

Subjective and objective outcomes of the PROSNAP total elbow arthroplasty for rheumatoid elbows

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Conflict of interest: None

[Objectives] The PROSNAP, a linked-type total elbow arthroplasty (TEA) by Kyocera, is designed for relatively small Asian patients and is characterized by component linkage with a snap-in structure. We investigated the subjective and objective outcomes of PROSNAP TEA for rheumatoid arthritis (RA). [Methods] We investigated 25 elbows of 24 RA patients (all female, mean age 65.6, mean RA duration 25.2 years). We evaluated the pre- and one-year postoperative elbow ROM, Japanese Orthopaedic Association (JOA) score, Mayo Elbow Performance Score (MEPS), Disability of the Arm, Shoulder, and Hand (DASH), Hand20, and Patient-related elbow evaluation (PREE). [Results] ROM significantly improved from 110° to 138° in flexion, from 55° to 67° in pronation, and from 60° to 73° in supination. JOA score increased from 47.6 to 89.1 and MEPS increased from 49.6 to 96.0 points. DASH and Hand20 improved pain, confidence, strength, and daily activities. PREE showed no improvement in throwing, but it improved significantly in pain, eating, and strength-related tasks. DASH (p=0.0039), Hand20 (p=0.0010), and PREE (p=0.000085) overall scores improved significantly using a significance test. [Conclusion] PROSNAP TEA for RA elbows improved elbow ROM, upper limb function, patient-reported outcome, and pain.

W77-5

Results of the silastic metacarpophalangeal joint arthroplasty in rheumatoid finger

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Conflict of interest: None

[Objectives] The MCP joint is one of the most frequently affected joints in rheumatoid arthritis (RA). In this study, we reviewed the results of silicon MP arthroplasty for RA fingers at our department. [Methods] Fifty-two patients with 190 joints who underwent silicon MP arthroplasty since 2000 were included in this study. There were 43 female patients and 9 male patients. The follow-up period ranged from 5 to 23 years. The postoperative range of motion, radiographic changes, and functional evaluation of the MP joints were examined in each case. [Results] The range of motion of the MCP joints improved from -71 degrees of extension and 90 degrees of flexion preoperatively to -4 degrees of extension and 58 degrees of flexion postoperatively, and radiological evaluation showed that ulnar deviation improved postoperatively. Loosening was found in 15 joints and breakage in 17 joints, and reoperation was performed in the two patients with broken implants. The MCP joint function evaluation according to Rittmeister showed good142 and fair48 joints, and ADL was improved due to improvement of pain and deformity. [Conclusion] Silicon finger arthroplasty performed at our department improved the MP joint extension angle and ulnar-deviation, and decreased pain.

W77-6

Short-term Outcomes of the Modified Zancolli Procedure for Rheumatoid Finger Deformities

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Conflict of interest: None

[Objectives] To evaluate the short-term outcomes of the modified Zancolli procedure for MP joint deformities in rheumatoid arthritis patients at our hospital. [Methods] 7 hands and 25 MP joints treated from February 2021 to July 2024 were reviewed. The group included 3 men and 4 women with a mean age of 63 years (range: 52-77). 6 cases were on the right hand and 1 on the left, involving the index (6), middle (6), ring (5), and little fingers (4). All were Larsen Grade 2, with Mitek mini anchors used. Evaluation included ulnar drift, MP joint ROM, and DASH score. [Results] MP joint ulnar drift improved from 5° (-10° to 39°) preoperatively to 4° (-16° to 19°) at final follow-up. ROM decreased from 30° (0° to 85°) -90° (75° to 100°) pre-op to 10° (0° to 30°) -80° (60° to 90°) post-op. DASH score improved from 10.8 (1.72 to 82.14) pre-op to 5 (5 to 13.39) at follow-up. Although DASH scores improved in all cases, some fingers showed worsened flexion angles and ulnar drift postoperatively. The decreased ROM may be due to the tendon advancement technique. Ulnar drift recurrence was more common in male cases, index fingers, and cases with severe bone and cartilage damage. [Conclusion] Careful patient selection is essential for achieving favorable outcomes with the modified Zancolli procedure.

English Poster Session

EP1-01

Optimal cancer screening in high-risk patients with dermatomyositis: A retrospective study of 44 cases

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Conflict of interest: None

[Objective] It is reported that the risk of developing cancer in patients with dermatomyositis (DM) may remain high for 3 to 5 years after DM diagnosis. The International Guideline for Idiopathic Inflammatory Myopathy-Associated Cancer Screening, published in 2023, recommends initial and annually repeated screening in patients at high risk of cancer. However, evidence for the optimal frequency of cancer screening is insufficient. This study aims to investigate the necessity of repeated screening. [Methods] We conducted a retrospective analysis of 44 patients with DM at our hospital. All the patients fulfilled Bohan and Peter classification criteria and were classified as being at high risk of cancer. We assessed screening modalities, detection of cancer and clinical characteristics of the patients. [Results] The average age at DM diagnosis was 61.2 years, with a mean follow-up period of 47 months and a mean interval from onset to DM diagnosis of 3.4 months. The initial screening including neck, chest, abdomen and pelvis CT scan (100%), upper (93.2%), and lower (81.8%) gastrointestinal endoscopy was conducted within 12 months after DM diagnosis (the percentages indicate the implementation rate of each examination). Nine patients were diagnosed with cancer; eight cases within 12 months of DM diagnosis through the initial screening and one in the 14th month. The standardized incidence ratio of cancer was significantly elevated in the first year (14.34; 95% confidence interval: 4.45-24.24), however it dropped to a level comparable to the general population in the second and subsequent years (0.84; 95% confidence interval: -0.76-2.45). [Conclusions] Our findings indicate that the initial cancer screening is beneficial in DM patients. Nevertheless, the low incidence of cancer in the second and subsequent years suggests that routinely repeating the intensive screening may not be necessary. Further studies with larger sample sizes are needed to confirm these results.

EP1-02

Association between triglyceride glucose index and carotid atherosclerosis in patients with systemic lupus erythematosus: a cohort-based study

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Conflict of interest: None

Objective: To investigate the association between triglyceride glucose (TyG) index and carotid atherosclerosis in systemic lupus erythematosus (SLE). **Methods:** This cross-sectional study in a tertiary care hospitals included 330 eligible consecutive SLE patients receiving carotid ultrasonography with integrated TyG index, calculated as ln [fasting triglycerides (mg/dL)×fasting glucose (mg/dL)/2]. According to the TyG index tertiles, the patients were categorized into three groups. Logistic regression models were applied to analyze the association of TyG index as continuous variables and tertiles with carotid atherosclerosis and carotid artery plaque. **Results:** Of 330 SLE patients included, 97.1% were female, with a mean age of 39.1±12.7 years and median disease duration of 95 (38-170) months. The frequency of carotid atherosclerosis was 10.3% (34/330) and the mean TyG index was 8.49±0.54. As compared with those without carotid atherosclerosis, patients with carotid atherosclerosis had significantly higher TyG index (8.87±0.82 vs. 8.45±0.48, p<0.001) (Figure 1). With increases in TyG index tertiles, the frequency of carotid atherosclerosis was increased, showing 3.7% for tertile 1, 9.1% for tertile 2 and 17.7% for tertile 3 (P=0.003). Multivariate logistic analyses showed that each 1-unit increase in TyG index was significantly associated with prevalent carotid atherosclerosis (unadjusted OR 3.84 (1.79-8.26); fully-adjusted OR 4.40 (1.52-12.69)). The unadjusted and fully-adjusted OR for occurrence of carotid atherosclerosis were 5.54 (1.83-16.80) and 4.19 (1.16-15.23) in patients with tertile 3 compared to patients with tertile 1 of TyG index (P for trend 0.006 and 0.042, respectively). Similar findings were found for the outcome of carotid artery plaque. **Conclusions:** The present study suggested that an elevated TyG index was associated with a higher risk of carotid atherosclerosis, independent of traditional cardiovascular risk factors and SLE-related factors.

EP1-03

Gut Microbiome Dysbiosis in Asian Patients with Knee Osteoarthritis

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Conflict of interest: None

[Objectives] We aim to evaluate the differences in gut microbiome of patients with knee OA compared to healthy controls. [Methods] We used the baseline data from patients with knee OA recruited to a randomized controlled trial (NCT02176460), who gave baseline demographic variables and stool samples. Age and sex matched healthy controls (HC) were recruited from community. DNA were extracted from patients' and HC stool samples and the gut microbiome was assessed using metagenomic profiling. Alpha and beta diversity, taxonomic and functional profiling of metagenomic analysis were compared between knee OA and HC. [Results] Nineteen knee OA patients (100% female, mean age 57.5 years) and 19 age and sex-matched healthy controls (100% female, mean age: 56.6 years) were included (Table 1). The knee OA patients had been diagnosed with moderate to severe knee OA: 68.4% Grade 3 KellgrenLawrence (KL) severity and 31.6% with Grade 4 KL severity. Both knee OA patients and HC showed similar ratio of Bacteroidetes to Firmicutes at phylum level (Figure 1A). At the genus level, there was increased abundance of Romboutsia and Streptococcus genus (both p<0.05) (Figure 1B) and decreased abundance of Bilophila, Hungatella, Lachnoclostridium and Massilimicrobiota genus (all p<0.05) in knee OA patients compared to HC. At the species level, knee OA patients had increased abundance of Prevotella bivia (p<0.05), and decreased abundance of Bacteroides sp, Bilophilia sp, Blautia obeum, Hungatella sp, Clostridium sp, Parabacteroides diatasonis (all p<0.05). There were differences in expression of Kyoto Encylopedia of Genes and Genome (KEGG) function proteins between OA patients versus HC (Figure 1C & 1D). Alpha diversity (p=0.39), and beta-diversity (p=0.09) were not significantly different between OA patients versus HC. [Conclusion] There are differences in gut microbiome composition between patients with knee OA and healthy controls. which may suggest possible link to pathogenesis.

EP1-07

Association of male microchimrism with severity of clinical manifestation in sclerodermic patients registered in scleroderma clinic at Hafez hospital in Shiraz

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Conflict of interest: None

[Objectives] Microchimerism is defined as the presence of non-self and circulating cells in a host. The current study aimed to assess the effect of microchimerism on scleroderma major organ involvements. This cross-sectional study was conducted on 56 scleroderma patients registered in a tertiary rheumatology center of Shiraz Univer- sity of Medical Sciences. Information on the patients' demographics and disease complications was gathered through a review of medical records. Skin score was applied to better assess skin thickening. High Resolution CT-scan as well as pulmonary function test (PFT) results were also used to investigate pulmonary involvement in patients. Y chromosome serum levels were measured using Phenol Chloroform Extraction protocol and following real-time PCR. [Methods] Fifty-six scleroderma patients with a mean age of 46±10 years were recruited in this study (58.9% with diffuse scleroderma and 41.07% with limited scleroderma). Other than skin thickening, the most common clinical presentation among the patients was interestitial lung disease (67.8%). [Results] No significant difference was found between Y chromosome levels of patients with either lung, cardiac, renal, or gastrointestinal involvement and those who did not have these complications. Y chromosome serum levels based on the results of PFT were also shown to have no significant difference. Moreover, no association was demonstrated between serum Y chromosome and skin score. The serum level of chromo-

some Y has no impact on the severity and frequency of major organ involvement in Iranian scleroderma patients. [Conclusion] unlike previous literatures, it was concluded that the serum level of chromosome Y has no impact on severity and frequency of major organ involvement in iranian scleroderma patients. this finding proposed the possible role of genetic and ethnical differences in disease presentations around the world which mandates further regional investigations.

EP1-08

Clinical predictors of organ damage at diagnosis in primary Sjögren's syndrome

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Conflict of interest: None

[Objectives] To elucidate the factors associated with organ damage at the time of diagnosis in primary Sjögren's syndrome (SjS). [Methods] All consecutive patients with primary SjS who visited Keio University Hospital between April 2012 and August 2024 were included. We retrospectively collected the following clinical data: age, sex, tear production by Schirmer test, saliva production by gum test, time from the onset of symptoms to diagnosis, the presence of autoantibodies, and laboratory findings. We analyzed factors associated with the severity of glandular symptoms and the presence of extraglandular organ manifestations at the time of diagnosis with primary SjS. [Results] A total of 333 patients with primary SjS were identified. The mean age was 66.8±15.4 years old, and 94.6% were female. The mean duration from symptom onset to diagnosis was 48.2±55.1 months. Positivity of anti-SSA, anti-SSB and anti-centromere antibodies were 70.2%, 34.7% and 8.7%, respectively. The mean values of Schirmer and gum test were 4.6 mm/5 min and 5.45/10 min. Of note, the diagnostic duration time from symptom onset was negatively correlated with the results of gum test (r=-0.17, p=0.02). Serum IgG levels were significantly higher in patients with interstitial nephritis and pulmonary hypertension than those without (interstitial nephritis; 2749±216.6 vs 1841±40.4 mg/dL (p<0.0001), pulmonary hypertension; 3149±269.6 vs 1843±39.9 mg/dL (p<0.0001)). [Conclusion] This study highlights that delayed diagnosis and elevated serum IgG levels are linked to organ damage at the time of diagnosis. These findings underscore the importance of early detection and management of systemic inflammation to prevent irreversible organ involvement in primary SjS.

EP1-09

Association between IgG4-related disease and peripheral blood eosinophil

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Conflict of interest: None

[Objectives] IgG4-related disease (IgG4RD) is characterized by peripheral blood eosinophilia in 20-40% of patients, but its clinical characteristics remain unclear. This study aims to investigate the characteristics of IgG4RD patients with eosinophilia. [Methods] We conducted a retrospective analysis of IgG4RD patients who visited our department between April 2004 and April 2024. The patients were divided into two groups: those with peripheral blood eosinophil counts of 300/μL or more and those with less than 300/μL. Clinical backgrounds and treatment outcomes were compared between the two groups. This study included patients who scored 20 or higher according to the 2019 ACR/EULAR classification criteria. [Results] A total of 44 patients met the ACR/EULAR classification criteria, of whom 23 (52.3%) exhibited eosinophilia at the time of IgG4RD diagnosis. The eosinophilia group had a higher proportion of males (91.3% vs. 47.6%, *p*=0.002) and a greater number of affected organs (median 4 vs. 3, *p*=0.040). This group also showed a trend towards a higher frequency of malignancies (52.2% vs. 23.8%, *p*=0.052) and elevated levels of serum IgG and IgG4/IgG ratio (median 2341 mg/dL vs. 1645 mg/dL, *p*=0.098, 0.41 vs. 0.28, *p*=0.074). There were no differences in the treatment approaches or recurrence rates post-treatment. [Conclusion] In IgG4RD patients with eosinophilia, there is a tendency toward higher serological activity and a greater number of affected organs. Additionally, careful attention should be paid to the potential for malignancy.

EP1-10

Mortality in patients with psoriatic arthritis: A systematic review and meta-analysis

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Conflict of interest: None

[Objectives] The debate persists regarding whether patients with psoriatic arthritis (PsA) face an increased risk of mortality. We aimed to ascertain the magnitude of all-cause mortality risk in patients with PsA compared to the general population through a systematic review and meta-analysis. [Methods] We conducted a comprehensive search of PubMed, EMBASE and Cochrane Library for studies published from inception to December 2023. STATA meta-analysis software was used to calculate the pooled risk estimates for mortality, represented as standardized mortality ratio (SMR). [Results] Among the 3,889 articles identified in our research, 20 studies were included for analysis. Overall, our findings revealed a 1.12-fold increased risk of death among PsA patients compared with the general population (meta-SMR: 1.12, 95% CI 1.09-1.15). Subgroup analyses showed that mortality risks were elevated in Asian countries (meta-SMR: 1.28, 95% CI 1.04-1.57), within population-based studies (meta-SMR: 1.13, 95% CI 1.02-1.25), and among the studies including over 1000 patients (meta-SMR: 1.12, 95% CI 1.01-1.25). Malignancy, cardiovascular and cerebrovascular diseases, as well as infection/respiratory diseases, emerged as the most frequent causes of mortality. [Conclusion] Our analysis suggested an approximately 12% increase of mortality among patients with PsA compared with the general population. More attention should be paid to malignancy, cardiovascular and cerebrovascular diseases, and infection/respiratory disease among PsA patients.

EP1-11

Prevalence and Associated Factors of Cognitive Disorders in Patients with Systemic Lupus Erythematosus: A Cross-Sectional Study Conducted in Urmia

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Conflict of interest: None

Objectives: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can significantly impact the central nervous system, leading to a range of neuropsychiatric manifestations, including cognitive impairment. This study aimed to investigate the prevalence and associated risk factors of cognitive impairment in a cross-sectional study of SLE patients. ***Methods:*** Comprehensive patient data were collected from 71 SLE patients, including demographics, clinical characteristics, and body mass index (BMI). Disease activity, cognitive function, anxiety and depression levels was measured using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2000), Mini-Mental State Examination (MMSE), Beck Anxiety Inventory and Beck Depression Inventory, respectively. ***Results:*** The prevalence of cognitive disorders among SLE patients was 31%. 86.3% of those with cognitive disorders were illiterate (or only completed middle school), compared to 39.5% in the non-cognitive disorder group (p=0.002). The mean age of patients without cognitive disorders was significantly lower (36.95±11.45 years) than that of those with cognitive disorders (45.5±12.18 years) (p=0.006). The mean disease activity score for patients with cognitive disorders was marginally higher (5.67±5.2) than for those without (3.26±2.94) (p=0.05). Depression scores were higher in patients with cognitive impairment (15±8.32) compared to those without (11.67±6.19) (p=0.05). Significant associations between cognitive disorders and increasing age (OR=1.65; 95% CI: 1.04-6.17; p=0.05), high-

er depression scores (OR=1.7; 95% CI:0.99-6.99; p=0.045), and lower educational levels (OR=14; 95% CI: 1.62-120; p=0.02) were foud. ***Conclusion:*** The findings indicate a high prevalence of cognitive disorders among patients with SLE, with significant relationships identified between cognitive impairment and factors such as advanced age, low educational attainment, elevated disease activity scores, and increased depression levels.

EP1-12

Determining Temporomandibular joint involvement in Lupus and Sjogren's patients by Ultrasound and comparing it with Clinical findings

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Conflict of interest: None

[Objectives] Temporomandibular joint (TMJ) involvement is one of the causes of musculoskeletal pain in adults. Rheumatological diseases, including Rheumatoid Arthritis (RA), Seronegative Spondyloarthropathies (Spa), Lupus (SLE) and Sjogren's (SS) disease. But few studies have been conducted on the prevalence of TMJ involvement in SLE and SS and the risk factors which can affect them. [Methods] A total of 51 patients, including 41 patients with SLE (selected based on SLICC criteria) and 10 patients with SS (based on ACR/EULAR criteria), who were selected from the patients referred to the Rheumatology Clinic of Shariati Hospital during 9 months, were included in the study. A rheumatologist performed a TMJ examination and then they were referred to a radiologist for ultrasound (US). Patients divided in 3 groups (all patients, SLE and SS patients). Their demographic information, important laboratory data such as ESR, CRP, dsDNA, complement, Major organ involvement and Drugs was obtained by questionary form and all information was recorded. [Results] The frequency of TMJ involvement was reported to be 57% of all patients, 70% of Sjogren's patients by US which was significantly more than physical examination (PE). 39% in All patients and 30% in Sjogren's patients (P-Value < 0.05). Although the detection rate in lupus patients by US (54%) was higher than the PE (41%), but it wasn't statistically significant. The degree of concordance between US and PE, was reported 70% in all patients. the highest concordance was in lupus (73%) and the lowest Concordance was reported in Sjögren's (60%). Cortical irregularity by US and Jaw deviation by PE was the most involvement in all patients group. [Conclusion] It seems TMJ involvement is common in SLE and SS, and it is necessary to pay more attention to this joint in routine PE. Although studies have been done on the use of US in diagnosis of TMJ involvement in diseases such as RA. It's use in other diseases such as SLE and SS is missed.

EP1-13

Gender differences in hyperuricemia and the association between hyperuricemia and colorectal cancer in Korean population

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Conflict of interest: None

[Objectives] The prevalence of hyperuricemia has been increasing not only in men but also in women, but they have the different epidemiological characteristics of hyperuricemia. Cancers related to the digestive system, such as colorectal cancer are easily affected by environmental factors including diets which is closely associated with hyperuricemia; however, its relationship is still unclear. In this study, the characteristics of hyperuricemia in Korean men and women and the relationship between colorectal cancer and hyperuricemia were investigated. [Methods] We analyzed nationwide data from the Korea National Health and Nutrition Examination Survey of 11685 men and 15420 women. Chi-square tests and Student's t-tests were used to examine the differences in variables between the hyperuricemia and normouricemia groups. Multiple logistic regression models were used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for the prevalence of colorectal cancer patients with hyperuricemia. [Results] The overall prevalence of hyperuricemia in Korea was 13.7% (men, 21.3%; women, 7.9%). In men, hyperuricemia was prevalent in those under 50 years of age, and in women, in those over 60 years of age. Obesity, hypertension, and dyslipidemia had high prevalence rates in the hyperuricemia group in both men and women, and in particular, hypertension and diabetes were closely related to hyperuricemia in women than in men. Alcohol consumption was related to hyperuricemia in men, but not in women. The prevalence of colorectal cancer with hyperuricemia was 0.67%, but there was no significant difference in prevalence of colorectal cancer between the hyperuricemia and normouricemia groups (men, OR 1.13, 95% CI 0.65-1.94; women, OR 1.66, 95% CI 0.80-3.45). [Conclusion] Women were more likely to have hyperuricemia at an older age and to suffer from diabetes and hypertension than men. However, there was no significant association between hyperuricemia and colorectal cancer.

EP1-14

Comparative Analysis of Clinical and Pathological Features in the First Renal Biopsy of Lupus Nephritis Patients: A Study Across Rheumatology and Nephrology Cohorts

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Conflict of interest: None

Objectives: Lupus nephritis (LN) significantly contributes to the morbidity and mortality in systemic lupus erythematosus (SLE). Renal biopsy is the gold standard for LN. Given that nephrologists typically conduct these biopsies, it's intriguing to explore potential differences in biopsy indications and clinical characteristics of LN patients between rheumatology and nephrology departments. Furthermore, the expanded indications for renal biopsies in the 2019 EULAR/ERA-EDTA guidelines prompt the question of whether physicians are more actively following these guidelines and performing renal biopsies. Methods: We analyzed biopsy-proven LN patients from rheumatology and nephrology departments from January 2011 to July 2024. Indications for renal biopsies, and clinical and pathological characteristics were recorded and compared between departments and between pre- and post-2019 subgroups. Results: We included 543 patients with biopsy-proven LN, with 195 in rheumatology and 348 in nephrology. Rheumatology patients had longer SLE disease duration and more frequent extrarenal manifestations. They also had higher positivity rates for auto-antibodies (Sm, rRNP, nRNP) but lower serum creatinine levels, fewer urinary red cells, and a lower activity index (AI, 7 vs. 8). Clinical variables, histological classes, and chronic index (CI) were similar between departments. The post-2019 group (n=275) showed reduced SLEDAI scores, and a significant decrease in urinary red cells and casts. However, no differences in histological classes or AI/CI scores were observed between pre- and post-2019 groups. Notably, the percentage of isolated proteinuria as an indication for renal biopsy increased after 2019. Conclusions: Biopsy indications were similar between rheumatology and nephrology cohorts. Physicians appear to have become more proactive in performing renal biopsies after 2019, with a decrease in urinary sediment abnormalities and an increased proportion of isolated proteinuria.

EP1-15

Association of hematological composite scores with RPDAI, RPDAM, autoantibodies and specific medication regimens in patients with relapsing polychondritis

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Conflict of interest: None

[Objectives] This study aims to explore the associations between hematological composite scores and specific items of the relapsing polychondritis (RPC) Disease Activity Index (RPDAI), the total score of the RPC Damage Index (RPDAM), autoantibodies, and the effects of different medications. [Methods] 73 RPC patients and 73 age- and sex-matched healthy controls were recruited from our hospital from January 1st 2008 to September 30th 2024. Hematological composite scores calculated included CLR, CAR, NLR, PLR, LMR, and SIRI. The Spearman method was used to analyze the correlation between these indexes and the demographic characteristics of RPC patients, specific scoring items of RPDAI, total scores of RPDAM, antibodies, and medications. Multivariate regression analysis was used to assess the relationship between these indexes and the included characteristics. [Results] Compared to controls, RPC patients had significantly lower levels of LMR, and higher levels of other indexes included. CAR correlated with auricular chondritis. CAR was negatively correlated with MMF treatment, and NLR was negatively correlated with HCQ treatment. After multivariate analyses, we found that proteinuria was associated with higher CLR, NLR, PLR and SIRI levels, as well as lower LMR levels. Respiratory chondritis with acute respiratory failure was associated with higher NLR and PLR levels. Higher RPDAM was associated with higher NLR levels. It was found that the positive result for anti-SSA was associated with higher CAR and LMR levels, while the positive result for p-ANCA was associated with higher PLR levels. We also discovered that MTX was associated with lower CLR. [Conclusion] Incorporating clinically accessible hematological composite scores into routine evaluations can aid in evaluating disease activity and assessing disease severity, and informing clinical treatment strategies.

EP1-16

Study on the effect and mechanism of methotrexate on serum uric acid in patients with rheumatic and musculoskeletal diseases

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Conflict of interest: None

[Objectives] Studies have shown that MTX combined with Peglotricase treatment can enhance the efficacy of lowering uric acid by inhibiting the production of anti-PEG antibodies. Given that MTX can inhibit the activity of ADA, it is possible that MTX inhibits the activity of ADA in cells, resulting in a decrease in serum uric acid. The purpose of this study was to clarify the effect of MTX on serum uric acid in patients with RMDs and its mechanism of action on serum uric acid. [Methods] The clinical data of 349 patients with RMDs who used methotrexate for more than 24 weeks and 429 patients with RMDs who did not take methotrexate were collected. The differences of serum uric acid concentration and incidence of hyperuricemia were compared between the two groups. A total of 106 patients with RMDs who received MTX for the first time and continued for 24 weeks were included. The levels of serum adenosine deaminase in RMDs patients before and after 24 weeks of continuous use of MTX were detected, and the changes of serum levels before and after MTX use were compared. PBMC of patients with initial medication were collected and divided into two groups: group A and group B. Group A was added with MTX at a concentration of 1 mg/L, and group B was a negative control without drugs. The activities of ADA in cells of two groups were detected. [Results] At week 0 and 24, the difference of the serum uric acid concentration and the incidence of hyperuricemia in the non-methotrexate group and the methotrexate group and inthe initial use of methotrexate group was statistically significant. The serum ADA level at week 0 and 24 was also significant. The intracellular ADA activity in group A was significantly lower than that in group B, the difference was statistically significant. [Conclusion] MTX, as a DMARDs, reduced the serum uric acid level and the incidence of hyperuricemia in RMDs during the treatment of RMDs, and reduced the serum ADA levels in RMDs patients. MTX also inhibited the production of ADA.

EP1-18

The First Case of Dulagutide-induced Leukocytoclastic Vasculitis

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Conflict of interest: None

Introduction: Leukocytoclastic vasculitis (LCV) is a small vessel vasculitis that is largely limited to the skin. LCV typically presents with symmetrical non-blancheable purpuric papules, though cutaneous manifestations may include ulcers, vesicles, and pustules. LCV has a wide spectrum of etiologies including malignancy, infections, vaccines, and medications. Of the medications attributed to LCV, GLP-1 agonists, such as dulaglutide, are an extremely rare cause with two case reports of semaglutide causing LCV. We report the first case of biopsy-proven LCV caused by dulaglutide. **Case Report:** a 57-year-old male with history of type 2 diabetes, obesity, polycythemia, and hypertension was started on dulaglutide for management of diabetes. He received a total of six weekly injections. Four days after his last injection, he developed non-blancheable palpable purpuric lesions. Dulaglutide was discontinued. He was seen in the emergency room where he had bloodwork negative for Rheumatoid factor, ANA, ENA, anti DNA, hepatitis A, B, C, and HIV serology. Skin biopsy revealed leukocytoclastic vasculitis with IgG and C3 deposition in the superficial vessel. The rash resolved after a one week course of prednisone. Patient was not started on any other new medications during this time. **Discussion:** Our case adds to the literature of two other cases implicating GLP-1 agonism in the development of LCV. The pathophysiology underlying this association is unclear. On literature review, dulaglutide has been associated with the development several inflammatory conditions at different layers of the skin including bullous pemphigoid, pyoderma gangrenosum, and granulomatous panniculitis. This suggests that dulaglutide hypersensitivity may be associated with immune dysregulation or autoimmunity, which could contribute to vasculitis. **Conclusion:** We present the first biopsy proven case of LCV due to dulaglutide. Further studies are required to elucidate the pathophysiology of this association.

EP1-19

Relapse of Adult Onset Still's Disease (AOSD) Complicated by Cardiogenic Shock Secondary to Myocarditis in a Diabetic Filipino

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Conflict of interest: None

Background: Adult Onset Still's Disease (AOSD) is a rare inflammatory disorder presenting as fever, arthritis or arthralgia, and salmon-pink nonpruritic maculopapular rashes In the Philippines, there is paucity of data in terms of its epidemiology. A relapse of disease following years of quiescence is rarely reported. Because of its similar presentation with other more common inflammatory disorders, it remained to be under-diagnosed and rarely considered in many cases. **Case Report:** This is a case of a 51-year-old diabetic male, diagnosed case of AOSD, presenting as fever and arthritis in 2010. He received regular Tocilizumab infusions for a year, achieved quiescent disease activity, and was subsequently lost to follow-up. He came in to our institution due to generalized body weakness and high-grade fever. He likewise presented with arthralgia, myalgia, and sore throat. Examination showed cervical lymphadenopathy, S3 gallop, and weak muscle tone. He subsequently developed cardiogenic shock secondary to myocarditis. Diabetic ketoacidosis (DKA) and heart failure with reduced ejection fraction likewise complicated his course. Ancillaries showed persistent leukocytosis in the absence of infection, and transaminitis. Inotropic support was instituted. He was given methylprednisolone pulse therapy followed by intravenous tocilizumab. After treatment regimen, hemodynamic stability, improvement of ejection fraction, and resolution of DKA was achieved. Symptoms of AOSD, namely fever, arthralgia, sore throat, and transaminitis, resolved. **Conclusion:** This case report contributes to the broader understanding of AOSD by documenting disease relapse following a long quiescent period. Adult Onset Still's Disease should be one of the considerations for patients presenting with fever and presence of maculopapular rash without a clear cause. It summarizes the key aspects of the case, acknowledges the challenges faced, and emphasizes the importance of a multidisciplinary approach.

EP1-20

A Rare Co-existence of Limited Scleroderma and Celiac disease

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Conflict of interest: Yes

Background: Systemic sclerosis is a rare autoimmune disease-causing thickened skin, vasculopathy and involvement of internal organs. Celiac disease (CD) is also an autoimmune disorder which affects the digestive system triggered by gluten intake. Their association has been described in previous studies and case reports but published literature is limited. **Case Presentation:** Here, we describe a rare case of a 36-year-old female, diagnosed of Celiac disease since 2019, recently consulted due to Raynaud's phenomenon and fatigue. It was noted on physical examination that patient has sclerodactyly of distal digits. Moreover, she has strong family history of autoimmune disease (Sjogren's syndrome). With this pertinent information, she was worked up for possible autoimmune etiology. Pertinent results were as follows: ANA 1:640 Centromere pattern, Lupus Panel Negative, Anti Jo-1 Negative, Sclerodermal marker result: positive Anti centromere A and Anti Centromere B and also high Gliadin Antibody IgA 119 U/ml, negative C3 (49.8 mg/dL), C4 (15.7 mg/dL), low CRP (0.15) and ESR (<1). These results confirm the diagnosis of limited scleroderma in a patient with celiac disease. Further work up was requested to rule out common systemic involvement of scleroderma but revealed normal pulmonary function test, normal echocardiography including pulmonary artery pressure, as well as normal creatinine and urinalysis. Patient was managed symptomatically and was advised for regular monitoring. **Conclusion:** Association of different autoimmune diseases in an individual is common. Thus, co-existence of Celiac disease and Scleroderma has been reported in the past, but the scarcity of published studies is one evidence of its' rarity. Published observational studies have contradicting results with limited number of participants. But reports of association between the two, must guide us in diagnosis of possible similar cases in the future.

EP1-21

Successful IVIG and Glucocorticoid Treatment in a Filipino Female with Autoimmune Encephalitis: A Case Report

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Conflict of interest: None

[Objectives] To present a case of a Filipino Female with autoimmune encephalitis who respond well on IVIG and Glucocorticoid Treatment [Case Report] A Thirty Five year old female who initially presented with one week history of sleep disturbance and generalized malaise. She had no underlying systemic disease, nor intake of alcohol or substance abuse. On initial evaluation at the Emergency Department, she had stable vital signs and was afebrile, with good orientation and appropriately answers to questions and appropriately answers to questions. Work up showed hyponatremia with leukopenia. She was initially managed Primary Insomnia, Euvolemic Hyponatremia and Urinary Tract Infection. Six hours later, she developed new onset fever, tachycardia, with slow response time and blank stares. Examination demonstrated supple neck, MMTs Three over five on upper and lower extremities. Cranial MRI and EEG were unremarkable. CSF fluid analysis revealed elevated CSF IgG. Infectious work up and encephalitis panel were negative. Autoimmune workup revealed positive ANA Homogenous pattern, Hypocomplementemia pANCA positive, IV Immunoglobulin for five days and Methyprednisolone pulse therapy for 3 days was were initiated with marked improvement in her neurologic status. With continuous physical and occupational therapy, the patient was subsequently discharged improved. The patient is maintained on tapering oral glucocorticoids [Conclusion] Autoimmune encephalitis can manifest initially in various ways. Early recognition and treatment are needed to avoid neurological sequelae and complications. Delay in immunotherapy may contribute to poor outcomes.

EP1-22

Symptom characteristics reported by patients with Sjögren's syndrome when they first visit a specialist

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Conflict of interest: None

[Objective] Sjögren's syndrome is an autoimmune disease that causes chronic inflammation throughout the body. Although the diversity of subjective symptoms is considered to be a characteristic of this disease, the clinical significance of this diversity is unclear. In this study, we focused on subjective symptoms at the time of the first visit to the internal medicine specialist outpatient clinic and examined their characteristics. [Methods] The subjects were patients who first visited our department between April 2023 and March 2024 and were clinically diagnosed with Sjögren's syndrome. Subjective symptoms were extracted from the questionnaire (multiple choice and free description) at the time of the first visit and from the medical records, and their characteristics were descriptively clarified and analyzed for association with physical findings, severity, etc. [Results] Of the 292 patients who first visited our department, 99 were clinically suspected of having Sjögren's syndrome, and 50 were definitively diagnosed. The average age was 67 years, and 86% were women. The number of subjective symptoms was statistically significantly higher than other collagen diseases, and the types of subjective symptoms were diverse, including dry symptoms, systemic symptoms, and gastrointestinal symptoms. [Conclusion] Sjögren's syndrome patients present with many and varied subjective symptoms at their first visit to the internal medicine specialist clinic, and the many and varied subjective symptoms are thought to be characteristic of this disease. Further studies involving a larger number of cases are necessary to clarify the clinical significance.

EP1-23

Amylodosis - Retrospective case s...

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Conflict of interest: None

Objectives: The Literature from Indian Subcontinent is scare regarding amyloidosis. We Aimed at studying the clinical profile of the patients with amyloidosis, their epidemiology, risk factors, clinical features and prognosis. **Method:** This a retrospective analysis of the out patient and in patient electronic medical records of the patients visiting rheumatology clinic from a single centre in south India from September 2020 to September 2023. Patient demographics, co morbidities, clinical features, musculoskeletal examination findings, internal organ involvement, laboratory findings including biopsy findings and bone marrow report and treatment details and survival data were analysed and entered. **Results:** A total of 5 patients were diagnosed to have Amyloidosis in this study period from Sep... 2020 to September 2023. The presenting symptoms were polyarthralgia or polyarthritis, excertional dyspnea. Classical feature of Amyloidosis like maeroglossia, Shoulder fat pad sign, peri orbital oozing was present in one patient. Strikingly 4 out of the 5 patients has features of serositis (pleural, pericardial, ascites). Bleeding manifestations (coagulopathy or Gi bleed or periorbital ooze) were present in 4 out of 5 patients. Echo features of amyloidosis was present in 3 patients Hepatomegaly with obstructive pattern of liver enzymes was present in 2 patients. Biopsy feature of amyloidosis either (fat pad, renal, GI, Bone marrow) were available in 4 out of 5 patients. 2 patients out of 5 died. **Conclusion:** Amyloidosis is a relatively rare condition caused by the accumulation of diverse normal and abnormal proteins in various bodily tissues. The success of medical management is predicated by the earliest possible diagnosis. Effective therapy cannot be instituted unless the type of amyloid is correctly identified. AA amyloidosis complicating Chronic Inflammatory Condition usually presents with Renal involvement (proteinuria) and histological confirmation with Renal Biopsy is important.

EP1-24

Incidence of ana positivity after the administration of biological drugs and their clinical co relation.

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Conflict of interest: None

Objective: To evaluate the prevalence and significance of ANA positivity following the administration of biological agents in Indian Subcon-

tinent patients with autoimmune rheumatological diseases. Methods: Pilot prospective cohort analysis involving 100 patients with autoimmune rheumatological diseases who were initially ANA negative at baseline. The cohort included patients with axial spondyloarthritis (AxSpA) and ANCA vasculitis. Patients with AxSpA, diagnosed according to the 2009 ASAS criteria, and treated with biological agents were followed at a tertiary care center in India from January 2021 to December 2023. ANA levels were measured before and after 3, 6, 9, or 12 months of biological therapy. Changes in ANA positivity, clinical outcomes, and correlations with disease activity were analyzed. Results: Out of the 100 patients enrolled, 69 (69%) completed the study. All participants were ANA negative at baseline. After biological therapy, ANA positivity developed in 4 patients (5.9%). Despite this increase, there was no significant correlation between ANA positivity and clinical disease activity, as measured by the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the visual analog scale (VAS) for pain, suggesting effective therapeutic response despite changes in ANA status. Additionally, 28 patients were not able to continue biological therapy, highlighting challenges related to the financial sustainability of biological therapy in the developing countries Conclusion: Biological therapies for AxSpA are associated with an increase in ANA positivity in these patients, although this change does not appear to impact clinical disease activity. The rise in ANA titers may reflect disease-related changes or treatment effects rather than a direct correlation with therapeutic efficacy. Further longitudinal studies are needed to understand the clinical significance of these findings and to refine the interpretation of ANA results during biological therapy.

EP1-25

Eosinophilic Granulomatosis with Polyangiitis Presenting as Hepatic Lesions: Two Case Reports and a Comprehensive Literature Review

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Conflict of interest: None

[Objective] Liver involvement in eosinophilic granulomatosis with polyangiitis (EGPA) is rare. We report two cases of hepatic lesions in EGPA and review the literature to elucidate its clinical significance. [Methods] EGPA cases with biopsy-proven eosinophilic liver infiltration were identified using PubMed; the search terms were “eosinophilic granulomatosis with polyangiitis”, “Churg-Strauss syndrome”, and “liver”. [Results] Case 1: A 66-year-old man presented with fever and right upper quadrant pain. He had eosinophilia and elevated hepatobiliary enzymes and was positive for MPO-ANCA; CT showed multiple hepatic lesions. A liver biopsy showed hepatocellular necrosis and eosinophilic infiltration. Thereafter, the patient had an asthma attack and developed sensory neuropathy. The findings led to an EGPA diagnosis. Recurrent eosinophil and hepatobiliary enzyme elevations were noted during steroid tapering, indicating a relapse. Since the availability of mepolizumab, he has been maintained on prednisolone (PSL) 3 mg. Case 2: A 39-year-old man with asthma and eosinophilic sinusitis presented with jaundice, abdominal pain, paresthesia, and lower-limb purpura. He showed eosinophilia, multiple mononeuropathies, and eosinophilic infiltration on skin and liver biopsies, leading to an EGPA diagnosis. He achieved remission with mepolizumab and PSL 3 mg. Five cases of liver involvement in EGPA have been reported. The said patients often developed right upper quadrant pain and cholestatic liver dysfunction, which improved rapidly after therapy initiation. To date, no specific imaging findings are known. Liver biopsy showed portal eosinophilic infiltration, necrotizing vasculitis, and granulomas. [Conclusion] It is important to recognize that EGPA can affect the liver. Liver biopsy can be a valuable tool in diagnosing EGPA. The multiple hepatic hypoattenuations and hepatocellular necrosis due to eosinophils in our case have not been reported previously.

EP1-26

Subacute progressive interstitial lung disease in elderly-onset male systemic lupus erythematosus

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Conflict of interest: None

Although interstitial lung disease (ILD) is relatively rare pulmonary involvement of systemic lupus erythematosus (SLE), rapidly progressive cases have been reported as “acute lupus pneumonitis (ALP)”. However, cases of subacute progression of SLE-ILD have not been well recognized. Here we report an elderly-onset male SLE patient with subacute progressive ILD, neuropsychiatric (NP) and renal disease, which was ameliorated by Rituximab (RTX), Anifrolumab (ANI) and corticosteroids. A 71-year-old man had a history of facial erythema and alopecia one year before admission. Then the patient developed dry cough and gradual progression of dyspnea on exertion (DOE) three months before admission. one month before admission, slight consolidation in both lower lobes of the lungs was detected on chest high resolution computer tomography (HRCT). From the same time, he began to have NP symptoms, such as cognitive disfunction and apathy. He visited a referral hospital due to the worsening of DOE a week before admission. He had mild consciousness disorder, fever and hypoxia. Laboratory test revealed thrombocytopenia, elevated serum anti-DNA IgG, low complement level and urinary protein. Chest HRCT showed extensive ground-glass opacity at both upper lobes and patchy-consolidation at whole lungs. He was diagnosed as SLE with progressive ILD, NP and renal involvement and was admitted to our hospital. We started treating the patient with methylprednisolone pulse therapy. Sequentially, we introduced RTX because of the favorable treatment efficacy to both SLE-ILD and NP-SLE. We additionally administered ANI, as the patient’s NP symptoms did not improve, and he had a history of skin rashes, which has been reported to be associated with a type 1 interferon signature. A month after admission, his manifestations dramatically improved with no serious complications. Our report suggests that subacute progression of ILD should be taken into account as a distinct clinical course of SLE-ILD.

EP1-28

Bridging Gout and Diabetes: A Deep Dive into Risk Dynamics and Interconnections

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Conflict of interest: None

Objectives This review aims to explore the bidirectional relationship between gout, an inflammatory arthritis marked by elevated serum uric acid, and type 2 diabetes mellitus (T2DM), a global metabolic disorder. It evaluates how hyperuricemia exacerbates insulin resistance and chronic inflammation and assesses the impact of urate-lowering therapies on managing both conditions. Methods A comprehensive review of literature was conducted using databases like PubMed and Scopus. Studies investigating the relationship between hyperuricemia, gout, and T2DM were selected. The role of monosodium urate crystals, inflammatory pathways, oxidative stress, and metabolic syndrome in disrupting glucose metabolism and insulin signaling was analyzed. The effectiveness of urate-lowering therapies, especially allopurinol, in reducing gout flares and improving insulin sensitivity was reviewed. Results The review finds that gout patients are at higher risk of developing T2DM, with a prevalence as high as 19%. Hyperuricemia and monosodium urate crystals trigger inflammation, impairing insulin signaling and glucose metabolism. Metabolic syndrome, often present in gout patients, further aggravates the development of T2DM through oxidative stress and endothelial dysfunction. Urate-lowering therapies, particularly allopurinol, show potential in reducing gout flares and improving insulin sensitivity. Conclusion Gout and T2DM are linked by shared metabolic dysfunctions. Effective management of both diseases requires an integrated approach involving lifestyle changes and pharmacological treatments. Urate-lowering therapies hold promise for managing both gout and T2DM. Future research should focus on personalized treatment strategies tailored to gout patients’ metabolic profiles and developing clinical guidelines to address both diseases.

EP1-29

Successful Management of Refractory Antiphospholipid Antibody-Positive Immune Thrombocytopenia in Early Pregnancy: A Case Report

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Conflict of interest: None

[Background] Antiphospholipid antibody-positive immune thrombocytopenia (aPL-positive ITP) carries a significantly higher thrombotic risk with thrombopoietin receptor agonist (TPO-RA) use compared to ITP without antiphospholipid antibodies (aPL). Careful monitoring and anticoagulant therapy are thus essential. We report a case of refractory aPL-positive ITP in early pregnancy successfully managed with TPO-RA and low molecular weight heparin (LMWH) following pregnancy termination, resulting in improvement without the need for splenectomy. [Case] A 33-year-old woman, 6 weeks pregnant with her second child, presented with petechiae and severe thrombocytopenia (lowest 3,000/μL). Testing revealed triple-positive aPL and ANA at a titer of 1:80, with no other signs of SLE, leading to a diagnosis of aPL-positive ITP. Her first pregnancy was uncomplicated, with no history of intrauterine growth restriction, hypertensive disorders, thrombosis, or miscarriage. She was transferred to our hospital after initial treatment with PSL 0.5 mg/kg and platelet transfusions (PT) failed. At our hospital, she received PSL 1 mg/kg, mPSL pulse therapy, IVIg, and HCQ without notable effect, so rituximab (RTX) was initiated. However, her platelet count dropped to 10,000/μL two weeks after the first RTX dose. Due to concerns about fetal risk, the patient and her family opted for pregnancy termination at 10 weeks. Following termination, the addition of LMWH and eltrombopag led to sustained platelet normalization, thus avoiding splenectomy. No complications, including thrombotic events, were observed. Remission has been maintained post-RTX with immunosuppressive therapy, including MMF, HCQ, and low-dose PSL. [Clinical Significance] This case demonstrates that for severe refractory aPL-positive ITP, combining TPO-RA, LMWH, and immunosuppressants allowed for effective management without thrombotic complications, offering a potential alternative to splenectomy.

EP1-30

Case series of pathological fractures associated with glucocorticoid-induced osteoporosis (GIOP)

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Conflict of interest: None

[Background] Clinicians should consider various risk factors of fractures. [Objectives] To show case series of pathological fractures associated with glucocorticoid-induced osteoporosis (GIOP) and to make clear the characteristics of pathological fractures associated with GIOP. [Methods] Seven patients are shown here, who have pathological fractures induced by GIOP. [Results] (Case 1) 52-year-old male. Daily doses of 20 mg of prednisolone (PSL) due to atopic dermatitis. He injured his 4 lumbar vertebrae fractures. Bone mineral density (BMD) was 125% of the young adult mean (YAM) value. (Case 2) 75-year-old male, receiving haemodialysis for 4 years due to chronic kidney disease. BMD was 86% YAM. He had been taking PSL 15 mg/day and injured his pelvis. Later he suffered from cerebral infarction. (Case 3) 85-year-old female. Daily doses of 6 mg of PSL due to idiopathic thrombocytopaenic purpura. She had a fresh fracture of the first lumbar vertebral body, in addition to an old fracture of the third lumbar vertebral body. (Case 4) 84-year-old male, receiving 5 mg of PSL. He had old fractures of the thoracic vertebrae. BMD was 135% YAM. He suffered from COVID-19 infection. (Case 5) 86-year-old male. Daily doses of 9 mg of PSL due to retroperitoneal fibrosis. He had a fresh fracture of the first lumbar vertebral body. (Case 6) 82-year-old female, receiving 5 mg of PSL and minodronate. She had a fresh fracture of the patella. (Case 7) 86-year-old female. Daily doses of 3 mg of PSL and alendronate due to polymyalgia rheumatica. She had a fresh fracture of the pelvis. [Conclusion] The characteristics of pathological fractures induced by GIOP are as follows: 1) multiple fractures, 2) complications perhaps induced by glucocorticoid, 3) fractures with high bone mineral density, 4) fractures of male, 5) scarcely injured bone healing, 6) classical antiresorptive treatment may be not sufficient for preventing GIOP but novel anabolic therapy can prevent fragility fractures induced by GIOP.

EP1-32

Combination Therapy With Limaprost alpha And Nefidipine For Digital Necrosis And Raynaud's Phenomenon In A 16-year-old Girl Without Autoimmune Disease; Case Report

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Conflict of interest: None

[Objectives] Raynaud's phenomenon is defined as occasional ischemia of the distal parts of the extremities. Ischemia may be idiopathic as in primary Raynaud's disease or instigated by a comorbidity as in Raynaud's syndrome. Research has shown that enhanced vascular reactivity is attributable more the local factor and less to abnormalities in the central nervous system. Local factors are classified as vascular, nervous, and intravascular. [Methods] A 16-year-old girl has visited the clinic complaining of abnormal sensarion with necrosis at the right 2nd fingertip shince recent months. [Results] CBC 8300-13.7-144k ESR 2 mm/hr CRP 0.12 Anti-CCP: negative FANA: positive 1:160 ENA panel: negative dsDNA: negative It fully recovered 3 months after administration of Opalmon (Limaprost alpha) 5ug as limaprost and Adalat orso 30 mg/tab (Nefedipine 33 mg). [Conclusion] We have experience in completely recovering digital necrosis with Limaprost alpha and nefidepine in 16-year-old girl, so we would like to share it together. Problem of Medicine: Safety for children is not established or there have no experience in children. The administration of this drug is not recommended because the safety and effectiveness of children under the age of 18 are not established. Question: Do we have other safe medicines to treat digital necrosis as a Raynaud's pheonomenon in children?

EP2-01

Risk of New-Onset Inflammatory Central Nervous System Diseases After Tumor Necrosis Factor Inhibitors Treatment for Autoimmune Diseases

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Conflict of interest: None

[Objectives] To evaluate the risk of inflammatory inflammatory central nervous system (CNS) diseases after tumor necrosis factor (TNF) inhibitors therapy and assess the difference in risk among different types of underlying autoimmune diseases, or TNF inhibitors. [Methods] Separate searches were conducted across PubMed, EMBASE, and the Cochrane Library from inception until March 1, 2024. Observational studies assessing the association between anti-TNF therapy and inflammatory CNS diseases relative to a comparator group. The risk ratio (RR) was used as the effect measure of the pooled analysis. [Results] Eighteen studies involving 1,118,428 patients with autoimmune diseases contributing over 5,698,532 person-years of follow-up were analyzed. The incidence rates of new-onset inflammatory CNS events after initiating TNF inhibitors ranged from 2.0 to 13.4 per 10,000 person-years. Overall, exposure to TNF inhibitors was associated with a 33% increased risk of any inflammatory CNS diseases compared to conventional therapies (RR=1.36, 95%CI 1.01-1.84), mainly attributed to demyelinating diseases (RR=1.38, 95% CI 1.04-1.81). Secondary analyses revealed a similar risk of inflammatory CNS diseases across different types of underlying autoimmune diseases (rheumatic diseases: RR 1.36, 95%CI 0.84-2.21; inflammatory bowel disease 1.49, 95%CI 0.93-2.40; P for subgroup=0.74) and TNF inhibitors (anti-TNF monoclonal antibodies versus etanercept: RR 1.04, 95%CI 0.93-1.15). [Conclusion] Compared to conventional therapies, exposure to TNF inhibitors exposure was associated with a 36% increased risk of inflammatory CNS diseases, irrespective of background autoimmune diseases or TNF inhibitor types.

EP2-02

Prevalence and associated factors of nonalcoholic fatty liver disease in individuals with rheumatoid arthritis: A nationally representative cross-sectional study

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Conflict of interest: None

Objectives: To determine the prevalence and associated factors of nonalcoholic fatty liver disease (NAFLD) in rheumatoid arthritis (RA) population using a nationally representative sample of the general US population. Methods: This cross-sectional study utilized data on US adults aged over 20 years old from the National Health and Nutrition Examination Survey (2017 to 2018). RA was defined by self-reporting of a diagnosis by the physician. NAFLD was diagnosed by controlled attenuation parameter scores of over 274 dB/m using vibration controlled transient elastography in the absence of other liver diseases. Weighted multiple regression analysis was further performed to assess the independent risk factors. Results: Of 224 participants with RA included, the weighted prevalence of NAFLD and advanced liver fibrosis was 47.0% and 8.0%, respectively. There was a numerically higher prevalence in RA patients than control group without arthritis regarding NAFLD (47.0% vs. 40.0%, adjusted OR 0.96, 95% CI 0.77-1.20, p=0.500) and advanced liver fibrosis (8.0% vs. 5.2%, p=0.12). Univariate analysis showed that RA patients with concomitant NAFLD were likely to have metabolic comorbidities including obese, central obesity, diabetes and hyperlipidemia and increased levels of triglyceride, fasting plasma glucose, HbA1c, liver enzymes and hsCRP levels. Further weighted multivariable logistic regression showed central obesity (OR 1.69, 95%CI 1.32-2.17, p=0.007) and diabetes (OR 1.30, 95%CI 1.01-1.67, p=0.047) were significantly associated with prevalent NAFLD in patients with RA. Conclusion: In a nationally representative sample of US adults, approximately one in two RA patients had NAFLD. Central obesity and diabetes are predisposing factors for NAFLD in RA. Our results highlight the importance of active NAFLD screening in RA population, especially for high risk subsets.

EP2-03

Use of Biologics After Cancer Diagnosis in Rheumatoid Arthritis Patients Undergoing Biologics -A Single-center Study

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Conflict of interest: None

[Objectives] Biologics (bDMARDs) have greatly contributed to improvemnet in quality of life in rheumatoid arthritis (RA) patients. However, due to concerns for immune surveillance pathways, bDMARDs are often avoided in cancer patients. Recent studies have reported that bDMARDs use does not increase the risk for cancer relapse in RA patients with a previous history of cancer. However, there is scarce data regarding bDMARDs use and their safety to continue bDMARDs after a recent cancer diagnosis. Our study aims to gather information on the actual conditions of bDMARDs use and their outcomes in RA patients undergoing bDMARDS after being diagnosed with cancer. [Methods] We created a cohort of RA patients who were diagnosed with cancer while undergoing treatment with bDMARDs (January 1st 2009~December 31st 2023), and evaluated the continuation, discontinuation, and restart of bDMARDs and the overall survival. [Results] Among 550 patients undergoing bDMARDs, 67 patients were diagnosed with cancer. bDMARDs administered at the time of cancer diagnosis included 23 (34%) TNF-a inhibitors, 34 (51%) IL-6 inhibitors, and 10 (15%) CTLA-4 inhibitors. There was a great variation for the type and stages of cancers observed. bDMARDs were continued in 25 patients (37.3 %). Skin and gastrointestinal tract cancer had a higher rate for continuing bDMARDs. Among 42 patients (62%) who discontinued bDMARDs, 15 (36%) restarted bDMARDs. There were totally 19 deaths (28%), 14 (21%) due to cancer, and 5 (7.5%) due to pneumonia or other infections. Most of the deaths due to cancers were from those who discontinued bDMARDs. [Conclusion] Since the study is a retrospective cohort with a limited number of patients, it was not possible to statistically clarify the safety of continuing bDMARDs when dealing with a high variation of cancers and patient background. Further researches are needed to verify the safety of bDMARD, so that patients can receive the best choice of treatment for both cancer and RA.

EP2-04

Human T-cell leukemia virus type 1 (HTLV-1) infection may increase the prevalence of pulmonary airway lesions in patients with rheumatoid arthritis (RA): a cross-sectional observational study

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Conflict of interest: None

[Objectives] The aim of this study was to characterize pulmonary lesions in HTLV-1-positive patients with RA. [Methods] Thirty HTLV-1-positive RA patients who had previously been evaluated for pulmonary lesions using high-resolution CT (HRCT) were enrolled. Ninety age- and sex- matched HTLV-1-negative RA patients were selected as controls for each HTLV-1-positive RA patients. All participants were enrolled from HTLV-1-positive RA Miyazaki Registry. All clinical information was retrospectively collected from registry database and medical records. The findings of pulmonary lesions on HRCT, RA disease activity scores, complication, and detail of antirheumatic regimen were compared between two groups. The association between the value of HTLV-1 proviral load (PVL) and characteristics of pulmonary lesions was evaluated in HTLV-1-positive RA patients. [Results] At the time of HRCT imaging, there was no difference in age or disease duration between the two groups. However, both DAS28 and CDAI, SDAI values were higher in HTLV-1 positive RA group than inHTLV-1 negative RA group (3.14 v. s 2.47, p= 0.05. 6.4 v. s 3.3, p= 0.01, 7.28 v. s 3.47, p= 0.01, respectively). The use of glucocorticoids tended to be higher and the use of biologics tend to be lower in HTLV-1 positive RA group than in HTLV-1 negative RA group (70% vs. 36%, 33% vs. 61%, respectively). In HRCT findings, approximately 50% of both groups had abnormal findings, and bronchiolitis was more common in the HTLV-1-positive RA group than in the HTLV-1-negative group. There were no differences in the frequency or pattern of interstitial pneumonia between the two groups. No consistent trends were found between the HTLV-1 PVL and the characteristics of lung lesions. [Conclusion] The prevalence of pulmonary airway lesions such as bronchitis and bronchiectasis may have increased in HTLV-1-positive RA patients compared to HTLV-1-negative RA patients.

EP2-05

Among human T-cell leukemia virus type 1 (HTLV-1)-positive rheumatoid arthritis patients with high HTLV-1 proviral load (PVL), some patients may have an increased HTLV-1 PVL during antirheumatic therapy ~Could this be a sign of the development of adult T cell leukemia?~

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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 rheumatoid arthritis (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 at 2019, 56 patients whose HTLV-1 PVLs were measured at least twice during the observation period from 2019 to 2023 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 (n=12) and non-increased group (n=44). Clinical characteristics including treatment details were compared between increased and non-increased groups. Furthermore, the population of HTLV-1 infected cells analyzed by flow cytometry (HAS-Flow) was compared between the two groups. [Results] In 2019, there were no differences in age between the two groups. However, the median PVL was 2.53 and 0.46 copies/100PBMCs, which were significantly higher in the increased group ($p<0.001$). The median PVL of the increased group increased to 6.41 copies/100PBMCs by 2023. The median DAS28 values were higher in the non-increased group than in the increased group (1.84 vs 2.71, $p< 0.05$). The rates of methotrexate, tacrolimus, and biological agent/JAK inhibitor use tended to be higher in the increased than in the non-increased group (50.0% vs 43.2%,33.3% vs 22.7%,41.6% vs 29.6%, 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. No patients developed ATL during the observation period of this study. [Conclusion] Some HTLV-1-positive RA patients with high PVL appear to have an increase in PVL during antirheumatic therapy. Since increased PVL was known as a risk factor for developing ATL, further research is needed to elucidate what types of antirheumatic treatments affects ATL development.

EP2-06

Clinical parameters for prediction of inflammatory arthritis in patients with arthralgia: a prospective cohort study

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Conflict of interest: None

[Objectives] Multiple trials for inflammatory arthritis (IA) prevention have been done with variable success. The need for risk stratification in arthralgia suspicious for progression to IA is imminent. The aim of this study is to identify clinical parameters associated with IA development. [Methods] Patients with arthralgia without arthritis were recruited and followed up till clinical diagnosis of any type of IA. Univariate analysis exploring the association between baseline clinical symptoms and biomarkers with development of IA was performed. Multivariate logistic regression models were built to identify independent predictors. [Results] This is a preliminary analysis of the first 139 patients [Age: 52.6±10.9, 76.3% female, median symptom duration: 47 weeks (IQR: 59 weeks)] who had at least 6 months follow up. As of 2024, the median follow-up duratoin was 51 weeks (IQR: 42 weeks). 23 (16.5%) patients developed IA, with a median follow-up of 30 weeks (IQR: 40 weeks). Patient who developed IA had shorter symptom duration (39.0±27.8 vs 72.0±82.9, p=0.031), higher acute phase reactant level (ESR: 40±24 vs 24±15 mm/hr, p<0.001; CRP: 8.9±15.3 vs 2.0±4.3 mg/L, p<0.001] and higher titre of autoantibodies [RF: 127±220 vs 46±93 IU/ml, p=0.004; ACPA: 60±71 vs 20±50 EU/ml, p=0.002] at baseline when compared to those who did not reached endpoint. They were also more likely to experience presence of anamnestic joint swelling, positive squeeze test and difficulty in holding fist at baseline. In multivariate logistic regression analysis, CRP (OR: 1.07, 95% CI: 1.00-1.14, p=0.042), ESR (OR: 1.04, 95% CI: 1.01-1.07, p=0.008) and symptom duration (OR: 0.98, 95% CI: 0.97-0.99, p=0.033) were independent predictors of IA development. [Conclusion] Shorter symptom duration and elevated inflammatory markers could predict the development of arthritis in patients presented with joint pain. Whether therapeutic intervention can prevent arthritis in at risk individuals should be investigated.

EP2-07

Impact of Oral Health on Rheumatoid Arthritis in Children Aged 5-10 Years: A Cross-Sectional Analysis of Inflammatory Markers and Clinical Outcomes

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Conflict of interest: Yes

[Objectives] This study explores the relationship between oral health and RA severity in children aged 5-10, focusing on inflammatory markers and clinical outcomes. [Methods] A cross-sectional study was conducted with 100 children, aged 5-10 years, including 50 diagnosed with RA and 50 healthy controls. Oral health assessments included plaque index, gingival index, and decayed, missing, and filled teeth (DMFT) scores. Blood samples were collected to measure inflammatory markers, including C-reactive protein (CRP) and interleukin-6 (IL-6). Parental questionnaires gathered data on dental hygiene practices, and clinical evaluation assessments RA disease activity and joint involvement. [Results] Children with RA exhibited significantly poorer oral health, with higher plaque and gingival indices compared to controls ($p < 0.01$). Elevated CRP and IL-6 levels correlated with poor oral hygiene and higher DMFT scores in RA patients, indicating a link between oral inflammation and systemic disease severity. RA patients with frequent oral hygiene practices demonstrated lower levels of inflammatory markers, suggesting that improved oral health may help manage systemic inflammation in children with RA. [Conclusion] Poor oral health is associated with elevated inflammatory markers and increased disease severity in children with RA. These findings underscore the importance of regular oral hygiene and dental care as part of comprehensive RA management in pediatric patients. Integrating oral health education into RA care plans could offer a cost- Effective strategy to mitigate systemic inflammation and improve clinical outcomes in young patients.

EP2-08

Difficult-to-Treat Rheumatoid Arthritis among Elderly RA from the KOBIO Registry

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Conflict of interest: None

[Objectives] 'Difficult-to-treat (D2T)' rheumatoid arthritis (RA) indicates a subpopulation of patients who fail to achieve low disease activity or remission despite multiple cycles of b/tsDMARDs. Elderly patients with RA have some characteristics including higher disease activity or higher prevalence of comorbidities. This study aims to search for characteristics of D2T RA among elderly patients with RA. [Methods] Data of RA patients who were treated with b/tsDMARDs were extracted from the Korean College of Rheumatology Biologics registry and analysed. [Results] Among 516 elderly RA patients who were same or older than 65 years and treated with b/tsDMARDs, 54 (10.5%) were diagnosed with D2T RA, and age (OR=0.91, p=0.012), RAPID3 (OR=1.082, p=0.044), and prior use of leflunomide (OR=0.446, p=0.009) were associated with D2T RA. The drug survival rate of b/tsDMARDs didn't differ between elderly patients with D2T RA and those not (p=0.53). The drug survivals of individual b/tsDMARD differed in elderly patients with D2T RA (p=0.024), while those didn't differ in those without D2T RA (p=0.16) during 8 years. In Kaplan-Meier curve, discontinuation and switching of b/tsDMARDs didn't differ in elderly patients with D2T RA and tocilizumab was the least switched drug in elderly patients without D2T RA (p=0.0064). Proportion of drug withdrawal due to inefficacy was higher in D2T RA patients compared to those without D2T RA (63% vs. 29.7%, p=0.0005). DAS28, SDAI, CDAI, and RAPID3 were significantly higher in elderly patients with D2T RA compared in those not at 1st and 2nd follow up. [Conclusion] Younger age, poorer patient's reported disease status, and less use of leflunomide might contribute to D2T RA among elderly patients. The drug switching of b/tsDMARDs did not differ among elderly patients with D2T RA, while those differed among elderly patients without D2T RA.

EP2-09

Carotid and coronary atherosclerosis in patients with rheumatoid arthritis treated with tocilizumab

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Conflict of interest: None

[Objectives] Cardiovascular disease is main complication in rheumatoid arthritis (RA) and biologic agents including TNF inhibitor and IL-6 antagonist might affect progression of atherosclerosis. [Methods] Coronary angiographic computer tomography, carotid ultrasound and pulse wave velocity (PWV) were conducted in patients with RA who were treated by tocilizumab and those not. [Results] Twenty-one female RA patients who were treated with tocilizumab during 3.3 ± 1.7 years and age-matched 11 female RA patients with csDMARDs participated. TCZ group had longer RA duration (11.8 ± 6.3 vs 8.7 ± 4.7 years, p < 0.001), lower DAS28 score (1.9 ± 1.2 vs. 2.7 ± 1.0, p = 0.033) than non-TCZ group. There's no difference of lipid profiles between two groups. In comparison of coronary computer tomography and carotid Doppler, 33.3% (7/22) patients and 18.2 % (2/11) had coronary plaque (p = 0.373), and 76.2% (16/22) and 45.5% (5/11) patients had carotid plaque (p = 0.832), and 47.6% (10/22) and 45.5% (5/11) patients had progression of carotid plaque during 1 year (p = 0.909) in TCZ and non-TCZ group. Mean carotid IMT were 0.67 ± 0.11 mm and 0.69 ± 0.12 mm (p = 0.843), and Mean PWV levels were 6.2 ± 0.85 and 7.38 ± 1.48 (p = 0.068) in TCZ and non-TCZ group. Any patients didn't have the progression of carotid IMT and 38.1% (8/22) and 22% (2/11) patients had the progression of PWV (p = 0.322) in TCZ and non-TCZ group. [Conclusion] While the study population was limited, no significant progression of atherosclerosis in the coronary and carotid arteries or no endothelial dysfunction was observed in RA patients who were receiving TCZ.

~~EP2-10~~

~~**Effect of achieving sustained SDAI remission on erosion healing in early rheumatoid arthritis -a one-year prospective HR-pQCT study**~~

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~~The Chinese University of Hong Kong, Hong Kong~~

~~Conflict of interest: None~~

~~[Objectives] Rheumatoid arthritis (RA) is chronic inflammatory disease with progressive joint destruction. The association between radiographic joint damage progression independently of disease activity and functional impairment need to be confirmed in the early stage of RA (ERA) with most patients demonstrating little baseline joint damage on radiography. vHigh-resolution peripheral quantitative CT (HR-pQCT) is a novel technique for detailed bone microstructure analysis allowing volumetric assessment of bone erosions. vThe aim of this study is to ascertain whether achieving sustained simply disease activity index (SDAI) remission can lead to better structural outcome by HR-pQCT then less function loss. [Methods] a single-center prospective, hospital-based, cohort study. Patients receiving an intensive treatment protocol were grouped by achieving sustained SDAI remission at 6, 9 and 12 months (SDI group) or not (non-SDI group). HR-pQCT of the second to fourth metacarpophalangeal joints were performed at baseline, month 6 and one-year. Erosion healing was defined as 1) a decrease in erosion volume exceeding the smallest detectable change (SDC). [Results] After 12 months, a significant reduction in erosion volume and marginal osteosclerosis was observed in both groups. The SDI group showed a lower incidence of erosion progression (0% vs 16%, p=0.135) and exhibited a higher rate of erosion healing (56% vs 29%, p=0.083) compared with the non-SDI group. In the GEE model, patients in the SDI group showed a higher likelihood of erosion healing (OR: 2.976, 95% CI: 1.0-8.9, p=0.050). The changes in erosion depth and width were similar between two groups. [Conclusion] vAchieving sustained SDAI remission could improve erosion healing and limit erosion progression in patients with ERA.~~

EP2-11

Reliability and Availability of the 2017 EULAR-OMERACT Scoring System for Ultrasound Synovitis Assessment: Results from a Training and Reading Exercise

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Conflict of interest: None

Objective: To evaluate the availability and reliability of the European League Against Rheumatisms Outcome Measures in Rheumatology Synovitis (EULAR-OMERACT) scoring system among radiologists with different levels of musculoskeletal ultrasound (US) experience in assessing synovitis in patients with rheumatoid arthritis (RA). **Method:** The patients with RA were retrospectively recruited from January 2020 to March 2022. Five radiologists with different levels of US experience were recruited for the reader study (R1-5), which included two parts. The participating radiologists first read 120 gray-scale (GS) and 120 Doppler US images twice, before and after a standard training program. In the first part, they semi-quantitatively scored the images from 0 to 3 based on the EULAR-OMERACT scoring system. In the second part, they read and scored 165 paired GS and Doppler images two times in one month using the EULAR-OMERACT scoring system. The correlation between the sum of the GSUS and power Doppler US (PDUS) image scores and the clinical scores was assessed. **Result:** The intra-rater agreement of the five radiologists was good for the EULAR-OMERACT scoring system, with κ ranging from 0.72 to 0.94 for GSUS and from 0.81 to 0.97 for PDUS. The inter-rater agreement among the experts was good to very good in the EULAR-OMERACT scoring system (κ: 0.76-0.94 for GSUS and 0.80-0.96 for PDUS). The sum of the GSUS and PDUS scores in the EULAR-OMERACT scoring system was moderate to highly positively correlated with the clinical scores (ρ of GSUS: 0.58-0.79, ρ of PDUS: 0.57-0.70 for disease activity score in 28 joints C-reactive protein) after training. **Conclusion:** The EULAR-OMERACT scoring system is reliable for evaluating synovitis in RA and shows potential for disease assessment and follow-up in patients with RA.

EP2-12

Rheumatoid Factor and Cystatin C: Unveiling an Independent Association in a Large Cohort from the UK Biobank

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Conflict of interest: None

Background/Objective: Cystatin C has demonstrated superior accuracy over serum creatinine in detecting early renal impairment and predicting long-term outcomes in cardiovascular diseases. However, its relationship with rheumatoid factor (RF) raises concerns, as glucocorticoid treatment and hyperthyroidism are known to elevate nonrenal Cystatin C levels. This paper investigates the intricate correlation between Cystatin C and RF, exploring the potential interference of RF with Cystatin C measurement. Methods: We utilized data from the UK Biobank study to assess the association between rheumatoid factor (RF) and cystatin C. Spearman's ranked correlation was employed using quartiles of cystatin Cand RF, while Pearson's correlation was applied with their actual values. To examine the independence of this association, a linear regression model was constructed, controlling for age and weight as covariates. Results: Pearson's correlation revealed a significant positive correlation between rheumatoid factor (RF) and cystatin C in 37,894 participants (r = 0.04830, p < 0.0001). Similarly, Spearman's correlation yielded comparable results (r = 0.05407, p < 0.0001). Upon controlling for age and weight, a linear regression analysis demonstrated that RF maintained an independent and statistically significant association with cystatin C (regression coefficient = 0.004, p < 0.001), with the model explaining 13.24% of the variance (adjusted R-square). Conclusion: In conclusion, our study, utilizing a large cohort from the UK Biobank, identified a significant and independent association between rheumatoid factor (RF) and cystatin C levels. Further research is warranted to explore the clinical implications and potential therapeutic implications of thisassociation.

EP2-13

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. **Conclusion:** 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.

EP2-14

Perception of Rheumatoid Arthritis patients on the use of Telemedicine utilizing a Telemedicine Perception Survey Tool

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Conflict of interest: None

[Objectives] The rationale for conducting a perception study among RA patients regarding telemedicine usage is rooted in the need to ensure patient-centric care, assess the impact of telemedicine on care delivery and patient experience, identify potential barriers, and inform healthcare policymakers to optimize RA management. [Methods] A cross-sectional study is a design. Target population would be all individuals diagnosed with Rheumatoid arthritis who are eligible for or potentially utilizing telemedicine services for follow-up care. [Results] The high levels of patient satisfaction and willingness to continue with telemedicine follow-ups, coupled with efficient consultation times and minimal waiting periods, underscore the effectiveness and appeal of telemedicine in managing RA. These findings suggest that telemedicine not only meets patient needs effectively, but also offers a streamlined and patient- friendly approach to healthcare. [Conclusion] The data highlights both the opportunities and challenges associated with telemedicine in delivering healthcare services to RA patients, offering valuable insights for healthcare providers and policymakers. High levels of convenience and time-saving benefits are evident, consistent with previous research indicating widespread acceptance among RA patients. However, slight indications of usability challenges suggest the need for improvement in telemedicine platform design and user training. Ensuring robust security measures is crucial to maintaining patient safety and privacy during telemedicine consultations. Addressing patients questions and concerns effectively, along with offering a hybrid model of telemedicine and in-person consultations, can enhance patient experiences. Continuously monitoring telemedicine utilization patterns and tailoring services to patient preferences and clinical needs are essential for optimizing telehealth practices in rheumatology care.

EP2-15

Safety and Effectiveness of Etanercept Biosimilar LBEC0101 for Rheumatic Diseases in South Korea: Real World Post-marketing Surveillance Data

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Conflict of interest: Yes

[Objectives] LBEC0101, as the third approved biosimilar of etanercept in Korea, represents an important step in expanding treatment options for autoimmune diseases like ankylosing spondylitis (AS), rheumatoid arthritis (RA), psoriatic arthritis (PsA), plaque psoriasis (PsO) and juvenile idiopathic arthritis (JIA). This post-marketing surveillance (PMS) study aimed to evaluate its safety and efficacy in real-world clinical settings in Korea. [Methods] The study, conducted from March 2018 to March 2022, involved a prospective, multi-center, open-label, observational phase IV design. It included both patients new to etanercept and those switched from the reference etanercept, with LBEC0101 administered weekly through subcutaneous injections. Safety assessment covered the incidence of adverse events (AEs), adverse drug reactions (ADRs), and serious adverse events (SAEs). Effectiveness was measured using the Disease Activity Score-28 (DAS28) for RA, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for AS, and the count of tender and swollen joints for PsA and JIA. [Results] The study enrolled 372 subjects, with 351 included in the safety analysis: 176 with RA, 164 with AS, 10 with PsA, and 1 with JIA. The overall incidence of AEs, ADRs, and SAEs was 35.33%, 15.67%, and 2.56%, respectively. Effectiveness results showed significant reductions in disease activity scores. [Conclusion] This PMS successfully provided long-term (up to 52 weeks) real-world data on the efficacy and safety of LBEC0101 for treating RAs and AS. While the study observed a higher incidence of adverse events and reactions compared to other studies, these were generally less severe. Factors such as concurrent medications and conditions, including possible links to the COVID-19 vaccine, were considered in the analysis. The study's findings are significant, although direct comparisons with other studies are limited due to the non-head-to-head nature of the research.

EP2-16

Effect of biologic disease modifying anti-rheumatic drugs on thrombocytosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The data for thrombocytosis in rheumatoid arthritis (RA) and effect of biologic and targeted synthetic disease-modifying antirheumatic drug (b/tsDMARDs) is limited. This study aims to confirm the relationship between thrombocytosis and disease activity in patients with RA and to confirm the effect on thrombocytosis when using b/ts DMARDs. [Methods] Data of patients with RA receiving b/tsDMARDs were extracted from the Korean College of Rheumatology Biologics and Targeted Therapy registry. Patients whose thrombocyte count over $450*10^9$/L and under $450*10^9$/L were classified as patients with thrombocytosis and patients with normal platelet count. Their baseline characteristics and disease-associated parameters were evaluated. Disease activity [visual analogue scale (VAS), disease activity score 28 (DAS28), clinical disease activity index (CDAI), simplified disease activity index (SDAI)] and functional index [routine assessment of patient index data 3 (RAPID3), EuroQol-visual analogue scales (EQ-VAS)] at baseline and 1-year follow-up were assessed. [Results] Total 2122 patients were enrolled. Among patients 1909 patients (90.0%) showed normal platelet count and 213 patients (10.0%) had thrombocytosis. Thrombocytosis group had more swollen and tender joint counts, higher erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), DAS-ESR, DAS-CRP, SDAI, CDAI, RAPID3, white blood cell count and lower hemoglobin level. At 1-year follow-up, change of disease activity were larger in thrombocytosis for ESR, CRP, DAS-ESR, DAS-CRP, SDAI, tender joint count, RAPID3. Changes in disease activity according to medication differed between the two groups as tocilizumab was the most effective among b/tsDMARDs whereas JAK inhibitor was effective in patients with normal thrombocyte count. [Conclusion] Elevated thrombocyte count in patients with RA reflects higher disease activity and may predict that tocilizumab would be effective therapeutic choice.

EP2-17

Association between osaka prognostic score and mortality in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: Inflammation, nutrition, and immune status are closely related to the prognosis of rheumatoid arthritis (RA) patients. Osaka prognostic score (OPS) is based on a comprehensive score of inflammation, nutrition, and immunity. This study aims to explore the relationship between OPS and all-cause and cardiovascular death in RA patients. **Methods:** This study included RA patients from the National Health and Nutrition Examination Survey (NHANES) in the United States from 1999 to 2010. The OPS was calculated based on serum albumin, C-reactive protein, and lymphocyte count. The outcome variables are all-cause and cardiovascular death. Using a weighted Cox regression model to explore the link between OPS and mortality in RA patients. Subgroup analysis and sensitivity analysis validate the stability of the results. **Results:** This study included a total of 1,580 RA patients. During the follow-up period, 654 all-cause deaths and 189 cardiovascular deaths were observed. In the weighted COX regression model, high OPS was significantly correlated with all-cause mortality (OPS>1 vs. OPS=0, HR=1.81 (1.36-2.41, P<0.001)) and cardiovascular mortality (OPS>1 vs. OPS=0, HR=5.01 (2.62-9.57, P< 0.001)) in RA patients. Subgroup analysis showed no significant interaction between subgroups. Using a series of sensitivity analyses, it was also found that the results were stable. **Conclusions:** OPS can be used as a tool to evaluate the prognosis of RA patients. In clinical practice, doctors still need to pay attention to the inflammation, nutrition, and immune status of RA patients. **Keywords:** osaka prognostic score; rheumatoid arthritis; NHANES; all-cause mortality; cardiovascular mortality

EP2-18

Comparison of differentially expressed genes contributing to immunological pathogenesis in rheumatoid arthritis and osteoarthritis patients

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Conflict of interest: None

[Objectives] Characterizing differentially expressed genes of systemic rheumatoid arthritis (RA) compared to osteoarthritis (OA) is indispensable to understand immunogenic interactions, and how several key immune genes were closely associated with the susceptibility of RA. This study seeks to identify RNA expression based computational methodologies for analyzing and comparing RA and OA immune interactions, which affected the development and progression of RA compared to OA. [Methods] In the present study, 33 RA patients and 20 healthy controls microarray data (GSE55235, 55584, 55457) from the Gene Expression Omnibus (GEO) database were used to detect novel candidate risk genes for RA susceptibility. All raw files (CEL files) were directly downloaded from NCBI-GEO web site. The up- or down-regulated differentially expressed genes (DEGs) were identified and visualized by R packages 'affy' and 'ggplot2', windows based tools "cluster 3.0" and "JAVA treeview". The significantly enriched Gene Ontology (GO) gene sets were computed and visualized by using the DEGs from the Gene Set Enrichment Analysis (GSEA). [Results] Overall, the 354 DEGs, which were 209 up-regulated and 145 down-regulated, were identified in RA patients, and 248 DEGs, which were 110 up- and 148 down regulated genes were identified in OA compared to the expression of healthy control samples. Among these genes, 127 genes were overlapped in both RA and OA, and 227 genes with 64 down- and 163 up regulated genes were exclusively expressed in RA compared to OA, the highly up-regulated genes such *as CXCL13, IGHD, CXCL9, IGLL5, ADAMDEC1*, and *CXCL10* were closely implicated in immune system process including lymphocyte, T cell, and cytokine activation. [Conclusion] Identifying novel candidate immune genes and its immune interactions in RA patients compared to OA will shed light on the underlying pathogenic mechanism between RA and OA, which finally provide clinical tools for assessing RA between OA in patients.

EP2-19

Rheumatoid arthritis-associated lymphoproliferative disease in our experience

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Conflict of interest: None

[Objective] To investigate cases of lymphoproliferative disease that occurred during treatment for rheumatoid arthritis. [Patients and methods] In our case study, there were 11 cases of RA-associated LPD. There were 2 males and 9 females. We investigated about the age at onset of RA, age at onset of RA-associated LPD, prescription at onset, period from onset of RA to onset of LPD, duration and amount of MTX administered until onset of LPD, site and clinical symptoms of lymphoma, LDH and IL-2R value at onset, EB virus infection, concomitant medications, clinical course and RA treatment after onset. [Results] The average age at onset of RA was 51.1 years. The average age at onset of RA-associated LPD was 68.7 years. The MTX dose at onset of LPD was 7.2 mg/week. The period from onset of RA to onset of LPD was 17.6 years. The duration of MTX administration until onset was 11.6 years. Lymphoma often developed in the cervical lymph nodes, but swelling of the inguinal and thyroid lymph nodes was also observed. Extranodal lesions were also observed in the parotid gland, liver, tonsils, retroperitoneal tumors, and palate, showing a variety of sites of development. Six cases showed high LDH at the time of onset. All cases showed high IL-2R at the time of onset. Four of the seven confirmed cases were positive for EB virus. One case each of adalimumab and tacrolimus was used as concomitant medication. In five of the 11 patients, lymph node swelling improved simply by discontinuing MTX and the patient is now under observation. Seven patients underwent biopsy, and all were diagnosed with diffuse large B-cell lymphoma. One of these patients improved simply by discontinuing MTX. Six patients received R-CHOP therapy for up to six courses. One patient also underwent peripheral blood stem cell transplantation. [Conclusion] Although all cases of RA-associated LPD in our experience are alive at the present time, careful follow-up is also required for each RA and lymphoma in the future.

EP2-20

Rheumatic manifestations among HIV-positive attending the ART Centers

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Conflict of interest: None

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. **Conclusion:** Our research suggests the need for regular screening of Rheumatoid factor (Rf) to determine arthritis in HIV-infected patients.

EP2-21

Efficacy and safety of JAK1 selective inhibitors for rheumatoid arthritis: a single-center retrospective case series

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Conflict of interest: None

[Objectives] Clinical trials have shown that JAK1 selective inhibitors upadacitinib (UPA) and filgotinib (FIL) are effective for rheumatoid arthritis (RA) in which existing treatments are ineffective. However, in clinical practice, these treatments are often administered to patients who are not eligible for clinical trials, and the purpose of this study is to examine their usefulness in clinical practice. [Methods] All cases in which UPA or FIL was administered for RA in our department from April 2020 to October 2024 were included. Clinical information was collected from medical records and descriptive statistical analysis was performed. [Results] Thirty-five cases of JAK1 selective inhibitors (23 UPA cases, 12 FIL cases) were enrolled. The age distribution of patients at the start of the study ranged from their 20s to their 90s, with a mean age of 60s. Seventeen UPA cases and nine FIL cases were women (74%). Before the initiation of JAK1 selective inhibitors, patients were receiving either MTX or biologics, but these were deemed ineffective, so JAK1 selective inhibitors were initiated. The initial dose was 15 mg in 14 UPA patients and 7.5 mg in 9 patients. FIL was 200 mg in 8 patients and 100 mg in 4 patients. DMARDs were changed to UPA in 18 patients and FIL in 7 patients, and additional combination therapy was used in 5 patients with both UPA and FIL. The therapeutic effect of UPA was remission in 19 cases, ineffective in 1 case, and indeterminable in 3 cases, while the therapeutic effect of FIL was remission in 7 cases, effective in 2 cases, ineffective in 1 case, and indeterminable in 2 cases. Regarding safety, no adverse events that interfered with RA treatment were observed during the observation period. [Conclusion] Although this was an initial study of a small number of cases, JAK1 selective inhibitors were effective and safe for RA patients in whom MTX and/or biologics were ineffective. Verification in more actual clinical cases is expected in the future.

EP2-22

Rheumatoid Arthritis - Patient Initiated Follow-up (PIFU): Experience from a tertiary centre Rheumatology Clinic in Peshawar, Pakistan

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Conflict of interest: None

[Objectives] Rheumatoid arthritis is the most common autoimmune inflammatory arthritis requiring regular monitoring and follow up. Patient Initiated Follow-up (PIFU) model allows patients to request an appointment at a time of need and convenience. Different socioeconomic groups may respond differently to PIFU models for clinic appointments. [Methods] Patients diagnosed with rheumatoid arthritis with stable disease are guided regarding PIFU model to arrange clinic review. This is arranged by the patients contacting the hospital clinic booking team. [Results] Challenges experienced by the patients and clinicians using the PIFU model include: 1. Socioeconomic factors effecting patient decision to attend for clinic reviews. 2. Phone connectivity problems leading to delay in appointment booking. 3. Patients attending clinics in flare up due to non-adherence to drug therapy. 4. Clinic appointments taking longer due to patients attending during flare up of disease. [Conclusion] PIFU model helps empower patients to arrange their clinic appointments when required. Consideration needs to be given to different socioeconomic factors whilst implementing PIFU model in rheumatology clinics. Patient inclusivity and education is important prior to embarking on PIFU model in rheumatology outpatient clinics. This is particularly important in low and middle income countries. The use of digital health tools needs to be considered to enhance the patients experience to supplement the PIFU model.

EP3-01

Single-cell RNA Sequencing Analysis of the Effect of Anifrolumab on B Cells of Patients with SLE

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Conflict of interest: Yes

[Objectives] Anifrolumab (ANI), a human monoclonal antibody to the type I interferons receptor subunit 1, was recently approved for the treatment of systemic lupus erythematosus (SLE). Sub-analyses from the phase III TULIP trials showed that the efficacy of ANI correlated with reductions in interferon-stimulated genes (ISG) expression at 12 weeks post-treatment. The B cell compartment of patients with SLE show many alterations including altered IGH gene usage and clonal expansion. This study was performed to assess the impact of ANI on the B cell compartment. [Methods] We performed single-cell RNA sequencing of peripheral blood CD19-positive cells from five SLE patients treated with ANI at our institution before and 12 weeks after treatment. [Results] The patients were all women with a mean age of 45.8 ± 9.0 years, an average disease duration of 15.4 ± 8.2 years, and a mean prednisolone dose at ANI initiation of 5.2 ± 2.8 mg. The proportion of unswitched memory B cells (USM) decreased in all cases after ANI treatment, along with an increase in somatic hypermutation ratio (SHM) and a trend toward a decrease in Gini index in USM. Clinically, four out of five patients showed a reduction in SLE Disease Activity Index 2000 scores or corticosteroid tapering within 12 weeks, while one patient achieved neither. ISG expression decreased across all B cell clusters in the four responsive patients, but the non-responsive patient had persistently low ISG expression. This non-responsive patient had a higher proportion of atypical B cells which also demonstrated clonal similarity with other B cell populations. This trend was seen both before and after ANI treatment. [Conclusion] After ANI treatment, most patients showed a decrease of ISG expression in B cells and a reduction of the proportion of USM, along with an increase in SHM. ISG status and atypical B cell levels might help identify patients more likely to be responsive to ANI, and additional cases are needed to confirm this.

EP3-02

Tacrolimus reduced cell viability of rheumatoid arthritis fibroblast-like synoviocytes through inhibition of autophagic flux

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Conflict of interest: Yes

[Objectives] We aimed to investigate the effect of tacrolimus on human fibroblast-like synoviocyte-rheumatoid arthritis (HFLS-RA), and determine whether it induces apoptosis. [Methods] Cell viability and cell cycle progression were analyzed using hemocytometry and flow cytometry, respectively, after treating HFLS-RA with tacrolimus. Western blot analysis was performed by pretreating the cells with the autophagy inhibitors 3-Methyladenine (3-MA) and Bafilomycin A1 (BafA1) to determine the effect on expression of proteins LC-3 and p62. To analyze the effect of tacrolimus on lysosomal function, flow cytometry analysis was performed using LysoTracker, and Immunofluorescence was confirmed via double-staining for LAMP-1 and LC-3. [Results] When HFLS-RA was treated with tacrolimus at 40 μM, 60 μM, and 80 μM, the cell viability decreased in a concentration-dependent manner to 20%, 60%, and 93%, respectively, and in a time-dependent manner to 8 h (23%), 16 h (53%), and 24 h (65%), respectively. Regarding the cell cycle progression, the number of cells in the sub-G1 stage increased in a concentration-dependent manner (un: 6.05%, 40 μM: 11.5%, 60 μM: 33.45%, and 80 μM: 61.5%). Increased LC-3 II protein expression and decreased p62 protein expression were off-

set when cells were treated with 3-MA, but not when they were pretreated with BafA1. Immunofluorescence staining confirmed an increase in the formation of LAMP-1 puncta, however, LC-3 was distributed homogeneously throughout the cytoplasm, and puncta were barely formed. When cells were co-treated with BafA1, puncta formation increased in cells stained for LAMP-1, and LC-3. [Conclusion] Our findings suggest that lysosomal dysfunction during tacrolimus induction of autophagy in RA may result in lysosome accumulation in cells and cell death. Further research is needed to elucidate the precise mechanism by which tacrolimus induces cell death by lysosome dysfunction in autophagy.

EP3-04

Sustained Elevation of Soluble Immune Checkpoint Proteins during Development of ACPA-positive rheumatoid arthritis

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Conflict of interest: None

[Objective] We aimed to investigate the association between serum soluble forms of immune checkpoint proteins (sICPs) levels at baseline and the future development of RA in ACPA+ at-risk individuals (ARI). [Methods] ACPA+ ARI without clinical arthritis, newly diagnosed ACPA+ RA patients and ACPA- healthy controls (HC) were enrolled (n = 40, 24 and 33, respectively) and sera were collected at baseline. ARI were clinically followed and the second sera were collected at the time point of RA diagnosis (referred as progressors). The 10 sICPs were measured by Meso Scale Discovery (MSD) assay and their levels at baseline and their longitudinal changes were analyzed. Values of ACPA and RF were categorized as negative (< cut-off), low (> cut-off and ≦ 3x cut-off) and high (> 3x cut-off). Cut-off values for sICPs were determined by Youden index and hazard ratio (HR) for time-to RA diagnosis between group was estimated by Cox model. [Results] At baseline, soluble programmed cell death 1 (sPD-1) was significantly elevated in ARI and RA, while soluble lymphocyte-activation gene 3 (sLAG3) was significantly elevated in RA and numerically elevated in ARI, compared to HC. Of 40 ARI, 15 (38%) developed RA and 14/15 progressors were $ACPA^{high}$. In 27 $ACPA^{high}$ ARI, HR (95% CI) of developing RA was 7.53 (1.69 to 33.6) in the RF^{high} group vs. the $RF^{-/low}$ group, 19.7 (2.41 to 161) in the $RF^{high}sLAG3^{high}$ group vs. the $RF^{-/low}sLAG3^{low}$ group, and 19.1 (2.26 to 161) in the $RF^{high}sPD\text{-}1^{high}$ group vs. the $RF^{-/low}sPD\text{-}1^{low}$ group. In the $RF^{high}sLAG3^{high}$ or $RF^{high}sPD\text{-}1^{high}$ group, higher proportions of ARI progressed to RA at one year compared to the only RF^{high} group (75%, 86% and 57%, respectively). The levels of sLAG3 and sPD-1 remained elevated in the progressors from baseline to the post-RA visits. [Conclusion] Elevation of sLAG3 or sPD-1 in combination with RF was the risk factor of imminent development of RA in $ACPA^{high}$ ARI and these levels of sICPs showed sustained elevation.

EP3-05

The significance of MS4A4A expression on peripheral blood monocytes and synovial tissue macrophages in patients with rheumatoid arthritis and its involvement in the pathogenesis

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Conflict of interest: None

[Objectives] Membrane Spanning 4-Domains A4A (MS4A4A), a protein expressed on monocytes and M2 macrophages, shows disease-specific upregulation in peripheral blood monocytes of rheumatoid arthritis (RA) patients. This study investigated the role of MS4A4A expression in peripheral blood monocytes and synovial tissue macrophages in the pathogenesis of RA. [Methods] Blood and synovial samples from 6 RA and 8 osteoarthritis (OA) patients undergoing joint replacement were analyzed cross-sectionally. Using flow cytometry, we assessed MS4A4A expression in blood monocyte subsets and synovial macrophages, and compared CX3CR1 expression between MS4A4A-positive and MS4A4A-negative monocytes. [Results] MS4A4A expression was significantly higher in RA patients compared to OA patients across all monocyte subsets, particularly in non-classical monocytes (p=0.014). Synovial infiltrating macrophages from RA patients showed significantly higher MS4A4A expression compared to OA patients (p=0.0019). MS4A4A expression correlated positively between blood monocytes and synovial infiltrating macrophages (r= 0.61, p=0.021). Furthermore, MS4A4A-positive monocytes exhibited significantly higher CX3CR1 expression than MS4A4A-negative monocytes (p=0.0001). [Conclusion] We found upregulated MS4A4A expression in both blood monocytes and synovial infiltrating macrophages of RA patients. The correlation between MS4A4A expression in blood monocytes and synovial infiltrating macrophages, coupled with increased CX3CR1 expression on MS4A4A-positive monocytes, suggests an enhanced synovial migration capacity. Since MS4A4A shows increased expression in M2 macrophages and promotes M2 macrophage polarization, MS4A4A-positive monocytes in RA may contribute to inflammation resolution through synovial tissue infiltration. These findings provide new insights into the potential role of MS4A4A in RA pathogenesis and suggest its potential as a biomarker for disease prognosis and treatment response.

EP3-06

Exploring the Role of EBI3 and IL-27 in Imiquimod-induced Splenomegaly

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Conflict of interest: None

[Objectives] Epstein-Barr virus-induced 3 (EBI3) is part of the heterodimeric cytokine IL-27, which regulates immune responses. Its gene expression is induced by Toll-like receptors (TLRs). Chronic immune activation, such as repeated imiquimod (IMQ) treatment (a TLR7 agonist), leads to splenomegaly and cytopenia due to enhanced splenic function, but the mechanisms are unclear. This study investigates the role of EBI3 and IL-27 in IMQ-induced splenomegaly and hematologic abnormalities. [Methods] Wild-type and *Ebi3* knockout (KO) mice were treated repeatedly with IMQ. Spleen size and blood counts were measured to assess splenomegaly and cytopenia. Flow cytometry and histology evaluated splenic myeloid cell populations and extramedullary hematopoiesis. RNA sequencing (RNA-seq) of spleen tissues examined type I interferon (IFN)-related gene expression. The impact of IL-27 on type I IFN-related gene induction was tested in bone marrow-derived macrophages. [Results] IMQ-treated wild-type mice developed significant splenomegaly and bicytopenia (anemia and thrombocytopenia). Myeloid cells in the spleen increased, with extramedullary hematopoiesis confirmed by histology. RNA-seq revealed upregulated type I IFN-related genes in IMQ-treated spleens. EBI3-deficient mice showed less severe splenomegaly and cytopenia under IMQ treatment. IMQ raised *Il27a* expression (encoding IL-27p28) in the spleen and blood, while IL-27 stimulation upregulated type I IFN-related genes in macrophages, even without type I IFN. [Conclusion] The results indicate that EBI3 and IL-27 promote IMQ-induced splenomegaly and cytopenia by driving type I IFN-related gene expression and myeloid cell expansion. EBI3 deficiency alleviates these changes, likely by reducing IL-27 levels. This study offers insights into the molecular basis of chronic infection-linked splenomegaly, identifying EBI3 and IL-27 as potential targets for treating immune-related splenic dysfunction.

EP3-07

Role and mechanism of SOX4 in mesenchymal stem cell senescence

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Conflict of interest: None

[Objectives] Mesenchymal stem cells (MSCs) are pluripotent stem cells. However, the replicative senescence associated with in vitro expan-

sion poses a significant barrier to the optimization of MSC-based therapies. Nuclear transcription factor SOX4 plays a pivotal role in MSC. This study aims to elucidate the mechanism by which SOX4 influences MSC senescence and to evaluate its therapeutic impact in collagen-induced arthritis (CIA) and systemic lupus erythematosus (SLE) mouse models, thereby offering novel insights to enhance the clinical efficacy of MSC treatments. [Methods] β-galactosidase staining was performed to assess cellular senescence in mesenchymal stem cells (MSCs). RT-qPCR and Western blot analyses were utilized to measure the expression levels of functional genes associated with MSCs. Flow cytometry (FCM) was applied to measure relevant functional markers of MSCs. The adipogenic and osteogenic potential of MSCs was determined through Oil Red O and Alizarin Red staining. In collagen-induced arthritis (CIA) and systemic lupus erythematosus (SLE) mouse models, lentiviral-mediated knockdown and overexpression of SOX4 were employed, followed by the assessment of disease-specific parameters. [Results] (1) MSCs exhibited signs of replicative senescence. (2) Following interference with the SOX4 gene in MSC-P3, there was a notable increase in senescence-related marker expression, a decline in immunomodulatory function, and a marked elevation in SASP gene expression. (3) Interference with the SOX4 gene in MSC-P3 also led to a significant increase in mitochondrial reactive oxygen species (mtROS) levels. (4) MSCs with overexpressed SOX4 demonstrated effective therapeutic outcomes in both CIA and SLE mouse models. [Conclusion] The promotion of mtROS production by SOX4 induces an senescent phenotype in MSCs. Overexpression of SOX4 in MSCs can ameliorate the symptoms in CIA and SLE mouse models.

EP3-08

TRIM6 Increases the Risk of Systemic Lupus Erythematosus by Reducing Interleukin-10 Levels: A Multiomics Mediation Mendelian Randomization Analysis

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is a common autoimmune disease closely associated with inflammatory responses. The relationships among inflammatory genes, proteins, immune cells, and SLE pathophysiology need to be further explored. [Methods] We obtained protein quantitative trait loci for 91 plasma inflammatory proteins ($P < 5 \times 10^{-8}$) and conducted Mendelian randomization (MR) analysis with SLE's GWAS (genome-wide association study) data. Significantly upregulated differentially expressed genes (DEGs) were identified from SLE's microarray data. Two-step mediation MR was performed using the expression quantitative trait loci of these DEGs to analyze the effects of the DEGs on inflammatory proteins and SLE. Phenome-wide MR was conducted to further investigate the causal relationship of inflammatory genes and different diseases. MR results were validated using differential expression, enrichment analysis, immune infiltration analysis, and machine learning methods in bulk RNA. [Results] *TRIM6* was identified as a potential risk factor for SLE (OR 1.24, 95% CI [1.00-1.55], $P = 0.046$), and its expression was correlated with neutrophils and plasma cells. Interleukin-10 (IL-10) levels were negatively associated with SLE (OR 0.25, 95% CI [0.12-0.51], adjusted $P = 0.013$) and potentially mediated the pathogenic effect of *TRIM6* on SLE. Phenome-wide MR indicated that inhibiting *TRIM6* expression decreased the incidence of secondary hypertension and disturbances of smell and taste. [Conclusion] IL-10 is possibly a protective factor for SLE. *TRIM6* may increase the risk of SLE by reducing IL-10 levels.

EP3-09

The CXCL9, CXCL10, CXLC11/CXCR3 Axis, a major role player in the pathophysiology of Interstitial Lung Disease in SKG mice

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Conflict of interest: None

[Background] Interstitial lung disease (ILD) is characterized by a combination of inflammation and fibrosis of the diffuse lung parenchyma, and is a common extra-articular manifestation in rheumatoid arthritis (RA). We have previously reported that myeloid-derived suppressive cells (MDSCs) are increased in the lung of SKG-ILD mice. The CXCL9, CXCL 10, CXLC11 (CXCL9, 10, 11) / CXCR3 axis is involved in local amplification loops responsible for sustaining inflammation in target organs, and the recruitment of diverse immune cells. The objective of this research is to elucidate the role of this axis in the pathophysiology of SKG-ILD. [Methods] SKG mice were used to obtain ILD models following an intraperitoneal (i.p.) injection of zymosan. A microarray and qPCR analysis of sorted MDSCs from different tissues was performed. The expression of CXCR3 in different cell populations was measured with flow cytometry (FC). We also performed an i.p. injection three times a week of the selective CXCR3 inhibitor (AMG 487) for 8 weeks in SKG-ILD mice. Matched controls (DMSO) were also used. To measure the effects of AMG487, we performed a lung histological analysis (H&E staining) using the ImageJ digital processing software. [Results] The microarray analysis showed that MDSCs in the inflamed lung overexpress CXCL9, 10, 11. The qPCR analysis of sorted MDSCs confirmed this result showing an increase of these chemokines in Lung in comparison with bone marrow. We next assessed by FC which particular cell population expressed CXCR3, and demonstrated a significant increase in the CXCR3+ population of MDSCs, macrophages, dendritic cells and Th17 cells in the ILD lung. Finally, the histological analysis revealed a significant decrease in the histological score for those mice injected with AMG487 (p=0.0293). [Conclusion] The CXCL9, 10, 11/CXCR3 axis has a major role in the pathophysiology of SKG-ILD and the inhibition of CXCR3 suggests a potential novel therapeutic strategy for RA-ILD.

EP3-10

Effectiveness of Biologic Therapy as Maintenance Treatment in Relapsing Polychondritis

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Conflict of interest: None

[Objectives] Although biologics (Bio) are increasingly used for maintenance therapy in relapsing polychondritis (RP), clinical evidence on their efficacy remains limited. This study aimed to evaluate the effectiveness of biologics in patients with RP. [Methods] We conducted a single-center, retrospective study of RP patients treated at our hospital between January 2000 and December 2022. Annual relapse rates were compared between patients before (pre-Bio term) and after (post-Bio term) initiation of Bio. Among patients receiving Bio, we further compared relapse-free survival and drug withdrawal rates between TNF inhibitors (TNFi) and IL-6 receptor inhibitors (IL-6Ri). [Results] A total of 59 RP patients were included in the analysis. Of these, 32 patients were treated exclusively with glucocorticoids and immunosuppressants, while 27 received Bio. The mean annual relapse rate was significantly lower in the post-Bio term compared to the pre-Bio term (0.0±0.001vs. 0.42±0.15) times per patient-year, p<0.001). Among Bio users, there was no significant difference in relapse-free survival rates between TNFi and IL-6Ri groups at 1 year (85% vs. 69%) or 5 years (55% vs. 48%) (p=0.70). Multivariable Cox proportional hazard analysis, adjusted for confounders, found no difference in relapse risk between TNFi and IL-6Ri (HR 1.6, 95% CI 0.6-4.3). Similarly, no significant differences were observed between TNFi and IL-6Ri groups in drug withdrawal due to ineffectiveness (1 year: 10% vs. 18%; 5 years: 40% vs. 23%; p=0.38) or adverse events (1 year: 6% vs. 0%; 5 years: 20% vs. 0%; p=0.48). [Conclusion] Biologics reduced the annual relapse rate in patients with RP, supporting their use as maintenance therapy. No superiority was found between TNF-i and IL-6Ri in terms of effectiveness and safety.

EP3-11

Analysis of treatment resistance in systemic lupus erythematosus using RNA sequencing of sequential PBMC samples

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) includes treatment-resistant cases that can hinder remission. We attempted to extract factors associated with treatment resistance by analyzing the RNA sequences of sequential PBMC samples before, one and three months after treatment. In addition, similar analysis was performed in the belimumab-administrated patients to compare factors of treatment resistance. [Methods] PBMCs were collected from 13 patients with systemic lupus erythematosus before standard therapy excluding belimumab, anifrolumab, and rituximab. Samples were also collected 4 and 12 weeks after treatment (total of 39 samples), and RNA sequencing was performed. Treatment response was defined as SLEDAI-2k was less than 4 after 12 weeks. Considering time-series factors, DEG analysis was performed between the treatment response and resistant groups, and enrichment analysis was performed. We also performed RNA sequencing of sequential PBMC obtained from eight patients who received belimumab (total of 24 samples). [Results] Of the 13 patients who received standard therapy, six were resistant and seven responded to treatment. The number of DEGs comparing before and after treatment was higher in the treatment response group (1813 in the response group, 366 in the resistance group, and 163 genes common to both groups). Many of the 203 genes found only in treatment resistance were related to interferon stimulated genes. Of the eight patients who received belimumab, three were in the treatment-resistant group and five were in the treatment-responsive group. The overlap between DEGs before and after treatment in belimumab-resistant cases and those found in standard treatment was small (421 in the BEL-resistant group, 46 in common with the GC-resistant group). [Conclusion] Treatment resistance in SLE is related to interferon stimulated genes, and there might be a different tendency in treatment resistance to belimumab.

EP3-12

Association between maternal and cord blood mass cytometric immune cell profiling with pregnancy outcome in pregnancies with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] The aim of this study is to determine the association between changes in immune cell profiling of maternal peripheral blood and cord blood and pregnancy outcome in pregnancies complicated by systemic lupus erythematosus (SLE) using mass cytometry. [Methods] Pregnant women with SLE (N=7) and healthy pregnant women (N=6) who attended St. Luke's International Hospital from August 2020 to December 2022 were included. 1) Mononuclear cells isolated from maternal peripheral blood at the third trimester and cord blood were analyzed using cytometry by time-of-flight (CyTOF). Dimensional reduction and clustering analyses were performed to compare immune cell populations between pregnant women with SLE and healthy pregnant women. 2) For pregnant women with SLE, the association between clinical features on pregnancy outcome and immune cell populations was analyzed. [Results] 1) Maternal peripheral blood from pregnant women with SLE had a significantly lower ratio for some T cell subsets such as gamma delta (gd) T cells (0.34% vs 1.43%), and a significantly higher ratio for some T and B cell subsets such as naïve CD8+ cells (21.15% vs 16.47%) and plasmablast (4.58% vs 1.68%) than healthy pregnant women. Cord blood of the children of pregnant women with SLE had a significantly higher ratio of naïve CD8+ cell (28.17% vs 17.05%) and gdT cell (0.58% vs 0.39%) than those of healthy pregnant women. 2) In pregnant women with SLE, only maternal gdT cell population had a significant association with pregnancy outcome, showing a positive correlation with weeks of gestation (ρ=0.857). [Conclusion] Maternal and cord blood exhibited different immune cell profiles in pregnant women with SLE compared to healthy pregnant women. In pregnant women with SLE, decreased frequency of gdT cells in maternal peripheral blood may be associated with adverse pregnancy outcomes such as premature delivery.

EP3-13

Hip abductor muscle composition predicts gait speed improvement after total hip arthroplasty for patients with osteoarthritis

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Conflict of interest: None

[Objectives] A recent study has shown that the minimum clinically important improvement (MCII) in gait speed after total hip replacement (THA) is 0.32 m/sec. Currently, it remains to be investigated what preoperative factors link to suboptimal recovery of gait function after THA. This study aimed to identify preoperative lower-limb muscle predictors for gait speed improvement after THA for hip osteoarthritis. [Methods] This study enrolled 58 patients who underwent unilateral primary THA. Gait speed improvement was evaluated as the subtraction of preoperative speed from postoperative speed at 6 months after THA. Preoperative muscle composition of the glutei medius and minimus (Gmed+min) and the gluteus maximus (Gmax) was evaluated on a single axial computed tomography slice at the bottom end of the sacroiliac joint. Cross-sectional area ratio of individual composition to the total muscle was calculated. [Results] The females (n=45) showed smaller total cross-sectional areas of the gluteal muscles than the males (n=13). Gmax in the females showed lower lean muscle mass area (LMM) and higher ratios of the intramuscular fat area and the intramuscular adipose tissue area to the total muscle area (TM) than that in the males. Regression analysis revealed that LMM/TM of Gmed+min may correlate negatively with postoperative improvement in gait speed. Receiver operating characteristic curve analysis for prediction of MCII in gait speed at $\geq$ 0.32 m/sec resulted in the highest area under the curve for Gmax TM with negative correlation. The explanatory variables of hip abductor muscle composition predicted gait speed improvement after THA more precisely in the females compared with the total group of both sexes. [Conclusion] Preoperative Gmax TM could predict MCII in gait speed after THA. Preoperative muscle composition should be evaluated separately based on sexes for achievement of clinically important improvement in gait speed after THA.

EP3-14

Expression and Clinical Significance of Long non-coding RNA lnc-DC in Kidney Tissue from Patients with Lupus Nephritis

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Conflict of interest: None

[Objectives] Long non-coding RNA (lncRNA) *lnc-DC* is known to regulate the STAT3 pathway involving cell proliferation, differentiation, and cytokine secretion, suggesting that it may play a role in systemic lupus erythematosus (SLE) pathogenesis. This study aimed to investigate the expression of *lnc-DC* in the kidney tissue of patients with lupus nephritis (LN) to provide new insights. [Methods] Total RNA was extracted from kidney tissue in 5 patients with LN and 4 controls using miRNeasy mini kit (Qiagen, Germany) according to the manufacturer's protocols. We performed quantitative real-time polymerase chain reaction (qRT-PCR) to measure the expression of *lnc-DC* in kidney tissue. Correlation analysis was used to analyze the relationship between *lnc-DC* and the activity indicators of LN. [Results] We examined kidney tissues obtained from 5 patients with LN (female 5, mean age 26.8±5.5 years) compared with 4 controls (female 1, mean age 69.0±10.8 years). Among 5 patients with LN, 2 were classified as LN class II+V, and the rest were classified as LN class

III, IV, and V. The mean duration between SLE diagnosis and kidney biopsy was 43.1±63.4 months. None of the LN patients had comorbidities except for one patient with pulmonary hypertension. The mean SLE Disease Activity Index 2000 (SLEDAI-2K) and non-renal SLEDAI-2K scores were 15.2±4.1 and 5.6±1.5, respectively. The relative expression of *lnc-DC* is significantly elevated in kidney tissue in patients with LN compared to those in the control group (P=0.016). In correlation analysis, the *lnc-DC* expression in LN tissue was significantly associated with higher levels of serum ESR (rho=0.900, P=0.037) and anti-dsDNA antibody (rho=1.000, $P < 0.001$). [Conclusion] Our study found that the lncRNA *lnc-DC* expression was markedly enhanced in kidney tissues in patients with LN, and it correlates with indicators of disease state, including ESR and anti-dsDNA antibody. These findings may provide a novel perspective on LN pathogenesis.

EP3-15

Identification of Systemic Lupus Erythematosus Subgroups based on Autoantibody Profile using Machine Learning Approach: Preliminary Findings from iLUPUS Study

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Conflict of interest: None

Objective: Recent studies in White European populations have successfully utilized machine learning (ML) approaches to develop algorithms for subgrouping SLE patients based on autoantibody features. We aimed to utilize the ML approach to subgroup the Malay SLE patients based on their autoantibody profile and to investigate the relationship between the identified SLE subgroups and clinical manifestations. **Methods:** Feature selection was performed using a random forest (RF) model to determine the most influential SLE-associated autoantibodies in 191 Malay SLE patients based on their autoantibody profile for SLE subgroup differentiation. Based on these selected features, unsupervised cluster analysis was conducted to identify distinct SLE subgroups and it's relationship with specific clinical manifestations and disease activity was investigated using logistic regression. **Results:** The RF assessment demonstrated that anti-SSA IgG, anti-Ro52 IgG, and anti-nRNP-SM IgG autoantibodies with the respective mean decrease accuracy value of of 27.32, 25.28, and 19.49 are key markers in distinguishing among the identified SLE subgroups. We identified four distinct subgroups: Subgroup 1 (26.18%) was characterized by anti-Ro52 IgG (78%) and anti-SSA IgG (88%) autoantibodies; Subgroup 2 (35.08%) by anti-nRNP-sm IgG (68.1%); Subgroup 3 (12.04%) by anti-histone IgG, anti-nucleosome IgG, and anti-nRNP_sm IgG (91.3%); and Subgroup 4 (26.70%) was autoantibody-negative. Subgroup 2 was associated with organ damage (OR 3.00, 95% CI 1.11-8.92), and Subgroup 3 with active disease (SLEDAI-2K≧6) (OR 5.65, 95% CI 1.30-29.99), mucocutaneous manifestations (OR 9.94, 95% CI 2.29-55.12), and renal involvement (OR 6.67, 95% CI 1.14-54.87). **Conclusion:** Our findings supported the utilization of ML approach in enhancing the precision of subgroup classification within Malay SLE and highlights the need for further studies across diverse ethnic groups to improve our understanding of ethnic variations in SLE.

EP3-16

25-hydroxycholesterol in the pathogenesis of rheumatoid arthritis

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Conflict of interest: None

[Objectives] We aim to investigate the mechanism by which 25-hydroxycholesterol (25-HC) promotes the inflammatory process of rheumatoid arthritis (RA) by regulating the phenotypic transformation of $CD4^+$T cells. [Methods] Patients diagnosed with RA along with gender and age-matched individuals with OA and healthy controls (HC), were recruited for this study. Peripheral blood mononuclear cells (PBMC) and synovial fluid mononuclear cells (SFMC) were collected. Atorvastatin was used at different concentrations to inhibit the mevalonate pathway and mevalonic acid was supplemented. CH25H was knocked down using small interfering RNA (siRNA). [Results] IL-10^+CD4^+T cells in PBMC/SFMC of RA patients exhibited significantly lower levels compared to HC/OA individuals, as did the expression of IL-10. Atorvastatin-induced inhibition of the mevalonate pathway resulted in a concentration-dependent reduction in the ratio of IL-10^+CD4^+T cells, and the expression of IL-10. This down-regulation effect by atorvastatin was reversed upon supplementation with mevalonate acid. Expressions of CH25H and LXR in $CD4^+$T cells of RA synovial tissue were increased, while levels of CH25H, LXR, and caspase-1 in $CD4^+$T cells of synovial fluid elevated. Knockdown of CH25H led to a significant decrease in the proportion of IL-10^-IFN-γ^+CD4^+T cells and an increase in the proportion of IL-10^+IFN-γ^-CD4^+T cells in RA patients. Supplementation with 25-HC reversed the siRNA-CH25H-mediated decrease in IL-10^+CD4^+T cells and reduced IFN-γ^+CD4^+T cell formation. Additionally, the expression of NLRP3 and capsase-1 p20 in peripheral blood $CD4^+$T cells was decreased, and this effect was eliminated upon supplementation with 25-HC. [Conclusion] In peripheral $CD4^+$T cells of RA patients, 25-HC may activate the NLRP3 inflammasome through the CH25H-LXR pathway, thereby inhibiting the phenotypic transformation of IFN-γ^+CD4^+T cells to IL-10^+CD4^+T cells, and ultimately promoting the inflammatory process in RA.

EP3-17

Depletion of MDSC Alleviated Atherosclerotic Lesions in ApoE-/- Mice

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Conflict of interest: None

[Objective] Atherosclerosis (AS) is a major cause of cardiovascular diseases, such as stroke and myocardial infarction. It is characterized by progressive stenosis caused by lipid accumulation and inflammation of the arterial wall. Immune cells are considered important players in plaque progression and rupture in AS. In recent years, myeloid-derived suppressor cells (MDSCs) have been found to be expanded in autoimmune diseases and cardiovascular diseases, but their regulatory role in these diseases remains controversial. Therefore, this study focuses on the role and mechanism of MDSCs in the development of $ApoE^{-/-}$ mice and provides new clues for finding more effective therapeutic targets for AS. [Methods] Flow cytometry (FCM) was used to detect MDSC and its subtypes in bone marrow, spleen and peripheral blood. $ApoE^{-/-}$ mice were injected intraperitoneally with 5-FU to clear MDSC, and the percentages of MDSC and its subtypes and $CD4^+$T cell subsets in bone marrow, spleen and peripheral blood were detected by FCM. The degree of AS vascular lesion was analyzed by oil red O and HE staining. Serum levels of four lipids were detected with lipid kit. FCM was used to detect the expression of MDSC CD80, CD86 and MHC II and glycolysis-related molecules at different times. [Results] The percentages of MDSC and its subtypes were increased in bone marrow, spleen and peripheral blood of $ApoE^{-/-}$ mice. After 5-FU clearance of MDSC, $ApoE^{-/-}$ mice had decreased plaque formation and decreased serum TG levels. The expression of M-MDSC CD80 and CD86 in peripheral blood of $ApoE^{-/-}$ mice increased in a time-dependent manner at different stages. The expression levels of M-MDSC glycolysis-related molecules HK2 and LDH in spleen of $ApoE^{-/-}$ mice were increased. [Conclusions] The reduction of MDSC through the administration of 5-FU resulted in amelioration of atherosclerotic lesions in $ApoE^{-/-}$ mice.

Poster Session

P1-001

Clinical characteristics of patients with rheumatoid arthritis at our hospital not proceeding to phase II despite not achieving remission

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Conflict of interest: None

[Objectives] Some patients with rheumatoid arthritis (RA) cannot proceed to phase II despite not achieving remission. We aim to clarify their clinical characteristics. [Methods] We investigated the background, reasons for not proceeding to phase II, RA disease activity and treatment and comorbidities in those eight cases. [Results] Seven of the eight patients were female, and one was male with an average age of 65.9 years and an average history of RA of 8.4 years. The reasons for not proceeding to phase II were drug prices in six patients, mental resistance in one patient and coexistence of non-tuberculous mycobacteria in one patient. The mean DAS28-CRP score was 3.37. Seven patients used Methotrexate (MTX) with an average dose of 9.4 mg/week. One patient did not use MTX due to interstitial pneumonia. Iguratimod was used in six patients and Salazosulfapyridine in four patients. Prednisolone (PSL) was used in six patients with an average dose of 7.5 mg/day. Comorbidities included polymyalgia rheumatica in one case and Behcet's disease in one case. [Conclusion] The reason for not proceeding to phase II despite not achieving remission was often due to drug prices. It became clear that many drugs including of high-dose PSL were used, nevertheless RA treatment was difficult to treat.

P1-002

Clinical evaluation of five cases of rheumatoid polymyalgia that changed diagnosis to rheumatoid arthritis during treatment

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Conflict of interest: None

[Objectives] Polymyalgia rheumatica (PMR) is difficult to differentiate from Rheumatoid Arthritis (RA), and there are cases in which the diagnosis is changed from PMR to RA. The purpose of this study was to evaluate the clinical characteristics of cases in which the diagnosis was changed from PMR to RA. [Methods] Data were collected retrospectively from patients newly diagnosed with PMR and changed diagnosis to RA during treatment at our hospital from May 2016 to September 2024. Patients who had started GC prior to the diagnosis of PMR were excluded. We analyzed clinical characteristics. [Results] Five patients were included, median age of onset was 72 years old, two were male. Three patients had acute onset, with no cases of sudden onset. The affected joints were proximal in all cases and peripheral joints in one case. The median CRP was 13.68. RF was positive in one case, but ACPA was negative in all cases. At the time of diagnosis change, 4 patients had new onset of hand arthritis. [Conclusion] Patients had an acute onset, proximal joints were the main site of involvement, and CRP was high. On the other hand, none of the cases had the sudden onset characteristic of PMR. It is important to take a detailed history and assess the peripheral joints during follow-up.

P1-003

Clinical study of subjective symptoms and physical findings in RA cases with hypersensitivity to pain

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Conflict of interest: None

[Objectives] To examine the correlation between subjective symptoms and physical findings in RA patients with hypersensitivity to pain. [Subjects] Control group (11 cases) RA group without pain hypersensitivity. Group A (6 cases) RA group with 4-10 painful points according to the 1990 ACR Classification criteria for FM (1990 FM criteria). Group B (7 cases): RA group that only meets the 1990ACR FMS classification criteria. Group C (10 cases): RA group that meets the 2010 classification criteria for FM (2010 FM criteria) or Wolfe's modified ACR preliminary diagnostic criteria for FM (Wolfe's modified criteria). [Methods] We examined issues, below TJC, SJC, TPC in 1990 FM criteria. PS-VAS, PGA, EGA, DAS28CRP, DAS28ESR, CDAI, SDAI. WPI and SS in 2010 FM criteria. Association of the CSI and the difference of clinical background and the physical findings among the above four groups were statistically examined. [Results] There were significant differences in PS-VAS, and PGA between the control and other 3 groups. There was a correlation between tender point count in 1990 criteria and TJC, WPI, and standard score in Wolfe's modified criteria. [Conclusion] RA group with pain sensitivity tend to have higher disease activity, particularly reflecting subjective symptoms such as PGA and TJC.

P1-004

Longitudinal changes in disproportionate articular pain (DP) in rheumatoid arthritis (RA) patients and their association with patient-physician assessment discrepancies

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Conflict of interest: None

[Objective] Last year, we reported that RA patients exhibiting disproportionate articular pain (DP), defined as having 28 tender joint counts exceeding swollen joint counts by more than 7, are characterized by high disease activity and predominance of small joint involvement, correlating with a discrepancy between patient and physician global assessments. This study aims to examine the longitudinal changes in DP. [Methods] We analyzed the proportion of DP, discrepancies in global assessments, disease activity, and trends in b/tsDMARDs usage among RA patients from *NinJa* 2019-2022. [Results] Among 9,015 patients, 193 (2.1%) exhibited DP in *NinJa* 2019. The persistent DP group maintained high disease activity and discrepancies in global assessments, while the DP-exiting group showed decreased DAS28-CRP but continued discrepancies, exceeding the overall rate of 11.0%. In this group, TNF inhibitors were predominantly used in *NinJa* 2019-2020, and JAK inhibitors were more commonly used in *NinJa* 2021-2022. [Conclusion] DP is associated with high disease activity. However, discrepancies persist even with improvements, suggesting a role of pain sensitivity in its etiology. The increased usage of JAK inhibitors indicates their potential efficacy in DP-RA, warranting future prospective studies.

P1-005

A Study on Mortality by Gender and Age Among Rheumatoid Arthritis Patients Using NinJa 2022

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Conflict of interest: None

[Objectives] To clarify mortality rates and major causes of death by gender and age among rheumatoid arthritis patients. [Methods] Using the *NinJa 2022* database, mortality rates and causes of death among rheumatoid arthritis patients were compared by gender. [Results] We analyzed 207 deaths (73 men, 134 women) among 17,501 patients (3,734 men, 13,767 women) in *NinJa 2022*. The overall mortality rate was 1.2%, with men at 2.0% and women at 1.0%, showing a higher rate in men. This trend held across age groups: mortality rates for men and women were 0.8% and

0.6% (male-to-female ratio 1.46) in their 60s, 2.0% and 1.0% (ratio 2.11) in their 70s, 4.7% and 2.5% (ratio 1.84) in their 80s, 7.7% and 4.2% (ratio 1.83) in their 90s, with male mortality nearly double that of females across all ages. Causes of Death: Respiratory diseases (pneumonia, interstitial pneumonia, lung cancer) were the leading cause in men, while heart failure and pneumonia were most common in women. [Conclusion] (1) Male rheumatoid arthritis patients showed higher mortality rates than females. (2) This gender difference persisted across all age groups, with men's rates almost double those of women. (3) Respiratory diseases were prevalent causes in men, whereas heart failure and pneumonia were common in women.

P1-006

Investigation of EBV production and the inhibitory effect of iguratimod on AKATA, Daudi and EBV-transformed B-lymphoblastoid cells

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Conflict of interest: Yes

[Objectives] EBV is known to be involved in the pathogenesis of RA, and NF-κB is activated in EBV-infected cells. Iguratimod suppresses the production of inflammatory cytokines by inhibiting NF-κB. In the present study, we investigated the involvement of inhibitory effect on NF-κB activity in EBV reactivation. [Methods] AKATA, Daudi, and B-lymphoblastoid cells (BLBC) were cultured with anti-human (α-h) IgG (AKATA), IgM (Daudi, BLBC) and iguratimod. 48 hours later, cells were stained with fluorescent. EBV DNA copy of cells was measured by real-time PCR. [Results] AKATA stimulated with α-h IgG and Daudi stimulated with α-h IgM showed enhanced production of EBER compared to no stimulation, which was suppressed in iguratimod. EBV DNA level was significantly increased in stimulating AKATA and significantly decreased in iguratimod. Furthermore, stimulation of BLBCs resulted in perinuclear staining of EAD antibodies, whereas EAD antibodies disappeared in iguratimod. [Conclusion] Iglatimod partially inhibited EBV reactivation, suggesting that suppressing EBV, which is thought to be involved in the pathogenesis of RA, may lead to a more fundamental treatment of RA.

P1-007

Stabilization of type 2 ryanodine receptor may improve autoimmune diseases

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Conflict of interest: None

[Object] We investigated the effects of stabilization of type 2 ryanodine receptor (RyR2) on DSS-induced colitis and experimental autoimmune encephalomyelitis (EAE). [Methods] We compared the severities of both DSS-induced colitis and EAE between control mice (wild type C57BL/6 mice) and V3599K KI mice which show stabilization of RyR2. Fecal microbiota transplantation with feces of control mice and V3599K KI mice was conducted two weeks before DSS was started. [Results] V3599K KI mice showed improvement of severities of DSS-induced colitis on day 7 ($p<0.05$) and EAE on day 14 ($p<0.05$). [Conclusions] These results suggest that stabilization of RyR2 may improve autoimmune diseases.

P1-008

CD14+ dendritic-shaped cells in rheumatoid arthritis synovial tissue have the potential to differentiate into osteoclasts

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Conflict of interest: None

[Objective] We reported that CD14+ dendritic-shaped cells in the synovial tissue of rheumatoid arthritis (RA) express CD90 around blood vessels in the sublining layer and differentiate into HLA-DR+ dendritic cells upon contact with lymphocytes in RA synovial tissue. In this study, we investigated the possibility of osteoclast differentiation of $CD14^{high}CD90^{int}$ cells. [Methods] After in vitro culture of RA synovial tissue, $CD14^{high}CD90^{int}$ cells were harvested and cultured in dendritic cell differentiation induction medium. Then, TNF-α and IL-6 were added in the medium, and the possibility of osteoclast differentiation was examined by TRAP staining. [Results] After dendritic cell differentiation, $CD14^{high}CD90^{int}$ cells showed more positive cells by TRAP staining than non-$CD14^{high}CD90^{int}$ cells. Furthermore, more positive cells were observed in the group of the cells co-cultured with lymphocytes. [Conclusions] It was suggested that $CD14^{high}CD90^{int}$ cells may have the possibility of osteoclast differentiation as well as dendritic cell differentiation in RA synovial tissue.

P1-009

HLA Haplotype Analysis in Japanese Patients with Palindromic Rheumatism

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Conflict of interest: None

[Objective] Palindromic rheumatism (PR) is a periodic arthritis whose factor is unclear, and it has been suggested that multiple genes may be involved in the pathogenesis of the disease. We have previously carried out whole genome sequencing (WGS) in Japanese patients with PR and investigated the effects of genetic rare variants (Kawara T et al., Kobe J. Med. Sci., 2024). Our analysis suggested that HLA-DQB1 is associated with its pathogenesis, and previous studies in other races have suggested an association with each HLA allele, including HLA-DQA1, DQB1, and DRB1. Accordingly, the purpose of this study was to clarify the details of each HLA haplotype associated with the disease. [Methods] HLA-DQA1, DQB1 and DRB1 HLA haplotypes were determined by direct sequencing of patients with PR, including two mother-child cases and one sporadic case. [Results] DQB1*05 and DRB1*08 were more likely to be accumulated in patients with PR than in the controls. On the other hand, HLA-DQA1 was considered to be less likely to be associated with disease. [Conclusion] It was suggested that HLA-DQB1 and DRB1 haplotypes is involved in the pathogenesis of Japanese patients with PR.

P1-010

Strategic Targeted Therapy for BCMA High-Expressing Autoreactive RP105-Negative B Cells Using t-SNE Method

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Conflict of interest: None

[Objectives] Refractory autoimmune diseases require novel therapy. One significant immune abnormality is autoantibody-producing B cells, particularly RP105-negative B cells. This study utilizes t-SNE analysis to identify pathogenic B cells and their specific antigens. [Methods] We performed t-SNE analysis on RP105 (-) B cells isolated from SLE patients using flow cytometry. We reviewed literature on RP105 in various diseases. [Results] Five subsets of RP105 (-) B cells exsist in autoimmune diseases. An increase in plasmablasts in SLE and activated B cells in IgG4-RD were found. Plasmablasts from SLE showed an increased BCMA/BAFF-R ratio. Although CXCR5 was present in early plasma cells under normal and persisted in late plasmablasts in IgG4-RD, it was lost in early in SLE. t-SNE analysis revealed over 20 distinct subsets of RP105 (-) B cells, surpassing previously reported categories. [Conclusion] Plasmablasts expressing high levels of BCMA are the most promising therapeutic target for SLE. BCMA-high expression RP105-negative B cells exhibit diverse subsets with varying ratios and molecular expressions specific to

each disease. Identifying pathogenic B cells and their antigens is essential for developing innovative therapeutic strategies tailored to individual autoimmune conditions.

P1-011

B Cells and Autoantibodies in MPO-ANCA Positive Temporal Arteritis

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Conflict of interest: Yes

[Objectives] Lymphocyte infiltration into the vessel wall is involved in temporal arteritis. This study aimed to investigate the role of B cells infiltrating MPO-ANCA positive temporal arteritis by analyzing their antigen specificity. [Methods] CD45-positive cells were sorted from two temporal artery biopsy specimens, and single-cell RNA-seq analysis was performed to obtain B cell receptor (BCR) sequences and gene expression profiles (GEX). Antibodies based on the variable region sequences of clonally expanded B cells were tested for reactivity to neutrophils and MPO antigen using immunostaining, fluorescence assay, flow cytometry, and ELISA. [Results] BCR sequences and GEX data from 131 B cells were obtained from two MPO-ANCA positive cases. Antibodies from 13 expanded B cell clones showed two clones reacting with neutrophils and the MPO antigen. GEX analysis divided lesional B cells into two groups, with MPO-reactive antibodies producing B cells in the same subset. [Conclusion] In MPO-ANCA positive temporal arteritis, self-reactive B cells infiltrating the lesion produce MPO-ANCA, potentially contributing to neutrophil-driven inflammation through the produced antibodies.

P1-012

The effects of CaMKII and mitochondrial reactive oxygen species on the pathogenesis of fibrosis in systemic sclerosis skin fibroblasts

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Conflict of interest: None

[Objectives] Prior research suggests that inhibiting CaMKII blocks fibrosis progression, and that mitochondrial oxidative stress can activate CaMKII. We investigated CaMKII and mitoROS effects on fibrotic pathology in systemic sclerosis (SSc) skin fibroblasts. [Methods] Dermal fibroblasts were isolated from diffuse cutaneous SSc patient biopsies and treated with CaMKII inhibitor KN93 or mitoROS quencher Mitoquinol (MitoQ) for 72 hours. Gene expression was analyzed by qPCR and Western blot. Fibroblast functions were assessed via cell migration, gel contraction, and proliferation assays. [Results] CaMKII inhibition by KN93 markedly reduced fibrosis-associated gene expression in SSc fibroblasts and suppressed their proliferation, migration, and gel contraction. Similarly, neutralizing mitoROS with MitoQ decreased fibrotic gene expression and impaired SSc fibroblast functions. MitoQ's anti-fibrotic effects were achieved by preventing CaMKII oxidation. [Conclusion] KN93 and MitoQ inhibit fibrosis-related functions in SSc fibroblasts, indicating CaMKII and mitoROS as key factors in SSc fibrotic pathology.

P1-013

Senescence-Associated Secretory Phenotype of Type II Alveolar Epithelial Cells contribute to the Pathogenesis of Bleomycin-Induced Interstitial Lung Disease

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Conflict of interest: None

[Objectives] The pathogenesis of interstitial lung disease (ILD) in rheumatic diseases remains unclear. We previously reported that type II alveolar epithelial cells (AT2) produce inflammatory senescence-associated secretory phenotype (SASP) factors contributing to ILD in a bleomycin-induced ILD (BLM-ILD) mouse model. This study aimed to comprehensively analyze SASP in ILD by RNA-seq in BLM-ILD model. [Methods] We generated *Sftpc-Cre; R26-tdTomato* mice, AT2 reporter mice, and induced BLM-ILD. AT2 collected pre-instillation and on days 3 and 14 post-instillation of BLM were analyzed by RNA-seq, with ontology analysis on genes upregulated post-instillation. Additionally, senescence was induced in A549 (AT2 cell line) via BLM, followed by immunofluorescence for phosphorylated IRF3 (pIRF3) and quantitative RT-PCR analysis of interferon-stimulated genes (ISGs). [Results] Genes upregulated on days 3 and 14 post-BLM instillation included those in the p53 pathway, indicating cellular senescence, and ISGs linked to the type I interferon (IFN-I) response. In the BLM-treated A549, translocation of pIRF3 protein and upregulation of ISG expression were observed. [Conclusion] Our findings suggest that in BLM-ILD, SASP-acquiring AT2 produce IFN-I and ISGs, which potentially contributing to ILD.

P1-014

Effect of JAK inhibitors on osteoblast differentiation

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Conflict of interest: None

[Objectives] Currently, five types of JAK inhibitors are indicated for rheumatoid arthritis in Japan. Here, we will report on the effects of various JAK inhibitors on osteoblast differentiation. [Methods] Using mouse MC3T3-E1 cells, JAK inhibitors (Baricitinib: Bari, Peficitinib: Pefi, Filgotinib: Filgo) were added and cultured. The degree of mature osteoblasts was evaluated by Alizarin Red S staining and alkaline phosphatase staining. [Results] Bari and Pefi showed an inhibitory effect on osteoblast differentiation, but Bari particularly inhibited osteoblast differentiation more strongly. On the other hand, Filgo showed no inhibitory effect even at high concentrations and differentiated into mature osteoblasts. Correlating with these results, Osterixs expression, an osteoblast differentiation marker, was observed only in Filgo-treated cells. In addition, the expression of FOXM1 increased in Filgo-treated cells as well as in controls, but no change in FOXM1 expression was observed in Bari and Pefi treated cells. [Conclusion] Among the JAK inhibitors, Bari and Pefi suppressed osteoblast differentiation, while Filgo did not affect osteoblast differentiation. Furthermore, it was suggested that FOXM1 expression regulated by JAK signals may influence differentiation of mature osteoblasts.

P1-015

Role of LIGHT in eosinophilic vasculitis

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Conflict of interest: None

[Objectives] Eosinophilic granulomatosis with polyangiitis (EGPA) is an eosinophilic vasculitis associated with allergic airway inflammation. While patients with marked eosinophilia and severe asthma have a higher risk of developing EGPA, its mechanism is unclear. TNFSF14 (LIGHT), a TNF family cytokine, is found at higher levels in the sputum of severe asthma patients. LIGHT signals on lung structural cells through LTβR, contributing to asthma exacerbation. Since LTβR is highly expressed on vascular endothelial cells, we hypothesized that LIGHT may regulate its function and triggers vasculitis. Additionally, recent studies suggest ETosis, a type of eosinophil cell death, is related to EGPA pathology. Thus, we aimed to investigate the role of LIGHT in eosinophilic vasculitis and ETosis. [Methods and Results] RNA-seq analysis of LIGHT-stimulated vascular endothelial cells revealed upregulation of eosinophil adhesion molecules. LIGHT-stimulated endothelial showed increased cell death when co-cultured with activated eosinophils. LIGHT did not induce ETosis in eosinophils, nor was ETosis observed in the co-culture system. [Conclusion] LIGHT might contribute to endothelial cell damage mediated by eosinophils. Further research is required to elucidate LIGHT's role in EGPA

pathogenesis.

P1-016

Analysis of the function and its quantification of citrullinated ITIH4 in arthritis

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Conflict of interest: None

[Objectives] Citrullinated ITIH4 (cit-ITIH4) is specifically expressed in RA plasma, and correlated with disease activity by semiquantitative methods. In this study, we investigated the function of cit-ITIH4 and its quantification. [Methods] ITIH4 and cit-ITIH4 expression in blood of K/BxN serum transfer arthritis (STA) and collagen-induced arthritis (CIA) was examined. The severity of arthritis and cells infiltrating joints and lungs were compared between wild-type mice (WT) and ITIH4 deficient mice (KO). Anti-cit-ITIH4 antibody in RA plasma was examined by ELISA. [Results] In STA and CIA, serum ITIH4 increased from the onset of arthritis, and cit-ITIH4 increased most at the extreme arthritis phase. There was no significant difference in the severity of STA or CIA and infiltrating cells to joints between KO and WT. However, neutrophil infiltration to the CIA lungs significantly increased in KO. Anti-cit-ITIH4 antibody in RA plasma tended to be elevated compared to healthy donors, however, there was no correlation with disease activity. [Conclusion] ITIH4 may inhibit neutrophil infiltration. Cit-ITIH4 may be a useful biomarker for arthritis, however, anti-cit-ITIH4 antibody had no correlation with disease activity, suggesting the need for a quantitative system for cit-ITIH4 itself.

P1-017

The role of ADAM-17 in lung fibroblasts

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Conflict of interest: None

[Objectives] In this study, we examined the expression and function of ADAM-17 in normal human lung fibroblasts (NHLF) to investigate the role of ADAM-17 in interstitial lung disease. [Methods] The expression of ADAM-17 in NHLF was confirmed by immunostaining, and ADAM-17 in the culture supernatant of NHLF co-stimulated with IL-6 and IL-6 receptor was measured by ELISA. Furthermore, to identify the role of ADAM-17 in inflammation in lung fibroblasts, the adhesion ability of monocyte (THP-1) to ADAM-17-suppressed NHLF was examined using siRNA. Finally, the expression of adhesion factors such as ICAM-1 in the supernatant of the NHLF was determined by ELISA. [Results] ADAM-17 is expressed in NHLF, and its production in NHLF supernatant was significantly upregulated by IL-6 and soluble IL-6 receptor stimulation compared to no stimulation. ADAM-17 knockdown in NHLF significantly decreased ICAM-1 and VCAM-1 in the cell supernatant, while there was no significant difference in the adhesive capacity. [Conclusion] ADAM-17 was expressed in NHLF, which are the major cells in interstitial lung disease, and a significant decrease in ICAM-1 and other factors in ADAM-17-suppressed NHLF supernatants was observed, suggesting that ADAM-17 is involved in the cleavage of adhesion factors.

P1-018

Early alterations in Peripheral Immune Cell Populations in Rheumatoid Arthritis Patients Following Adalimumab Therapy

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Conflict of interest: Yes

[Objectives] This study aims to examine the early alterations in peripheral blood immune cells in rheumatoid arthritis patients at 2 weeks after the initiation of adalimumab therapy. [Methods] The change of immune cell population was evaluated in 12 Japanese RA patients by multicolor flow cytometry. [Results] Two weeks after adalimumab treatment, significant increases were observed in effector memory $CD8^+$ T cells, Th1/17 cells, Tfh17 cells, and memory Treg cells. Conversely, there were significant reductions in naive $CD4^+$ T cells, Th2 cells, and activated Tfh2 cells. [Conclusion] Early changes in peripheral blood immune cells following adalimumab administration may have potential implications for the immunological effects of TNF inhibitors.

P1-019

Association between synovial fluid maresin levels and blood test parameters in patients with rheumatoid knee arthritis

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Conflict of interest: None

[Background] Maresin (MaR), a lipid mediator (LM), helps resolve inflammation. Our prior analysis in synovial fluid (SF) from RA and OA patients showed that SF MaR levels could distinguish RA from OA. However, SF collection is invasive and requires specialized skills. [Objectives] To find insurance-covered blood test parameters that could potentially replace the need for measuring MaR concentration. [Subjects and Methods] The study involved 10 RA patients undergoing TKA, during which SF was collected, processed, and MaR levels were measured via LC-MS/MS. Venous blood collected preoperatively was tested for (1) white blood cell count ($/mm^3$), (2) CRP (mg/dL), (3) anti-CCP antibody (U/mL), (4) MMP-3 (ng/mL), and (5) RF (mg/dL). Simple linear regression analyzed the correlation between SF MaR and each blood parameter. [Results] The correlation analysis yielded: (1) R^2=0.0001, P=0.978 (2) R^2=0.00625, P=0.828 (3) R^2=0.000192, P=0.971 (4) R^2=0.0763, P=0.440 (5) R^2=0.379, P=0.0583. No significant correlation was found for any parameter. [Discussion] MaR may specifically suppress joint inflammation, making it unlikely to correlate with systemic blood test parameters. [Conclusion] No significant correlation was found between SF MaR levels and blood test parameters in RA patients.

P1-020

Anti-integrin alpha9 antibody inhibits fibrocyte migration

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Conflict of interest: None

[Objective] Fibrocyte is one of the important effector cells in pulmonary fibrosis. We identified integrin alpha9 (ITGA9) as a surface marker of fibrocytes. In this study, we examined the effect of ITGA9 inhibition using lung fibrocytes. [Methods] Fibrocytes were induced from murine lung cells and treated with anti-ITGA antibody. The migration capacity and the expression of collagen, humoral factors were examined by transwell migration assay and quantitative polymerase chain reaction. A murine fibroblasts cell line was also evaluated in the same method. [Results] Anti-ITGA antibody inhibited the migration of both fibrocytes and fibroblasts. Anti-ITGA antibody tended to decrease the Col1a1 mRNA level in fibrocytes as well as Acta2 in fibroblasts. [Conclusions] ITGA9 inhibition may have the anti-fibrotic potential by suppressing fibrocyte and fibroblast migration.

P1-021

Investigation of chronic inflammation and aging factors associated with polymyalgia rheumatica (PMR)

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Conflict of interest: None

[Objectives] PMR mostly occurs in older people over 50, and that suggests a potential link between PMR and chronic inflammation and aging. We investigated the relationship between chronic inflammation and aging-related factors in patients with PMR. [Methods] (1) Using peripheral blood mononuclear cells (PBMC) from PMR patients and healthy controls (HC) over 50, we evaluated cyclin-dependent kinase inhibitors and senescence-associated secretory phenotype inducers via qRT-PCR. (2) Considering synovitis in PMR, we used human fibroblast-like synoviocytes (HFLS), performed IRF3 knockdown, and stimulated with IL-1β to analyze inflammatory gene expression. (3) The involvement of Type I IFN (IFN I) was assessed using reporter cells and serum samples. [Results] (1) *IRF3* was significantly reduced in PMR patients compared to HC before treatment, but increased after treatment, approaching HC levels. (2) IL-1β-stimulated HFLS exhibited significantly increased *TNFA*, *IL-1B*, and *MMP3* expressions by IRF3 knockdown, but *IL6* did not changed. (3) IFN I activity observed no significant difference between PMR patients and HC, unlike SLE with high IFN I expression. [Conclusion] Reduced IRF3 expression contributes to worsening PMR inflammation, on the other hand, IFN I may be unaffected by disease activity or treatment.

P1-022

In Vivo Finger Kinematics in Rheumatoid Arthritis Patients with Boutonniere Deformities Using Deep Learning

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Conflict of interest: None

[Objectives] Buttonhole deformity in rheumatoid arthritis causes PIP joint flexion and DIP joint hyperextension, significantly impairing hand function. Conventional motion analysis uses optical reflective markers that interfere with finger movements and require special equipment. OpenPose uses deep learning to estimate human body features from images or videos without needing special equipment or environments. This study aims to evaluate active finger movements in buttonhole deformations using OpenPose. [Methods] Four RA patients with buttonhole deformity (8 fingers) and four healthy volunteers (8 fingers) were included. Active extension movements were filmed from the ulnar side with a smartphone, and DIP, PIP, and MCP joint angles were calculated using OpenPose feature point estimation and compared. [Results] The PIP joint angle at maximum extension was significantly smaller in the buttonhole deformity group (130.2 vs. 195.8, p=0.0014). In the normal group, MCP extension was slower and more gradual, while in the buttonhole deformity group, MCP extension was steeper and preceded the other joints. [Conclusion] Deep learning evaluated active deformed finger movements in vivo, revealing characteristic movement features. OpenPose proved useful in analyzing finger kinematics.

P1-023

Examination of extensor and flexor tendons by ultrasonographic examination in cases with primary complaints of pain and stiffness in the hands and fingers, but without synovitis

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Conflict of interest: None

[Objectives] Usually, US of the hand only observes the extensor (Ex) side, but in many cases there are no findings on the extensor side and inflammation of the flexor (Fx) tendons are observed. We investigated the US findings of the flexor tendons in cases with finger symptoms. [Methods] Fx US was performed on patients with finger symptoms and 156 cases without arthritis were analyzed. Tendonitis were defined as swelling, fluid accumulation and positive PD signals of tendon, and positive PD signals at enthesis. [Results] Tendonitis were Ex (+) Fx (+) 27%, Ex (+) Fx (-) 3%, Ex (-) Fx (+) 63%, and extensor (-) Fx (-) 7%, with an overall Ex (+) 30% and Ex (-) 70%, and 90% of both Ex (+) and Ex (-) were flexor (+). The number of Tendonitis on the flexor side per case was significantly higher on the Ex side (+) at 4.7±3.2 compared to 3.7±3.1 on the Ex side (-) (p=0.021). The enthesitis was significantly higher on the Fx side at 7.6±3.0 compared to 2.6±3.2 on the Ex side (p<0.0001). [Conclusion] Tendonitis was found in 30% of cases on the extensor side alone, but were found in 90% when the flexor side was included. Clinical symptoms often coincide with flexor findings. It is necessary to observe the flexor side, especially when the patient shows the palmar side.

P1-024

Musculoskeletal Ultrasonography Findings in Rheumatoid Arthritis Complicated by Gout

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Conflict of interest: None

[Objectives] Double contour sign on musculoskeletal ultrasonography (MSUS) is often a pitfall in the diagnosis or exacerbation of rheumatoid arthritis (RA), although it is necessary to exclude gout. In this report, we describe a case in which gout attack was strongly suspected during the course of RA. [Case] A 65-year-old woman was diagnosed with RA one year ago based on bilateral wrists pain and blood tests that revealed RF 17 IU/mL and ACPA 289 U/mL. After that, the joint pain tended to improve with a weekly low-dose methotrexate pulse, but pain in the toes also appeared, and she was referred to our hospital. MSUS revealed the presence of synovitis of GS 3 and PD 2 in the right first MTP joint and hyper-echogenicity in the synovial membrane and double contour sign on the cartilage surface of the joint. She had been prescribed diuretics for leg edema at another hospital, her renal function was worsening, so the drug was discontinued and febuxostat 10 mg was started. The arthritis resolved quickly and spontaneously, and the patient was considered to have a gout attack. [Conclusion] In general, RA and gout are not frequently combined, but when they are present at the same time, the diagnosis becomes difficult because of the overlap of symptoms.

P1-025

Efficacy of Ultrasound-Guided Glucocorticoid Injections for Residual Synovitis

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Conflict of interest: None

Objective: Residual synovitis identified by power Doppler ultrasonography (PDUS) represents a risk for RA recurrence and bone destruction. This study assessed the efficacy of ultrasound-guided glucocorticoid (GC) injections for treating residual synovitis after cs/b/tsDMARDs therapy. **Methods:** RA patients with 1-2 swollen joints after ≧3 months of cs/b/tsDMARDs therapy were enrolled, confirmed by PDUS residual synovitis. Triamcinolone acetonide was administered under ultrasound guidance, with clinical and imaging assessments conducted at 3 and 12 months

post-treatment. **Results:** Thirty patients (36 joints) received GC injections. Median PDUS gray-scale (GS) scores of injected joints improved from 3 to 2 to 1, and PD scores improved from 2 to 0 to 0 at baseline, 3, and 12 months. Total GS and PD scores of finger/wrist joints, patient VAS, and CDAI also showed significant improvements. Patients achieving PDUS remission (total PD≦1) without DMARD intensification had lower baseline disease activity, fewer PDUS-detected synovitis sites, and lower GS and PD scores at baseline ($p<0.05$). **Conclusion:** Ultrasound-guided GC injections improved residual synovitis, though patients with high disease activity and extensive synovitis may require intensified DMARD therapy for remission.

P1-026

Optimal ultrasound guidance for PIP joint injections

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Conflict of interest: None

[Objectives] Recently, ultrasound guidance has been widely used for intraarticular injections. For the assessment of synovitis, proximal interphalangeal (PIP) joints are more commonly examined from the dorsal aspect. The aim of this study was to investigate which approach is more suitable for intraarticular injections of PIP joints: ultrasound guidance from the dorsal or volar aspect. [Methods] Patients with rheumatoid arthritis who were indicated for corticosteroid injections of PIP joint arthritis at Tokyo Metropolitan Tama-Nambu Chiiki Hospital were included. Both dorsal and volar aspects of PIP joints were evaluated with ultrasound, and cross-sectional areas of the joint space from each aspect were measured. Corticosteroid injections were performed with ultrasound guidance from the aspect that depicted the joint space more clearly. [Results] Four PIP joints were included in this study. In three of the PIP joints, the cross-sectional areas of the joint space were larger when examined from the volar aspect compared to the dorsal aspect. All injections were performed with ultrasound guidance from the volar aspect. [Conclusion] For intraarticular injections of PIP joints, ultrasound guidance from the volar aspect may be more suitable than from the dorsal aspect.

P1-027

Discontinuation of concomitant methotrexate in patients with rheumatoid arthritis treated with certolizumab pegol: A randomized, controlled trial (PRIMERA study)

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Conflict of interest: Yes

[Objectives] To compare the effect of discontinuing versus continuing methotrexate (MTX) alongside certolizumab pegol (CZP) on maintaining low disease activity (LDA) in rheumatoid arthritis (RA) patients already stable on combination therapy. [Methods] This multicentre, open-label, randomized, controlled trial included RA patients with sustained LDA (Clinical Disease Activity Index [CDAI] ≦10) for ≧12 weeks with CZP + MTX. Patients were randomized to either continue MTX (CZP + MTX group) or discontinue MTX after a 12-week reduction period (CZP group). The primary endpoint was the proportion of patients maintaining LDA without a flare (i.e., a CDAI score >10 or intervention with rescue treatments for any reason) at week 36. [Results] All 84 screened patients were randomized to the CZP + MTX group (n=41) and CZP group (n=43). Proportions (90% confidence interval [CI]) of patients who maintained LDA at week 36 were 85.4% (76.3 to 94.4%) in the CZP + MTX group and 83.7% (74.5 to 93.0%) in the CZP group. The difference (90% CI) between the two groups was -1.6% (-14.6 to 11.3%), with the lower limit of the 90% CI exceeding the non-inferiority margin of -18%. [Conclusion] Discontinuing concomitant MTX in RA patients on CZP is clinically feasible for maintaining LDA.

P1-028

A survey of pharmacists' shared decision-making in the face of an unstable supply of sarilumab

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Conflict of interest: None

[Objectives] In May 2024, limited sarilumab shipments prevented all patients from continuing treatment. Pharmacists engaged in shared decision-making, allowing patients to decide whether to continue with sarilumab. This issue was investigated due to the impact of unstable medicine supply on treatment decisions. [Methods] The study included patients using sarilumab as of May 2024 and excluded those whose treatment couldn't be changed by their doctor. Pharmacists engaged in shared decision-making with patients whose treatment could be altered, asking about their prioritized values, the impact of unstable supply, concerns about worsening disease, and side effects. [Results] Enrolled all 23 patients in the study, 6 were excluded, and 17 were included. Nine patients (53%) continued with sarilumab, five (29%) switched to tocilizumab, two (12%) switched to other drugs, and one (6%) switched to biofree. Ten patients prioritized efficacy, while seven prioritized safety. Additionally, ten patients mentioned that the unstable supply influenced their values. Among the eight patients who switched, six were concerned about worsening symptoms, and four were concerned about side effects. [Conclusion] The study showed that an unstable medicine supply significantly affects patients' values and anxieties.

P1-029

The effect of ozoralizumab in bio-naïve patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] We report the therapeutic effects of Ozoralizumab (OZR). [Methods] We analyzed five RA patients in our department who had an inadequate response to methotrexate (MTX) and started treatment with OZR, with follow-up for up to 12 weeks. We evaluated the treatment continuation rate, therapeutic effects, and complications up to 12 weeks. [Results] The cohort consisted of 4 women and 1 man, with a median disease

duration of 1.2 years, and the mean age at the start of OZR treatment was 72.6 years. All patients were also taking MTX, with an average dosage of 9.2 mg/week. The mean disease activity, as measured by DAS-CRP, improved from 3.76 at baseline (BL) to 2.47 at 4 weeks and 2.19 at 12 weeks. Similarly, SDAI improved significantly from BL average of 17.3 to 7.4 and 5.9 at 4 and 12 weeks. CRP levels also showed significant improvement, decreasing from 1.5 mg/dL at BL to 0.22 and 0.12 mg/dL at 4 and 12 weeks. No complications requiring drug suspension were observed, and all patients were able to continue OZR treatment for the full 12 weeks. [Conclusion] OZR has a molecular weight approximately 1/4 that of conventional IgG antibodies, making it more likely to accumulate at sites of inflammation. Along with improvements in disease activity, CRP levels also showed early improvement.

P1-030

Successful Discontinuation of Ozoralizumab in Established RA After Achieving Deep Remission

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Conflict of interest: None

[Background] Ozoralizumab (OZR), lacking CDC and ADCC activity, has limited evidence for discontinuation post-remission. [Clinical Course] A 78-year-old woman diagnosed with RA four years ago was maintained on salazosulfapyridine (500 mg/day). In June of Year X-1, she developed persistent left knee arthritis. Referred to our department in February of Year X, labs showed anti-CCP 345.6 U/mL, RF 44 IU/mL, CRP 2.64 mg/dL, MMP-3 457.0 ng/mL, and bilateral knee inflammation. MTX 10 mg/week showed limited effect, so OZR was started in May of Year X. After four weeks, CRP dropped to 0.6 mg/dL, and VAS improved from 86 to 11. By 12 weeks, she achieved Boolean remission, sustaining this state. In May of Year X+1, OZR was discontinued at her request, and six months later, remission persists on MTX 6 mg/week. [Discussion] Bio-free TNF therapy is supported, especially with antibody agents. In this case of established RA, OZR enabled remission sustainment post-discontinuation despite prior limited response. Among 74 GLM cases at our department, 46 were established RA; none maintained remission post-discontinuation. This case suggests OZR may allow sustained remission following deep remission. [Conclusion] OZR shows potential as a TNF inhibitor supporting drug-free remission in RA.

P1-031

The efficacy of Ozoralizumab to RA patients for short-term results

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Conflict of interest: None

[Objectives] To evaluate Ozoralizumab (ORZ) to RA patients for short-term results. [Methods] From July 2023, six cases treated with ORZ were evaluated by recording DAS28 (CRP). The average of DAS28 (CRP) was 4.2 points before use of ORZ. [Results] DAS28 decreased to 1.8 points at six month, CRP was also reduced from 3.1 to 0.11 at six month. [Conclusion] The therapy of ORZ was effective for short-term results.

P1-032

A case of palmoplantar pustular pustulosis (PPP) in which TNF preparations were effective against pustules

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Conflict of interest: None

[Case] A 55-year-old woman [Chief complaint] Deformed nails on both hands, swelling and pain in the right elbow and DIP joints of the 2nd to 5th fingers of both hands, and pustules on the palms and soles. [Present illness] From around the age of 52, numerous small pustules appeared on the palms and soles of the feet in the summer. She had been using over-the-counter medications for tinea but had not improved, and the condition had repeatedly disappeared and reappeared with desquamation. She visited a nearby dermatologist. A patch test showed a positive reaction to amalgam used for orthodontic treatment, so it was replaced, but the pustules did not improve. Around the same time, she began to develop deformed nails. About 6 months ago, arthritis in her joints had gradually increased, and she began to suffer from pain. She was suspected of having PPP disease and its arthritis. Bone scintigraphy revealed accumulation in the costoclavicular joint, and CT revealed bone sclerosis in the costoclavicular joint. The patient was diagnosed PPP. [Treatment] MTX could not be used to nausea, but azathioprine and tacrolimus relieved the joint pain, and the TNF agent adalimumab was effective against the pustules. We report the examination and treatment of this case, with review.

P1-033

Results of Ozoralizumab Use in Patients with Phase III Rheumatoid Arthritis

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Conflict of interest: None

Objective: To evaluate the outcomes of patients with ozoralizumab (OZR) for Phase III rheumatoid arthritis (RA). Methods: 28 phase III RA patients with induction of OZR were included. Patient background, disease activity, methotrexate (MTX) and prednisolone (PSL) combination rates, and reasons for canceling OZR were evaluated. Results: There were 12 cases of OZR efficacy and 16 cases of invalidity/dropout. The mean age at the start of treatment was 66.7 years for both cases, the mean duration of RA was 18.8 years for the effective cases and 19.3 years for the invalid/dropout cases, and The average number of previous bDMARDs was 2.7 for both cases. Mean SDAI was 14.9 at start and 3.76 at last follow-up for effective cases, and 14.8 at start and 14.9 at last OZR administration for invalid/dropout cases. The mean DAS28-ESR was 3.86 atfirstfirst and 2.81 at the last follow-up for the effective cases, and 3.95 at the first and 4.14 at the last OZR dose for the invalid/dropout cases. The reasons for canceling of OZR were inadequate response in 12 cases, fatigue in 2 cases, skin rash after dose in 1 case, and elevated blood pressure after dose in 1 case. Conclusion: OZR is also effective in Phase III RA patients, but care should be taken in cases of inadequate efficacy and side effects.

P1-034

The efficacy of ozoralizumab using ultrasound in patients with rheumatoid arthritis

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Conflict of interest: None

[objectives] Ozoralizumab is a next-generation anti-tumor necrosis factor-α antibody. In our knowledge, there were few reports in efficacy of ozoralizumab. We evaluated the efficacy of ozoralizumab using ultrasound (US) in patients with Rheumatoid arthritis (RA). [Methods] This study included 7 RA patients who performed US examination before and after ozoralizumab. Synovitis was evaluated using gray scale (GS)-score and Power doppler (PD)-score at 1-5MCP, 1-5PIP, 1-5 MTP, wrist, knee and elbow joint bilaterally. DAS28-CRP, SDAI, CDAI, GS-score and PD-score were evaluated at 0, 4, 12 weeks after ozoralizumab. [Results] Two patients were treated in combination with methotrexate, 5 patients were used ozoralizumab in first b/tsDMARDs. DAS28-CRP at 0, 4, 12 weeks were 3.8±1.4, 2.9±1.0, 2.8±0.8 (p=0.69). SDAI at 0, 4, 12 weeks were 21.0 ±5.6, 11.3±3.2, 10.9±2.8 (p=0.06). CDAI at 0, 4, 12 weeks were 20.6±5.2, 11.1±3.0, 10.8±2.8 (p=0.06). Change of GS scale was from 8.3±2.8 to 1.6±4.2 (p=0.03). Change of GS scale was from 5.1±2.1 to 0.4±2.1 (p= 0.02). US findings improved in all patients in ozoralizumab treatment. [Conclusion] Ozoralizumab was effective on US findings for patients with RA.

P1-035

A case of gout with inflammation at the finger flexor tendon enthesis and urate crystal deposition in the subcutaneous tissue of the finger pad

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Conflict of interest: None

[Case] A man in his 50s with a history of gout in the ankle and knee joints, who developed pain in his fingers, underwent US. On the extensor side the inflammation was observed in four nail beds, and the three-layer structure of the nail was lost, suggesting chronic inflammation of the nail bed. On the flexor side, the inflammation was observed at the all enthesis of the distal phalangeal flexor tendon, and the urate crystal deposition and PD signals were observed in the subcutaneous tissue of the right thumb pad. The urate crystal deposition, swelling, and synovial fluid accumulation were observed in the extensor flexor tendon and around the tendon. In addition, synovial fluid accumulation in the suprapatellar fossa and the medial flexor tendons of the ankle were observed, but the urate crystal deposition was not observed in either the 1st MTP joints. [Conclusion] We have previously reported at this conference that many of the sites where gout develops in large joints coincide with the sites where enthesitis is likely to occur. In this case, there was multiple tendon enthesitis in the fingers, and there was also increased tendon brightness and swelling and synovial fluid accumulation, so it is thought that persistent high uric acid levels can lead to the onset of gout.

P1-036

Configuration of tibial condyle is a risk factor of infrapatellar fat pad inflammation

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Conflict of interest: None

[Objectives] Angle of the tibial condyle posterior rotation was assessed in knees with infrapatellar fat pad pain. [Methods] Lateral knee radiograph at 90 degrees flexion was taken in all patients with infrapatellar fat pad pain since August1st 2023. Angle AW between the anterior cortex of the tibial shaft and the anterior wall of the tibial condyle, and Angle IP between the anterior wall of the tibial condyle and the patellar tenon were measured. Our previous study showed that mean and standard deviation of Angle AW and Angle IP were 14.7±6.0 degrees and 9.4±6.0, respectively. These data was used for the standard value. [Results] Sixty-four knees in 50 cases were assessed. The average age was 48.0 years old. There were 27 right and 37 left knees. The mean and standard deviation were 9.0±4.2 degrees and 5.9±3.5 degrees, respectively. Angle AW and Angle IP were significantly smaller in knees with infrapatellar fat pad pain. Because the infrapatellar space is narrower with smaller Angle IP, the fat pad may easily have inflammation. [Conclusion] The smaller tibial condyle posterior rotation is a risk factor of infra patellar fat pad inframmation.

P1-037

A case of gouty hand arthritis in which arthroscopic surgery was effective in diagnosis and treatment

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Conflict of interest: None

[Case] A 54-year-old man had been treated for gout for 5 years. Uric acid (UA) level had been stable for the past 4 months, but 1 month ago left wrist pain appeared. Steroid injection in the wrist joint was not effective, so he was referred to our department. On initial examination, swelling, redness, and tenderness were observed in his left wrist joint. Blood tests showed a high CRP of 2.84 mg/dl, but no evelation of UA. MRI showed findings of synovial proliferation and effusion in the wrist joint. Treated with the antibacterial agent (Cefalexin) for a week, the swelling was relieved, and CRP was decreased to 1.91 mg/dl. Cefalexin was finished, and NSAIDs was started with local rest, but the arthritis continued, so he was referred to the outpatient rheumatology department. The ultrasound examination showed synovitis in the wrist joint, and arthroscopic surgery was performed for diagnosis and treatment. There were synovial proliferation and white deposits in the joint, and the deposits were identified as UA crystals on speculum examination. The pain started to ease the day after surgery and no pain and recurrence at 6 months postoperatively. [Clinical Significance] Arthroscopic surgery can be minimally invasive in diagnosis and treatment and is useful for prolonged monoarthritis.

P1-038

Five Cases of Polyarthritis with Hyperuricemia

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Conflict of interest: None

Here we report five cases of polyarthritis with hyperuricemia. All patients were male. The average age was 57.4 years (47-70). Four patients had a history of drinking alcohol. Three patients had been diagnosed with hyperuricemia and two patients had been treated before the onset of the disease. Two patients had started taking antirheumatic drugs before their first visit to our hospital. UA was 8.1 mg/dl (4.4-11), CRP was 1.67 mg/dl (0.42-3.38), two patients had positive RF, and one had positive ACPA. US showed double contour sign in three, metastatic uric acid crystals (MSU) crystal aggregation in one, joint synovitis in four, and tenosynovitis in three. We administered urate-lowering drugs to all patients, NSAIDs to four patients, glucocorticoids to three patients (two patients were tapered and discontinued), and the anti-rheumatic drugs that had been administered previously were discontinued in both patients, while one patient was given an anti-rheumatic drug for rheumatoid arthritis. When it is difficult to prove tophus or MSU crystals, taking a medical history is important for diagnosis, but images can also be helpful. In particular, RF/ACPA-positive patients need to be monitored for changes in joint symptoms even after their uric acid levels have stabilized.

P1-039

Changes in Spinal Balance, Bone Density, and Bone Metabolic Markers Including Upper Cervical Spine in 39 Patients Treated with Tofacitinib for 5 Years

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Conflict of interest: Yes

[Objectives] In this study, we investigated the relationship between TOF treatment and spinal balance and osteoporosis in 39 rheumatoid arthritis patients treated with tofacitinib (TOF) for 5 years, based on changes in patient backgrounds over the 5-year period after treatment. [Methods] The subjects were 39 RA patients who started receiving TOF between December 2013 and May 2018 and continued for 5 years. Patient background at the start of treatment was as follows: average age: 67.5 years, disease duration: 15.4 years, Stage: 3.1, Class: 2.0, 20 patients taking PSL (average dose: 4.6 mg/day), disease activity DAS28ESR: 4.4, DAS28CRP: 4.1, CDAI: 17.7, SDAI: 20.0, SVA: 60.3 mm, ADI: 1.3 mm, Ranawat value: 14.6 mm, femoral neck YAM value: 75.9%, urinary NTX: 51.1nM BCE/mM/Cre, eGFRcys: 70.6 mL/min/1.73 m^2. [Results] After 5 years of treatment with TOF, disease activity improved to remission to low disease activity with mean DAS28ESR: 2.8, CDAI: 3.7, SDAI: 3.9, mean SVA: 65.3 mm, ADI: 1.4 mm, Ranawat value: 13.7 mm, YAM value: 79.1%, urinary NTX: 33.2 nM BCE/ The mean dose of PSL was 2.2 mg/day in 5 patients. [Conclusion] The results suggest that the continuous treatment with TOF may improve spinal balance, bone mineral density, and bone quality in patients whose disease activity was controlled.

P1-040

Study of continuation and fracture rates and treatment efficacy of semiweekly teriparatide in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The two-year continuation rate, treatment efficacy, and fracture rate when rheumatoid arthritis (RA) patients with osteoporosis were treated with semiweekly teriparatide (TPTD) were compared with non-RA patients. [Methods] We retrospectively investigated patients treated with TPTD between December 2019 and September 2022 at our hospital. 16 RA patients and 80 non-RA patients were treated with TPTD. [Results] The 2-year continuation rate was 68.8% for RA patients and 28.8% for non-RA patients. The reasons for discontinuation in non-RA patients were adverse events such as feeling unwell (31.2%), on the other hand, in non-RA patients were adverse events (30.1%), injection difficulty (8.8%), onset of other diseases (3.8%), and others such as transfer to a new doctor or admission to a facility (17.5%). After 2 years, the LSBMD change rate increased 1% in RA patients and 6.9% in non-RA patients; the HBMD change rate was -4.2% in RA patients and 6.3% in non-RA patients. During treatment, 13 RA patients had 0 fracture and 29 non-RA patients had 1 fracture during the treatment period. [Conclusion] RA patients were able to continue treatment longer with TPTD and No fractures were observed. TPTD was considered effective in RA patients.

P1-041

Safety Analysis of Switching from Denosumab to Zoledronic Acid in Rheumatoid Arthritis Patients

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Conflict of interest: None

[Objectives] Discontinuation of denosumab causes rapid bone mineral density loss and increases fracture risk. Long-term use increases risk of atypical fractures and osteonecrosis of the jaw. While switching to bisphosphonates is recommended, safety data is lacking. We aimed to verify if denosumab can be safely discontinued by switching to zoledronic acid in rheumatoid arthritis patients. [Methods] We analyzed records of nine rheumatoid arthritis patients who switched from denosumab to zoledronic acid at our clinic between October 2022 and October 2024. [Results] All subjects were female, with mean age 77.9±5.2 years. Mean YAM values for lumbar spine and proximal femur were 85.8±15% and 67.9±6.3%. Median bone metabolism markers were: TRACP-5b 256.5 mU/dL (IQR: 191.5-429.5), total P1NP 48.45 ng/mL (IQR: 19.425-69.9), 25 (OH)D 17.75 mg/mL (IQR: 14.7-22.225). Three patients had previous fractures, five had glucocorticoid use (mean maximum prednisolone: 9.0±7.3 mg/day). No new fractures occurred during observation. [Conclusion] Switching from denosumab to zoledronic acid may enable safe discontinuation in rheumatoid arthritis patients. However, continued follow-up is needed due to short observation period and small sample size.

P1-042

Efficacy of romosozumab as sequential therapy for bisphosphonate in glucocorticoid-induced osteoporosis

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Conflict of interest: None

[Objective] To evaluate the efficacy of romosozumab (ROMO) as a sequential therapy for bisphosphonate (BP) in glucocorticoid-induced osteoporosis (GIOP). [Methods] Patients with rheumatic diseases receiving BP and prednisolone 5 mg/day or more for at least 6 months were prospectively enrolled and either switched from BP to ROMO (ROMO group) or continued on BP (BP group). We measured bone mineral density (BMD) of the lumbar spine (L2-L4), femoral neck (FN) and total hip (TH) every 6 months and bone turnover markers every 3 months. [Results] Six patients in the ROMO group and 24 in the BP group were enrolled. The mean percent change of the lumbar spine BMD from baseline at 12 months was statistically higher in the ROMO group (ROMO: 12.5±10.3%, BP: 1.8±1.1%). The mean percent change in BMD of the FN and TH tended to be higher in the ROMO group (FN: 2.1±1.6%, 0.6±1.7%; TH: -0.02±3.7%, -2.6±1.1%). Serum P1NP level, a bone formation marker, increased in the ROMO group. Serum TRACP-5b, a bone resorption marker, decreased in the ROMO group and urine pentosidine, a bone quality marker, remained decreased in the BP group. No new fractures occurred. One patient in the ROMO group had a cerebral infarction. [Conclusion] ROMO as a sequential therapy for BP was suggested to be effective for GIOP.

P1-043

A case of the combination of evocalcet and romosozumab was effective in increasing bone mineral density in a patient with conservative treatment of primary hyperparathyroidism

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Conflict of interest: None

78-year-old woman with loss of consciousness, blood tests showed hypercalcemia. Intact PTH elevation and nodules on ultrasound and accumulation at the same site on 99mTc-MIBI scintigram were observed, leading to a diagnosis of primary hyperparathyroidism (PHPT). Conservative treatment was decided and evocalcet was started. Bone density T-score of the femoral neck was -3.7, alendronic acid was started based on the diagnosis of osteoporosis. One year after diagnosis, the T-score decreased to -4.1, and alendronic acid was replaced with romosozumab. One year after replacement, the T-score increased to -3.1. The patient progressed without complications of hypocalcemia. **«Clinical Significance»** PHPT is a disease in which parathyroid hormone levels are persistently elevated and bone resorption exceeds bone formation, resulting in a decrease in bone density. In this case, the patient was treated conservatively, but evocalcet and a bisphosphonate, which inhibits bone resorption, did not prevent the loss of bone density. Therefore, the combination of evocalcet with lomosozumab, which inhibits bone resorption and promotes bone formation, was shown to increase bone density. The use of romosozumab may be an option for the treatment of osteoporosis associated with conservative treatment of PHPT.

P1-044

A case report of the rheumatoid patient who got delayed bone union of periprosthetic knee fracture cured by Abaloparatide

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Conflict of interest: None

A-73-year-old woman fell at home and felt left thigh pain, then she was taken to our hospital by ambulance. She was diagnosed with periprosthetic knee fracture, and was admitted to our hospital. She was diagnosed with rheumatoid arthritis (RA) at the age of 51, and she had left total knee arthroplasty (TKA) at the age of 64 due to knee destruction by RA. At the time of her fracture, she was being treated for RA with methotrexate 6 mg/week and Upadacitinib 7.5 mg/day. She underwent open reduction & internal fixation (ORIF), but 7 months after surgery, there was no callus formation of fracture site in x ray, and she felt thigh pain. We suspected delayed bone union, then we administered Abaloparatide (ABL) to her for the purpose of bone union promotion. As a result, callus formation could be found 10 months after surgery, and she felt no thigh pain. 14 months after surgery, finally, she achieved good bone union of fracture site. [Clinical Significance] ABL is expected to have the effect of promoting bone healing, like Teriparatide. But there are few clinical reports of ABL's promoting bone healing effect, and there is no report on the use of ABL in RA patients. This is the first clinical report that RA patient achieved bone heal-

ing by ABL promotion.

P1-045

A case of a patient with RA who presented with an old ulnar fracture with characteristics of atypical fracture that occurred while on long-term bisphosphonate medication

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Conflict of interest: Yes

[Background] There have been scattered reports of atypical fractures of the ulna as well as the femur in patients on long-term bisphosphonate (Bp) therapy. We report here a case of suspected atypical fracture of the ulna in a patient with RA taking long-term bisphosphonate (Bp). [Age/Sex] 75 years old/ female [Chief complaint] Right elbow joint pain. [History of illness] The patient had been followed up by our department for about 25 years for RA with Stainblocker class 3 stage 3. He had no history of trauma, but had been aware of right elbow pain and swelling for 3 months. Imaging tests indicated a right ulna fracture, and he was referred to our department for surgical treatment. Simple radiographs showed a fracture of the right proximal ulna, osteosclerosis of the margins of the fracture and dislocation of the radial head. The patient had been taking Alendronic acid for about 15 years. The diagnosis was a pseudarthrosis of the right ulnar diaphysis, an old atypical fracture, and dislocation of the right radial head. The patient underwent reflesh of fracture site and plate fixation. Pain was improved and fusion was achieved. [Conclusion] It had many characteristics of atypical fractures, and we felt that continued Bp administration should be strictly avoided.

P1-046

Bilateral atypical femur fracture in a patient with breast cancer taking zoledronic acid and denosumab: a case report

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Conflict of interest: None

[Objective] The purpose of this case report is to present a case of atypical femoral fractures that occurred in a patient with breast cancer bone metastases who received long-term zoledronic acid treatment, and to raise awareness about the potential risks associated with this therapy. [Methods] A retrospective analysis was conducted on the clinical course of a 54-year-old female patient. The patient was diagnosed with stage IV breast cancer 8 years prior and received chemotherapy and zoledronic acid treatment for bone metastases. [Results] Fifty-seven months after initiating zoledronic acid treatment, the patient suffered an atypical femoral fracture in her right femur and underwent surgery. Twenty months later, the patient developed another atypical femoral fracture in her left femur and underwent intramedullary nail fixation. These fractures were suggested to be potentially associated with long-term use of zoledronic acid. [Conclusion] The use of zoledronic acid and denosumab in patients with bone metastases caused by breast cancer should be done cautiously, considering the risk of atypical femoral fractures. Long-term use of bone resorption inhibitors carries potential risks, and it is important to carefully evaluate the benefits and risks for individual patients.

P1-047

Elucidation of the mechanism of angiogenesis in the synovial membrane in knee osteoarthritis

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Conflict of interest: None

[Objectives] To investigate the mechanism of angiogenesis in the synovial membrane in OA. [Methods] Joint fluid, synovial membrane, and cartilage were collected from knee OA cases, and plasma was also collected from some cases. Control synovial membrane and cartilage were collected from autopsy cases. Cartilage tissue was subjected to a load equivalent to that applied in vivo in PBS, and the released factors were analyzed. Gene expression of VEGF-A and angiopoietin-1 and 2 (ANGPT1 and 2) in synovial tissue was examined, and protein levels in synovial homogenates, joint fluid, and plasma were measured. [Results] VEGF-A was abundantly released from OA cartilage by loading. The expression of ANGPT1 and 2 was significantly upregulated in OA synovium, but the expression of VEGF-A was not significantly different from that in control. VEGF-A was present in the synovial fluid and was abundantly extracted from synovial tissue. While the concentration of ANGPT2 was similar in plasma and synovial fluid, the concentration of ANGPT1 in joint fluid was about 1/10 of that in plasma. [Conclusion] VEGF-A released from cartilage accumulates in the synovial membrane via the joint fluid, and angiogenesis occurs in the synovial membrane by the action of VEGF-A and ANGPT2 in the joint fluid.

P1-048

Knee flexion and extension strength increases in the first year after total knee arthroplasty and correlates with an increase in lower extremity skeletal muscle mass

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Conflict of interest: None

[Objectives] Functional improvement for osteoarthritis of the knee (KOA) after total knee arthroplasty (TKA) involved in knee muscle strength. We evaluated the relationship between muscle strength (flexion + extension) and lower extremity skeletal muscle mass before and after surgery. And we also examined the influence of metals implants in the body. [Methods] Patients who underwent unilateral TKA for KOA at our hospital were measured lean mass (LM) by DXA of the lower extremities and muscle strength before and 1 year after surgery. LM were individually corrected for height (SMI). [Results] 125 patients (mean age: 75.2; female: 98; 89 had metal) were included. The mean LM before and after surgery was 6059.8/6190.4 g on the operative side ($p<0.01$, paired t-test) and 6301.4/6238.6 g on the non- ($p=0.32$), with significant improvement on the operative side. Muscle strength on the operative side increased significantly to 236.7/281 N (pre/postoperative: $p<0.01$). There was a positive correlation between the increase in muscle strength on the operated side and the increase in SMI ($p=0.014$, Spearman's rank correlation coefficient). [Conclusion] SMI and muscle strength on the operative side increased one year postoperatively compared to the pre, and the two were significantly correlated.

P1-049

Factors associated with gait speed 2 years after total knee arthroplasty in patients with knee joint disorders

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Conflict of interest: None

[Background and Objectives] Knee joint disorders reduce mobility. In this study, we aimed to measure the walking speed of patients who underwent primary TKA two years after surgery and to examine the factors that are most correlated with this. [Subjects and Methods] We investigated the relationship between basic attributes such as age and gender, walking pain VAS, clinical knee function assessment (KSS), skeletal muscle mass of the limbs (DXA method), quadriceps muscle strength, and range of motion. [Results and Discussion] The subjects were 149 people (123 women, average age 75.5 years). Walking speed two years after TKA (average 2.01 m/s) improved compared to preoperative speed (average 0.91 m/s), but there was no significant difference ($P=0.2$; paired t-test). In addition, a

multivariate analysis was performed with walking speed 2 years after surgery as the objective variable and age, sex, VAS for pain during walking, KSS, skeletal muscle mass of the limbs, quadriceps strength, and range of motion as dependent variables. As a result, quadriceps strength (extension) was significantly and independently associated with walking speed ($P < 0.01$). [Conclusion] Walking speed 2 years after TKA improved compared to preoperative, but the difference was not significant.

P1-050

A Case of Rapidly Progressive Peripheral Vasculitic Neuropathy Associated with Systemic Lupus Erythematosus

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Conflict of interest: None

[Case] A 48-year-old woman presented to our hospital with a history of recent cerebral infarction of unknown embolic origin and ongoing fever. Over the past three days, she had developed progressive lower limb weakness. On examination, she exhibited distal muscle weakness, accompanied by sensory deficits in the distal extremities. Laboratory investigations revealed low complement levels, positive anti-dsDNA antibodies, and pleural effusion, consistent with systemic lupus erythematosus (SLE). Intravenous steroid pulse therapy was initiated, but as neurological symptoms worsened, plasma exchange and intravenous cyclophosphamide were administered. Nerve conduction studies indicated progressive Wallerian degeneration, suggesting irreversible nerve damage. High-dose intravenous immunoglobulin therapy was administered, but no improvement was observed, leading to the patient's transfer to a rehabilitation facility. [Discussion] The prevalence of peripheral neuropathy associated with SLE is reported to range from 2-10%, with polyneuritis being the most common presentation. Early diagnosis and intervention are crucial for managing this condition. However, as illustrated in this case, despite prompt treatment, the disease can progress rapidly, leading to significant neurological deficits.

P1-051

A case of systemic lupus erythematosus started with asymptomatic protein-losing enteropathy

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Conflict of interest: None

41-year-old woman presented with eyelid edema for a half year. The albumin level dropped gradually without malnutrition and liver disfunction related to albumin synthesis, and loss of albumin was the most suspected. There were no gastrointestinal symptoms and nephritis or other renal problems from urinalysis causing loss of albumin. Systemic lupus erythematosus (SLE) was suspected from decrease of leukocyte and lymphocyte, positive antinuclear and anti-ds-DNA antibodies, hypocomplementemia. A gastrointestinal bleeding scintigraphy revealed protein leakage from the stomach, leading to the diagnosis of SLE with protein-leaking gastroenteropathy (PLE). The treatment of methylprednisolone 60 mg/day and hydroxychloroquine 200/400 mg/every other day were started. The albumin level improved significantly after 9 weeks of treatment, and the re-examined scintigraphy showed the disappearance of protein leakage after 12 weeks. Here we reported a case of SLE started with asymptomatic protein-losing enteropathy. It is reported a PLE with lesions in the upper gastrointestinal tract presents absence of gastrointestinal symptoms and results to be difficult to diagnose. We reported a case of SLE with asymptomatic PLE treated with steroids successfully.

P1-052

A case of systemic lupus erythematosus complicated by Scedosporium infection with brain abscess secondary to herpes zoster vesicular lesions

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Conflict of interest: None

[Case] A 41-year-old female diagnosed with systemic lupus erythematosus developed macrophage activation syndrome, and administered prednisolone (PSL) 60 mg/day with cyclosporine and mycophenolate mofetil following steroid pulse therapy. However, she did not achieve remission, PSL 15 mg/day or more was continued. After 6 months, she developed cellulitis and ulcers with blisters on her leg and was admitted to dermatology. Enterococcus faecium and herpes zoster virus antigen were detected from the ulcer with blisters, so we initiated antibiotics and acyclovir. From day 7, new papules and pustules were observed, and the escalation of acyclovir dose had little efficacy. On day 14, acute weakness of her right lower limb was observed, and MRI showed brain abscess. Scedosporium apiospermum was detected both from drainage fluid of brain abscess and pustules, and we administered voriconazole. Brain abscess was gradually shrank and skin lesions were recovered. She was discharged on day 44 with the dose of PSL tapered to 10 mg/day. [Clinical Significance] Scedosporium is classified as rare deep-seated mycosis, and immunosuppressed states are thought to be arisk factor. This case suggests that highly immunosuppressed state and pre-existing sources of infection may cause Scedosporium infections.

P1-053

The risk factors for relapse and infection and the relationship between those events and osteoporotic fracture occurrence in patients with long-term SLE

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Conflict of interest: None

[Objectives] In patients with a long disease duration, glucocorticoid (GC) dosage reduction with aggressive immunosuppressive drug can be often difficult due to clinical inertia. This study aims to clarify the risk factors for relapse and infection and the relationship between those and osteoporotic fractures in patients with a long disease duration of SLE. [Methods] This retrospective observational study included SLE patients consecutively treated from 2016 to 2023. Clinical data were investigated using electronic medical records. [Results] A total of 170 SLE patients were included. GC dosage decreased and immunosuppressant use increased. Relapse was observed in 12%, infection in 18%, and osteoporotic fracture in 7%. Relapse patients were younger than non-relapse patients, had higher rates of immunosuppressant use, and had more osteoporotic fractures. Compared with non-infection patients, infection patients were unable to reduce PSL by 2 mg or more, and more cases of osteoporotic fractures were observed. [Conclusion] In SLE patients with a long history of disease, there are cases further immunosuppressive treatment is required to prevent relapse, GC dosage reduction is effective to prevent infections, and decrease of both events may also lead to a reduction of osteoporotic fractures.

P1-054

A case of Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) secondary to systemic lupus erythematosus (SLE) caused by COVID-19 infection

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Conflict of interest: None

A 17-year-old male contracted COVID-19 in mid-January of year X,

recovering with symptomatic treatment. Two or three weeks later, he experienced nosebleeds and hematuria. A school checkup revealed 3+ blood in urine, 3+ protein, and purpura, leading to hospitalization in May. Diagnosis showed fever (38.3°C), CH50 14.0 U/mL, antinuclear antibody 80-fold, anti-dsDNA antibody >400/mL, and positive anti-Sm antibody, indicating SLE. Coagulation tests revealed PT activity 26%, factor II activity <6.3%, APTT 126.4 seconds, and positive lupus anticoagulant (LA), diagnosing LAHPS. Treatment with steroid pulse therapy, prednisolone, and cyclophosphamide resolved bleeding. PT and APTT normalized after two weeks, allowing renal biopsy, which indicated lupus nephritis type IV (A)+V. Renal function and proteinuria normalized after three months. LAHPS, a rare condition causing bleeding due to decreased PT activity despite LA positivity, often affects young children post-viral infection. It may resolve without treatment, but immunosuppressive therapy is used when associated with collagen diseases like SLE. This case is noteworthy as SLE, lupus nephritis, and LAHPS developed almost simultaneously post-COVID-19 infection, suggesting a potential link and making it a valuable case report.

P1-055

Characteristics and clinical practice of systemic lupus erythematosus (SLE) patients with thrombotic microangiopathy (TMA) in Japan: a case series study

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Conflict of interest: Yes

Objective: Atypical hemolytic uremic syndrome (aHUS) is a thrombotic microangiopathy (TMA) caused by excessive activation of the complement pathway, often with genetic abnormalities. Systemis Lupus Erythematosus associated TMA (SLE-TMA) is rare and has a poor prognosis, and is assumed to be aHUS-like. Methods: Clinical data from SLE-TMA patients (pts) between Jul 2020 and Dec 2023 were collected. Variants in the alternative pathway genes were examined. SLE without TMA (SLE-nonTMA) served as a control group. Results: 9 SLE-TMA and 11 SLE-non TMA pts were included in this study. The median (range) age, duration of SLE, and SLEDAI score of the SLE-TMA pts were 39 (15-63) years, 6 (0.1-21) years, and 18.5 (12-22), respectively. 8 pts with SLE-TMA received a treatment for TMA (5 pts received ≧2 therapies). 3/9 pts achieved complete remission, 5 pts did not achieve an improvement in renal function, and 1 pt was lost to follow-up. Rare missense variants were found in 6/9 SLE-TMA pts (3 had variants in 2 genes) and in 5/11 SLE-nonTMA pts. Conclusion: Variants in the alternative pathway genes were found in both groups, but variants were found in ≧2 genes in SLE-TMA pts. A combination of complement gene variants may be associated with TMA risk.

P1-056

A case of SLE-associated pancreatitis differentiated from drug-induced pancreatitis

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Conflict of interest: None

Case: In February X, 20s female developed fever and swelling of both eyelids and parotid glands, and was suspected to have Sjogren's syndrome due to strong positivity for anti-SS-A/B antibodies. Her condition temporarily resolved with antimicrobial treatment, but she developed fever again in April. In May, skin rash on both palms, arthralgia, pancytopenia, hypocomplementemia, positive urine protein, and positive anti-dsDNA antibodies were also found. She was diagnosed with systemic lupus erythematosus (SLE) and treatment was started with prednisolone (PSL) 40 mg /day (1 mg /kg /day). On the third day of treatment (DAY 3), abdominal pain appeared and was diagnosed as acute pancreatitis. Lupus pancreatitis or PSL-induced pancreatitis was considered, and PSL was changed to dexamethasone 6 mg, but the pancreatitis continued to worsen. Methylprednisolone semi-pulse therapy was administered on DAY8-11, and since then, SLE and pancreatitis have been improving well with post therapy of PSL, hydroxychloroquine and mycophenolate mofetil. Discussion: SLE-associated pancreatitis is often problematic to differentiate from glucocorticoid-induced pancreatitis. This report presents SLE-associated pancreatitis with some literature review.

P1-057

Significance of several kidney biopsy in treatment strategy of lupus nephritis

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Conflict of interest: None

[Objectives] Lupus nephritis is frequent exacerbated and requires a renal biopsy to determine the course of treatment. Therefore, we examined the impact on the treatment policy in case where a kidney biopsy was performed multiple times. [Methods] We retrospectively examined 384 biopsies performed in patients with SLE between 1975-2022, of which 106 performed two or more biopsies. We examined 42 studies since 2007. [Results] Of the 106 kidney biopsies performed two or more times, 40 were different from the previous pathological diagnosis. In 31 cases, 30 patients had enhanced treatment after the second biopsy, and in 30 of these cases, there was a change in pathological diagnosis. Of the treatment-enhanced patients, 14 had a PSL of 10 mg or more after 6 months, and 10 of them had not been able to reduce their dose below 10 mg after 1 year. On the other hand, all patients who received biologics after biopsy reinduction had a PSL of 10 mg or less by 12 months. [Conclusion] Multiple doses may be of high importance in determining treatment in refractory lupus nephritis. There were cases where steroids were required for a long time even if the treatment was enhanced, but since it was possible to reduce the amount of PSL in the case of biologics, the treatment content should also be considered.

P1-058

A case of systemic lupus erythematosus and antiphospholipid antibody syndrome with chorea as the initial symptom

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Conflict of interest: None

[Case] A 76-year-old woman presented with gait disturbance and dyskinesia for six years. Three months ago, she was referred to our hospital, where a magnetic resonance imaging (MRI) of the brain showed only small chronic ischemic changes. 2 weeks ago, she was admitted to our hospital. She presented dance-like involuntary movements. Systemic lupus erythematosus (SLE) was suspected due to positive anti-dsDNA IgG antibody and hypocomplementemia. The cerebral fluid (CSF) examination revealed no abnormalities, and the IL-6 of CSF was not elevated. Antiphospholipid antibody syndrome (APS) was strongly suspected due to positive lupus anticoagulant, antiphospholipid antibody. The patient was started on methylprednisolone pulse therapy and initiated on aspirin, followed by prednisone 45 mg, which showed rapid improvement in involuntary movements. [Clinical Implication] Chorea is a rare neurological complication with CNS lupus and APS and may be the first symptom. Both ischemic and immunologic mechanisms have been postulated. In this case, immunosuppressive treatment quickly normalized the APTT, and antibody titers of antiphospholipid antibodies decreased. The immune response

against the central nervous system mediated by antiphospholipid antibodies might play a major role.

P1-059

Three cases of systemic lupus erythematosus (SLE) in males with elderly onset

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Conflict of interest: None

[Objectives] Epidemiologically, SLE is more common in young women, with a male-to-female ratio of 1:8. We report three cases of first-episode SLE in elderly men. [Methods] Case report [Results] Case: (1) 72-year-old male. Chief complaint: polyarthralgia, edema of both lower limbs, convulsions, and impaired consciousness. Laboratory data: ANA 1280X, positive for anti-Sm Ab, hypocomplementemia, thrombocytopenia, positive urine protein, multiple abnormal signals in cerebral cortex and subcortex on MRI. (2) 75-year-old male. Chief complaint: polyarthralgia and shortness of breath. Laboratory data: ANA640X, positive anti-dsDNA Ab, hypocomplementemia, pleurisy, pleural effusion. (3) 85-year-old male. Chief complaint: polyarthralgia, leg edema. Laboratory data: ANA1280X, positive for anti-dsDNA Ab, positive for urinary protein. [Conclusion] The SLE GL was developed based on data from young women, who have a high incidence of SLE, and was not designed for the treatment of elderly men. Therefore, it is necessary to avoid excessive immunosuppressive treatment with reference to vasculitis, which frequently occurs in the elderly.

P1-060

A case of central optic lupus with intracranial hypertension

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Conflict of interest: None

A 52-year-old woman with systemic lupus erythematosus (SLE), scleroderma, and Sjögren's syndrome reported a sensation of "her brain being sucked in" in March of Year X, followed by diplopia in April. An ophthalmologist suspected optic neuritis and referred her to Hospital B, where MRI showed papilledema and bilateral optic nerve sheath enlargement, suggesting perineuritis. A lumbar puncture indicated elevated intracranial pressure (over 30 mmHg) but normal cerebrospinal fluid protein levels and cell counts. Due to suspected intracranial hypertension related to SLE, she was admitted to our department. Treatment began with steroid pulse therapy for central nervous system lupus, followed by a daily dose of 20 mg prednisolone. An IgG index of 1.128 indicated immune involvement, leading to intravenous cyclophosphamide therapy. Acetazolamide and topiramate were prescribed for intracranial hypertension. Although her diplopia improved and the IgG index showed positive changes, her intracranial pressure remained poorly controlled, requiring ongoing management. As this case shows, when diplopia and papilledema are present, it is important to suspect intracranial hypertension and proceed with a thorough examination, and to check for symptoms seen in SLE and elevated autoantibodies.

P1-061

A case of systemic lupus erythematosus (SLE)/mixed connective tissue disease (MCTD) in which multiple peripheral microscopic hematoma occurred during follow-up

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Conflict of interest: None

[Case] 29-year-old female [Chief Complaint] Pain in both palms and both ears [PHI] Noticed swelling and pain in the fingers of both hands that lasted for 1 hour in the morning since X-4 months. x-3 months The patient was previously referred to our department. Swelling of the entire fingers of both hands, ANA1280 times, anti-DNA, RNP, SS-A, CL, β2GP1 and LAC positive, C3 38, C4 3.7, and a diagnosis of SLE/MCTD with APS was made. For the primary prevention of hand symptoms and thrombosis, oral administration of PSL7.5 mg and aspirin100 mg was started. During a regular outpatient visit for x-1 weeks, a painful eruption was observed on both palms and ears and a painless aphthae on the hard palate. There was no fever, elevated CRP, elevated ESR, proteinuria, or hematuria. It was determined that the rash was caused by SLE/MCTD, and the dose was increased to PSL 30 mg. One week later, the oral aphthae disappeared, but the skin rash worsened and it was determined that the thrombotic pathology caused by APS was the main cause rather than the inflammation caused by SLE/MCTD. A skin biopsy was performed and warfarin was started, and the skin rash disappeared. Dermatopathological examination revealed no evidence of vasculitis, but fibrin thrombus was found in dermal capillaries and arterioles.

P1-062

A case of refractory pericarditis and pleuritis of systemic lupus erythematosus requiring multi-target therapy for remission induction

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Conflict of interest: None

A 39-year-old woman visited her local doctor in July due to arthralgia in her fingers. In the same month, she delivered her second child by Cesarean section. She was discharged from the hospital, despite that she had been experiencing dyspnea and chest discomfort since the delivery. After discharge from the hospital, she revisited her local doctor due to persistent joint pain. She was diagnosed with rheumatoid arthritis and started on salazosulfapyridine. In August of the same year, she developed fatigue and revisited her local doctor. She was suspected to have pericarditis and was admitted to the Department of Cardiology and was started treatment with ibuprofen and colchicine. As her condition did not improve, she was referred to our department. The patient was diagnosed with SLE due to fever, serositis, arthritis, positive antinuclear antibody, and positive anti-dsDNA antibody. The patient did not respond well to initial treatment, and hydroxychloroquine, tacrolimus, mycophenolate mofetil, NSAIDs, and colchicine were added sequentially, which led to successful tapering of steroid dose. Collectively, we have experienced a refractory case in which pleural effusion was refractory to high-dose steroid therapy. We report this case with a review of the literature.

P1-063

Clinical characteristics of three cases of VEXAS syndrome

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Conflict of interest: None

[Background] VEXAS syndrome is attracting attention as an acquired autoinflammatory disease. We investigated the clinical symptoms and treatment of three cases of VEXAS syndrome at our department. [Methods] We examined the clinical features of three cases of VEXAS syndrome treated at our department, as well as histological examinations of the rash, genetic testing, and the effectiveness of treatment. [Results] 1) All three cases were men aged 70 years or older (71-76 years old) and presented with fever, ear swelling, and rash. In two cases, the rash appeared before the ear swelling. 2) Blood tests showed macrocytic anemia in all cases, and vacuolar changes in myelocytes and erythroblasts in the bone marrow in one case. 3) Genetic tests showed *UBA1* c. 121A>C p. Met41Leu in two

cases and c. 122T>C p. Met41Thr variant in one case. 4) Histological examination of the rash revealed neutrophilic dermatosis in two cases and erythema in one case. 5) Corticosteroids were started at 30 mg in all three cases, and the treatment was very effective in treating fever, ear swelling, and rash. [Conclusion] VEXAS syndrome has characteristic clinical symptoms and laboratory findings, and early diagnosis is necessary.

P1-064

A case with novel NBAS gene mutations suspected of hemophagocytic lymphohistiocytosis

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Conflict of interest: None

[Introduction] Neuroblastoma amplified sequence (NBAS) is a protein involved in reciprocal transport between the endoplasmic reticulum and Golgi apparatus, and its Sec39 domain mutations cause infantile liver failure syndrome 2 (ILF2) and c-terminal mutations cause SOPH syndrome, and have been reported to complicate primary hemophagocytic syndrome. [Case] One year and 5 month old girl was brought to the emergency room with fever, vomiting, and diarrhea, as well as seizures and loss of consciousness. Marked elevation of hepatic enzymes and amylase, hyperammonemia and hypoglycemia were observed. At age 5 years, she had fever and vomiting, neutropenia, thrombocytopenia, increased atypical lymphocytes, elevated hepatic enzymes, high serum ferritin and high sIL-2 receptor. Both two episodes improved after several days of fluid management. Exome analysis reveals a novel heterocomplex variant of c. 7102C>T and c. 2727G>A in the *NBAS* gene. Thereafter, there was no evidence of liver damage at the time of fever, which was typical for ILF2. [Clinical Significance] To improve the prognosis of ILF2, it is important to control liver failure by therapeutic intervention in the early stage of fever. In patients with HLH associated with severe liver injury, this disease should be differentiated.

P1-065

Successful treatment with tofacitinib for juvenile spondyloarthris: a case report

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Conflict of interest: None

INTRODUCTION: The efficacy of ubatacitinib (UPA) in adult spondyloarthritis has been reported, but there is no report of its response in juvenile spondyloarthris (jSpA). Case: An 18-year-old female with persistent pain in her lower limbs and knees since the age of 7 years, diagnosed as juvenile idiopathic arthritis (JIA) at the age of 10 years. She was administered methotrexate and adalimumab, but the joint pain in her extremities gradually flared up. At age 16 she switched from adalimumab to abatacept (ABT), which was ineffective. The pain was more severe in the lumbar region, and the diagnosis was changed to jSpA after MRI findings of sacroiliitis. She was switched from ABT to UPA (15 mg/day) due to complications of atopic dermatitis. After initiation, pain and skin symptoms improved markedly, PSL was discontinued, and MRI MRI revealed subsidence of inflammation around the sacroiliac joint. Discussion: jSpA is a rare disease that is included in the adherence-associated arthritis type in the JIA classification. In this case, the diagnosis was triggered by the patient's back pain that increased after switching to ABT. Although csDMARDs and TNF inhibitors are the common treatment for jSpA, UPA may be an effective option for patients who do not respond to conventional therapy.

P1-066

A case of a 16-year-old boy with chronic recurrent multifocal osteomyelitis who is suspected of mycosis fungoides

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Conflict of interest: None

Case: The patient had bilateral thigh pain since the age of 7 years. At the age of 13 years, MRI scan showed multiple osteomyelitis. The patient was started on NSAIDs but symptoms did not improve, so glucocorticoid (GC), methotrexate (MTX) and bisphosphonate (BP) were used in combination and symptoms improved. The patient was then started on adalimumab (ADA) due to difficulties in reducing PSL. PSL and BP were discontinued after one year and MTX after two years; The patient had a good course with ADA alone, but at the age of 15 years, a skin rash appeared on the bilateral thighs and ankles, and psoriasis was suspected. However, a skin biopsy revealed MF and the ADA was discontinued. the skin symptoms did not improve after discontinuation of ADA, and pain developed in the lumbar back and hip joints, and MRI showed findings of osteomyelitis, leading to suspicion of recurrent CRMO. NSAIDs and PSL were restarted, but analgesic management was inadequate, and secukinumab and BP were started. Since then, the cutaneous and osteomyelitis symptoms have tended to improve. Discussion: MF is a very slowly progressing T cell malignant lymphoma of primary cutaneous origin; its association with various biological agents in the development of MF has been reported and is discussed.

P1-067

A Case of Malignant Lymphoma with Monoclonal Protein Exhibiting Rheumatoid Factor Activity, Difficult to Differentiate from Rheumatoid Arthritis

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Conflict of interest: None

A 78-year-old woman presented for evaluation of persistent elevated CRP levels. She had been diagnosed with rheumatoid arthritis (RA) 30 years prior and treated with bucillamine. After undergoing a ureteral stone removal procedure, her CRP levels remained elevated despite antibiotic treatment. Laboratory tests revealed elevated CRP (9.59 mg/dL) and RF (2322 IU/mL), leading to suspicion of RA exacerbation. However, physical examination showed no joint swelling or tenderness, and imaging revealed no bone changes. Joint ultrasound did not indicate synovial proliferation, leading to a mismatch between the clinical presentation and test results. Further CRP testing suggested a false elevation, and elevated serum IgA and IgA-λ-type monoclonal protein were identified. A CT scan revealed left axillary lymphadenopathy, and biopsy confirmed low-grade B-cell lymphoma. Class-specific RF tests showed elevated IgM and IgA-RF. Treatment with rituximab led to a decrease in CRP, IgA, and RF levels. This case suggests that the monoclonal protein had RF activity, resulting in a false-positive CRP and necessitating differentiation from RA. This case highlights the importance of reassessing abnormal test results when they do not align with clinical observations and has educational significance.

P1-068

Two cases of seronegative late-onset rheumatoid arthritis by synovial pathology at the time of arthroplasty

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Conflict of interest: None

[Objectives] More than 50% of patients with late-onset rheumatoid arthritis (LORA) are considered seronegative. We report two cases in which rheumatoid arthritis was diagnosed by pathologic examination of synovial tissue at the time of joint replacement surgery. [Methods] Case 1: 78-year-old woman, chief complaint of right shoulder and left hip joint pain, started taking PSL for suspected PMR due to high CRP level and ACPA/RF negative results. Left THA was performed. Intraoperative pathology of the synovial membrane showed evidence of rheumatoid arthri-

tis. She was started on MTX. Case 2: A 76-year-old woman presented with left knee arthralgia, negative for ACPA and RF. She was started on PSL, but her left knee joint destruction progressed rapidly over a 6-month period and she underwent left TKA. As in case 1, the diagnosis of RA was confirmed and treatment was initiated. In the two cases diagnosed as non-RA, one was diagnosed as idiopathic arthropathy and the other as crystal-induced arthritis. [Conclusion] LORA often presents subacutely or acutely in large joints and is often seronegative, so it may not meet the 2010 ACR/EULAR classification criteria. Although there are no specific histologic findings for RA, pathologic diagnosis could be useful in seronegative LORA.

P1-069

Comparison of Anti-CCP2 and Anti-CCP3 Antibodies in Early Rheumatoid Arthritis Patients and Healthy Volunteers

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Conflict of interest: None

[Objectives] We aimed to elucidate the positivity and agreement of anti-CCP2 and anti-CCP3 antibodies in early RA patients and healthy volunteers. [Methods] We included RA patients (n=86) within one year of onset and asymptomatic health check-up participants (HCs, n=498). Anti-CCP2 antibodies were measured at the first visit for RA patients, and anti-CCP3 antibodies were measured using frozen stored serum. For HCs, frozen stored serum was tested for both antibodies. The cutoff values were set at 4.5 U/ml for anti-CCP2 antibodies and 20 U/ml for anti-CCP3 antibodies; additional cutoff values of 40 U/ml and 60 U/ml were also evaluated. [Results] In RA patients, the positivity was 62% for anti-CCP2 antibodies, and 63%, 57% and 56% at cut off values of 20, 40, and 60 U/ml for anti-CCP3 antibodies. κ coefficient for anti-CCP3 antibodies at each cutoff value was κ=0.88, 0.86, and 0.83. In HCs, the positivity was 2% for anti-CCP2 antibodies, and 4%, 2%, and 1% for anti-CCP3 antibodies. κ coefficient was 0.49, 0.73, and 0.62, respectively. [Conclusion] In early RA patients, anti-CCP3 antibody positivity at 20 U/ml was comparable to anti-CCP2 antibodies, with the highest agreement. In HCs, anti-CCP3 antibodies at 40 U/ml had similar positivity to anti-CCP2 antibodies, with the highest agreement.

P1-070

Examination of serum amyloid b-40 autoantibodies and SAA protein in rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] Accumulation of amyloid b (Ab) is considered to be one of the factors that cause dementia, and its trends are being investigated. We have already developed an ELISA method for Amyloid b-40 autoantibody (anti-Ab-40), and investigated its relationship with the inflammatory marker SAA. [Methods] The subjects were 107 patients visiting a rheumatology outpatient clinic for the first time. 48 cases of internal rheumatoid arthritis (RA) (37 female, 11 male) and 59 cases of unknown arthritis (UA) (42 female, 17 male) were diagnosed. In addition to SAA, CRP, IL-6, RF, and ACPA antibodies were examined. [Results] The anti-Ab-40 antibody concentration (Mean±SE unit (u) was 19.8±2.9u in the RA group and 12.2±1.4u in the UA group, which was higher in the RA group than in the UA group ($p<0.01$). The SAA concentration (Mean±SEug/mL) was higher in the RAgroup, 64.8±16.2, and 32.8±11.4 in the UA group, but no statistically significant difference was observed. Regarding the relationship with aging, anti-Ab-40 antibodies had a negative relationship in both the RA group r=-0.455 and the UA group r=-0.244. [Conclusion] Autoantibodies against Ab-40 were higher in the RA group than in the UA group, and showed a tendency to decrease with age.

P1-071

A case of severe eosinophilic granulomatosis with polyangiitis (EGPA) with cardiac involvement successfully treated with multidisciplinary therapy including mepolizumab

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Conflict of interest: None

Case Presentation: An 18-year-old female without asthma history presented with purpura, dyspnea, and marked eosinophilia (24,000/μL). Imaging revealed ground-glass opacities, pleural and pericardial effusions, and cardiomegaly. Cardiac involvement was confirmed by positive troponin T, elevated CK-MB, and reduced ejection fraction (EF 30%). EGPA with myocarditis was diagnosed based on eosinophilia, sinusitis, and vasculitis on skin biopsy. Despite steroid pulse and cyclophosphamide therapy, the patient remained refractory. Mepolizumab was administered on day 22. By day 37, clinical symptoms, eosinophil count, troponin T, and CRP levels improved significantly. Follow-up echocardiography showed improved EF (50%). Conclusion: In EGPA, cardiac involvement is considered to be a serious complication, accounting for approximately 50% of deaths. Although MEP is recommended for severe cases refractory to remission induction therapy, the efficacy of MEP in patients with cardiac involvement has not been proven in large studies. This case suggests that treatment including MEP may be effective in the treatment of refractory EGPA with cardiac involvement.

P1-072

The influence of rheumatoid factor on cytokine measurement in rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] Rheumatoid factor (RF), an autoantibody against the Fc portion of IgG, is recognized in sera of patients with rheumatoid arthritis (RA) and other connective tissue diseases (CTD). In this study, we investigated the effect of RF interference on cytokine measurement in sera of RA patients. [Methods] Used in this study were sera from 8 RA patients (4 with low RF and 4 with high RF). Following the treatment with or without a blocking reagent (HeteroBlock), the concentrations of 10 cytokines in their sera were measured using two different types of multiplex immunoassay (MIA) (A and B) to analyse the effects of RF interference. [Results] Using the MIA A, 5 RA patients showed high levels of either IFN-α, IL-1β, IL-2, IL-6, IL-10, IL-12p70, IL-17A or TNF-α. However, HeteroBlock treatment resulted in a negative result in all of them except IL-6 level. In five RA patients, one of which showed low IgM RF level but high total RF level (including IgG). In the MIA B, there were no suspected false positives due to RF interference even without blocking treatment. [Conclusion] It was suggested that not only IgM RF, but also IgG or IgA RF, may affect multiplex system measurements. The possible presence of RF should always be considered in cytokine profiling of patients with RA and CTD.

P1-073

Association of nailfold videcapillaroscopy and organ damage in four cases of anti-Th/To antibody-positive systemic scleroderma

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Conflict of interest: None

Background: In systemic sclerosis (SSc), skin hardening severity and nailfold videocapillaroscopy (NVC) findings are associated with organ damage. Recently, an anti-Th/To antibody test has become available in Japan by A-Cube. This antibody often associated with organ involvement such as interstitial pneumonia and pulmonary hypertension, although skin stiffness is mild. Few studies have examined the relationship between this antibody and NVC findings. **Cases:** Between August 2022 and August 2024, of 18 patients with suspected SSc tested with A-Cube, 4 were positive for anti-Th/To antibodies. All patients had mild skin hardening (mRSS 0 [0-2]) and Raynaud's phenomenon was present in only two patients. The NVC showed a normal pattern in two patients and a non-specific pattern in two patients, none of whom had characteristic findings of SSc. The two patients with normal NVC required immunosuppressive therapy with glucocorticoids and rituximab for progressive interstitial pneumonia (IP). On the other hand, the two patients with a non-specific pattern were only followed up and showed no organ involvement. **Clinical Significance:** Organ involvement in anti-Th/To antibody-positive SSc patients is not predictable from NVC findings.

P1-074

Rheumatoid Factor in Healthy Individuals During the COVID-19 Pandemic

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Conflict of interest: None

[Objectives] Rheumatoid factor (RF) is a marker significant in diagnosing rheumatoid arthritis (RA) and assessing its disease state. However, RF lacks specificity, appearing positive in other diseases and sometimes in healthy individuals. Transient elevations in RF can also occur due to bacterial or viral infections and vaccinations. [Methods] We analyzed RF data from annual health screenings conducted at the Okayama Saiseikai Preventive Medicine Health Screening Center between 2018 and 2023 to identify any shifts in RF positivity rates over time. [Results] From 2018 to 2023, the RF positivity rates and average RF levels were as follows: 2018: Positivity rate 6.6%, mean RF 8.67±29.8 IU/ml, 2019: Positivity rate 6.9%, mean RF 8.59±21.3 IU/ml, 2020: Positivity rate 6.9%, mean RF 8.26±18.9 IU/ml, 2021: Positivity rate 7.8%, mean RF 8.54±19.1 IU/ml, 2022: Positivity rate 7.6%, mean RF 8.9±24.2 IU/ml, 2023: Positivity rate 7.5%, mean RF 9.03±25.5 IU/ml. A noticeable increase in both positivity rate and mean RF value was observed from 2022, aligning with the COVID-19 vaccination rollout. [Conclusion] COVID-19 vaccinations may have activated RF production, leading to higher RF positivity among healthy individuals, thus requiring careful consideration in RA diagnosis.

P1-075

Analysis of Rheumatoid Factor-Positive Cases in a Hospital Setting

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Conflict of interest: None

[Objectives] Rheumatoid factor (RF) lacks specificity for RA. This study examines RF-associated diseases and related factors. [Methods] From January to March 2024, RF levels were measured in 686 patients in our hospital's internal medicine department, analyzing their age, sex, kidney and lung impairment, liver disease, and medications. [Results] Among the 686 cases, 396 were RF-positive (mean ± SD: 93.3±275.1). Of 442 RA cases, 77% were RF-positive. Positivity rates were as follows: kidney disease (14%, 35 cases), PMR (24%, 25 cases), pSS (67%, 21 cases), vasculitis (38%, 16 cases), SSc (67%, 12 cases), psoriasis (9%, 11 cases), SLE (40%, 10 cases), lung disease (30%, 10 cases), PM/DM (33%, 6 cases), MCTD (66%, 3 cases), and other conditions (12%, 95 cases). RF > 200 was mainly found in RA cases, though some were linked to gastrointestinal cancer or ILD. In 442 RA cases (mean age 67.3±14.5 years; MTX use 57.4%, 8.0±2.8 mg; GC use 10.9%, 3.3±2.4 mg; Bio/JAKI use 37%), RF levels correlated with pre-existing lung disease and showed an association with ABT and JAKI use. [Conclusion] Although high RF values were mostly seen in RA cases, a few were associated with gastrointestinal cancer and ILD, warranting caution. High RF levels in RA patients were linked to lung disease.

P1-076

Quantitative Evaluation of Patient Characteristics Affecting Therapeutic Response to Biologics and JAK Inhibitors in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Biologics and JAK inhibitors play a key role in controlling rheumatic disease progression, though treatment responses vary among patients. Patient-specific factors like sex, age, and concurrent medications could influence treatment outcomes. This study aimed to assess the impact of these characteristics and the use of biologics or JAK inhibitors on ΔCDAI (3-month improvement measure) using Ridge regression. [Methods] We analyzed data from 304 rheumatoid arthritis patients, collecting details on one administered biologic or JAK inhibitor per patient, along with key characteristics (sex, age, concurrent drugs). ΔCDAI was set as the target variable, with model accuracy evaluated using R^2 and MSE. [Results] Ridge regression achieved an R^2 of 0.72 and an MSE of 57.86, indicating moderate predictive accuracy. Higher treatment efficacy was observed in males, with concurrent drug count and experience with biologics affecting responses. [Conclusion] Treatment efficacy varied significantly by patient characteristics, especially sex and treatment history. Current limitations in sample size and factor scope suggest that expanding these could improve predictive accuracy and support personalized treatment planning.

P1-077

Prognosis prediction after biologic or targeted synthetic disease-modifying anti-rheumatic drugs administration in a short-term

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Conflict of interest: None

[Objectives] We examined short-term results until 6 months after the initiation of biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs) and validated prognosis prediction indicators based on the activity classification of the Joint Index Vector (JIV-AC). [Methods] Patients who were administrated b/tsDMARD were selected. The mode of action grouped them. The changes in clinical indicators at 3 and 6 months were classified according to the JIV-AC for each action group. [Results] A total of 195 cases were recruited. At initiation, there were 18 in High Joint Activity (HJA), 104 in Moderate Joint Activity (MJA), 36 in Low Joint Activity (LJA), and 37 in Remission (REM). The cases that showed no improvement after initiation were 2 in HJA, 41 in MJA, 26 in LJA, and 6 in REM. The higher Vz in JIV showed significantly worse results. In patients who were given interleukin-6 inhibitor (IL6-i) and Janus Kinase inhibitor (JAK-i), higher serum albumin levels (ALB) tended to result in worse outcomes. [Conclusion] Low ALB represents IL-6 hyperactivity. Therefore, high ALB would reflect low IL-6 hyperactivity and lead to low response to IL6-i or JAK-i. The high Vz suggested a low response to b/tsDMARD, and the high ALB suggested a low response to IL6-i and JAK-i.

P1-078

Development of a Predictive System for the Effectiveness of treatment in Rheumatoid Arthritis Based on Very Early Changes in ePRO: A Study Overview

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Conflict of interest: None

[Objectives] Patient-reported outcomes (PROs) are increasingly vital in rheumatoid arthritis (RA) management, enabling patients to self-assess their condition. The widespread use of smartphones makes electronic PRO assessments (ePRO) feasible, allowing for real-time data entry and early symptom detection, which might be missed during in-person visits. This study investigates whether early treatment effects identified through ePRO in RA patients beginning molecular targeted therapy can predict long-term disease activity and joint damage. [Methods] RA patients at Nagasaki University Hospital starting biological agents or JAK inhibitors are included in this one-year prospective study. ePRO data, including visual analog scale, Health Assessment Questionnaire, and EQ-5D-5L, are collected at baseline, days 1, 3, 7, and 14, then biweekly. DAS-28, CDAI, SDAI and musculoskeletal ultrasound assessments will be conducted quarterly, and one-year bone changes will be evaluated using the modified total sharp score (mTSS) to analyze relationships with ePRO changes. [Results] The ePRO platform has been developed, and patient enrollment is in progress. [Conclusion] We showed the study protocol. Details on enrolled cases will also be reported at the time of conference presentation.

P1-079

An Examination of Three Cases Where Treatment Drugs Were Selected Based on Synovial Immunostaining in Patients Undergoing Multiple Surgeries

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Conflict of interest: None

[Objectives] Our study investigates the effectiveness of targeted therapies in rheumatoid arthritis patients based on synovial immunostaining patterns-Lymphoid type (L type) and Myeloid type (M type). We analyzed three cases undergoing multiple surgeries. [Case Summaries] Case 1: A 76-year-old female with a 6-month history of RA underwent arthroscopic rotator cuff repair (ARCR). Synovial tissue stained L type, initially treated with anti-IL-6, followed by JAK inhibitors after secondary inefficacy. Total knee arthroplasty (TKA) confirmed persistent L type; JAK inhibitors continued, maintaining remission. Case 2: A 78-year-old female on JAK inhibitors underwent reverse shoulder arthroplasty (RSA), with low inflammatory phenotype in synovial staining. Later TKA showed conversion to L type; remission was maintained on JAK inhibitors. Case 3: An 88-year-old female initially identified as M type during RSA was treated with TNF inhibitors. At TKA, her synovial tissue had converted to mixed (L & M) type; remission was maintained with anti-IL-6 agents. [Conclusion] JAK inhibitors are also beneficial for L type cases, suggesting that synovial phenotypes may evolve with treatment progression.

P1-080

Risk Factors Associated with Relapse after Methotrexate Reduction in Patients with Rheumatoid Arthritis in DAS28-CRP Remission

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Conflict of interest: None

Objective: This study aimed to identify risk factors for flare after tapering methotrexate (MTX) in rheumatoid arthritis (RA) patients in DAS28-CRP remission. **Methods:** We retrospectively analyzed RA patients in DAS28-CRP remission who tapered MTX between September 2023 and August 2024 in our outpatient clinic. Data on flare incidence and associated factors were collected, with univariate and logistic regression analyses to examine these factors. ROC curve analysis identified a DAS28-CRP cutoff value, along with sensitivity and specificity for predicting flare. **Results:** 39 patients were enrolled. Age was 69 years (median), MTX dose before dose reduction was 8 mg/week (median), 19 patients (48.7%) were treated with csDMARDs other than MTX and 11 patients (28.2%) with bDMARDs. Five patients experienced flare. Age, MTX dose before flare, csDMARDs, bDMARDs, glucocorticoid use, and RAPID3 showed no significant association with flare. Multivariate analysis showed that pre-taper DAS28-CRP was significantly related to flare risk (p=0.03). ROC analysis provided a DAS28-CRP cutoff of 1.44, with a sensitivity of 0.58 and specificity of 1.00. **Conclusion:** Pre-taper DAS28-CRP scores appear to be a key risk factor for flare in RA patients tapering MTX in remission.

P1-081

Development of a Circulating Cell-Free DNA Detection System for Treatment Response in Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] We previously demonstrated that circulating cell-free DNA (ccfDNA) increases in the blood and synovial fluid of rheumatoid arthritis patients, serving as a potential biomarker for early identification of those with favorable responses to biologic DMARD therapies. To replace the currently used qPCR, this study aimed to develop a novel detection system by generating antibodies targeting ccfDNA. [Methods] Synthetic ccfDNA was used to immunize BALB/c mice. After five immunization rounds, splenocytes were fused with the PAI myeloma cell line to create hybridoma clones. By using immunostaining and EMSA, we evaluated the nuclear staining properties of immortalized RA synovial cell line (MH7A) using culture supernatant and assessed the specificity to ccfDNA after antibody purification, respectively. A candidate antibody was further tested in an ELISA system to detect ccfDNA. [Results] Out of 165 culture supernatants, 44 exhibited nuclear staining in MH7A cells. Among these, one IgG antibody was found to be ccfDNA-specific by EMSA. The ELISA prototype demonstrated higher absorbance in ccfDNA-immobilized groups in a concentration-dependent manner. [Conclusion] A hybridoma line producing anti-ccfDNA antibody has been established, which enable to produce antibody for detecting ccfDNA.

P1-082

Joint Index Vector can predict future remission rate in patients with rheumatoid arthritis

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Conflict of interest: None

[Background] Joint Index Vector (JIV), which includes disease activity and functional damage on each independent axis, is a novel measure for RA, and future JIVs are able to be predicted using transform matrix calculated by stored data[1]. Preliminary study revealed that mean JIV scalars is negatively correlated with boolean remission rate. [Objectives] To esti-

mate 3-year-later boolean remission rate by the mean vector scalar (mV) of predicted JIVs. [Methods] Regression parameters and credible intervals (CI) were obtained by Bayesian estimation using remission rates and mVs in each year from *NinJa* (2002-2022). Predicted JIVs in 2010 were calculated with JIVs of 2007 and the transform matrix using data from 2004 and 2007. Predicted JIV in 2013, 2016, 2019 and 2022 were acquired in the same way. [Results] Estimated remission rates were obtained using the regression equation and mVs of predicted JIVs. The difference between actual and estimated rates was in around 2%. Two pairs of each mV and real remission rate were in 50%CI and the all including rest of 3 in 95%CI. [Conclusion] JIV, which has both activity and damage aspect, is a surrogate index for composite boolean remission and can predict a future remission rate.

P1-083

The Impact of Boolean 2.0 on Disease Activity and Functional Outcomes in Rheumatoid Arthritis: An Analysis of NinJa 2022

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Conflict of interest: None

[Background] PtGA reflects activity in 40 non-assessed joints beyond the 28- joint assessment. Boolean 2.0 relaxes PtGA criteria, raising concern about remission despite residual activity in these joints. [Objective] To assess changes in remission profiles under Boolean 2.0 and their relevance. [Methods] Using data of NinJa 2022, we identified patients achieving Boolean 1.0 (n=4657) and those achieving only Boolean 2.0 (n=1606). Analysis 1: We compared demographic backgrounds, treatments, joint counts (28 and non-assessed joints), and HAQ-DI. Analysis 2: Propensity score matching used covariates such as age, disease duration, sex, BMI, NSAIDs/GC use, joint counts, and hospitalization. We then compared joint counts and HAQ-DI between matched groups. [Results] Analysis 1: Significant differences were found in age, disease duration, sex, GC/NSAIDs use, b/tsDMARDs use, HAQ-DI, and joint counts. Swollen joint counts in non-assessed joints showed no significant difference. Analysis 2: There were significant differences in HAQ-DI and tender joint counts, but not in swollen joint counts. [Conclusion] Boolean 2.0 has relaxed PtGA criteria, reflecting residual tenderness but not swelling in non-assessed joints. It allows remission even with residual tenderness, which should be noted in practice.

P1-084

The relationship between PROMs with the "Okomarigoto Sheet" and disease activity, locomotive syndrome risk level, and physical function assessment in rheumatoid arthritis patients

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Conflict of interest: None

Purpose: To investigate the relationship between patient-reported outcome measures (PROMs) using the "Okomarigoto Sheet" (this sheet) and disease activity/locomotive syndrome risk level/evaluation of physical function. Methods: Subjects were 134 RA patients who visited our clinic from June to August 2024. We examined the relationship between the results of this sheet and disease activity (DAS28_ESR, SDAI, CDAI, Boolean 1.0/2.0), Locomo 25 score, and physical function (HAQ-DI). Results: In this population, the mean age was 76.4 years, 75.4% female, and the mean disease duration was 129.3 months. In the evaluation of disease activity and Locomo 25, there was a positive correlation with pain (VAS) and fatigue (VAS), while there was no association with stiffness (min.) on this sheet. HAQ-DI and this sheet showed positive correlations in pain, fatigue, and stiffness. In the self-assessment of three choices on this sheet, a relationship was found in disease activity, level of locomotion, and physical function. Conclusion: The patients with higher disease activity and Locomo 25 score feel more pain and fatigue. However, stiffness (min.) may be difficult to assess with objective measures. On the other hand, functional remission may be associated with improvement in PROMs.

P1-085

Low sarcopenia index associated with inadequate response to methotrexate in rheumatoid arthritis

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Conflict of interest: None

[Objectives] We performed a retrospective analysis of RA patients who first started MTX treatment in our department to determine the relationship between SI at baseline and the effect of MTX treatment. [Methods] Between April 2018 and March 2022, 30 patients who started MTX treatment after diagnosis of RA in our department and were followed up for 48 weeks and whose SI could be calculated at the start of treatment were included. We calculated SI= (serum Crea) / (serum CystatinC) *100. [Results] The median age was 68.5 years, 83.3% were female and the median DAS28CRP was 3.13. Univariate COX proportional hazards analysis for time to Bio-JAKi induction showed a significant difference in SI (HR 0.921 [0.851-0.996], p=0.0399). Disease duration and GC use were associated (both $p<0.15$). Multivariate analysis of these items showed that only SI was significantly different (HR 0.846 [0.741-0.966], p=0.0136); from the adjusted log HR curve for SI, SI=69.25 was considered the cut-off. The two groups were divided by this cut-off, but there were no significant differences in pre-treatment DAS28-CRP or BMI. [Conclusion] In this study, we analysed the association between the efficacy of MTX and SI in RA. Low SI was suggested to be associated with resistance to MTX treatment.

P1-086

Does complicated Sjogren's syndrome affect appetite status in patients with rheumatoid arthritis? ~Evaluation appetite state using CNAQ-J (Council of Nutrition Appetite Questionnaire scores for the Japanese)~

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Conflict of interest: None

[Objectives] To investigate the effect of secondary Sjogren's syndrome (SjS) on the appetite status in patients with rheumatoid arthritis (RA). [Methods] Eighty patients who were diagnosed with RA were enrolled into this study. The clinical information and CNAQ-J assessment was collected at periodical visit. Patents were divided into two groups according to complicated secondary Sjogren's syndrome as follows; 11 patients who was diagnosed as RA and SjS (RA+SjS group) and 74 RA patients without SjS (RA group). [Results] The proportion of female was higher in RA+SjS group (70.3% vs 100%, p=0.03). Although there were no differences in age and duration of RA, the body weight was lighter in RA+SjS group (58.8 kg vs 51.0 kg, p=0.04). No differences were found in the usage rate of methotrexate (MTX), predonisolone (PSL), and b/tsDMARDs. The dosage of MTX and PSL were not different as well. The se-

rum albumin level and hemoglobin value were not different between two groups. Despite no difference in the total score of CNAQ-J, the score in category C 'How often do you feel hungry?' tended to be low in RA+SjS group (p=0.0594). [Conclusion] There were no differences in parameters of CNAQ-J between two groups. It indicates some other factors may affects the low body weight in RA+SjS group.

P1-087

Preoperative disease activity and functional impairment in patients with refractory rheumatoid arthritis who required orthopedic intervention

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Conflict of interest: None

Introduction: There is no established treatment for difficult-to-treat (D2T) rheumatoid arthritis (RA). When pharmacotherapy fails, structural damage may require orthopaedic surgical intervention (OSI). We hypothesized that disease backgrounds differ between D2T and non-D2T RA in cases requiring OSI. **Methods:** We reviewed OSI cases from 2016 to 2023 with three years of preoperative follow-up. In cases of multiple OSIs within three years, the earlier surgery was analyzed. Medical information including medications were evaluated. Cumulative integrated disease activity and HAQ scores, and the use of biologic/targeted synthetic DMARDs (b/tsDMARDs), were compared between the D2T and non-D2T RA groups. **Results:** A total of 327 cases (37 males, 290 females) were analyzed, with an average age of 67.5 years and a mean disease duration of 18.3 years. The D2T RA group consisted of 65 cases. There was no significant difference in OSI sites between the groups. HAQ scores were significantly higher in the D2T group. Cumulative disease activity and HAQ scores were also significantly higher in the D2T group. **Conclusion:** In D2T RA cases requiring OSI, poor disease control and worsening functional impairment were observed over the three-year period, suggesting that surgery may have been delayed.

P1-088

About our efforts to achieve functional remission for rheumatoid arthritis patients who visit our clinic

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Conflict of interest: None

[Objectives] Patient with RA often evaluate as PROs. We explored with PRO indicators are important to patients with RA and considered efforts aimed at achieving functional remissions. [Methods] We quantified the EQ-5D and the Rheumatism Problem Checklist (RPC) of 80 patients with RA who visit our clinic and are treated based on the revised drug treatment algorithm of the 2024 RA, and used the ICER, a medical economic evaluation, to understand the PGA in PROs and to investigate whether they are approaching functional remission. [Results] Depending on the patient's condition, the treatment method varies from Phase1 to 3 of the revised drug Guidelines for the Treatment of RA. However, we are convinced that by deciding the treatment method and treating with SDM while taking into account PROs, we can provide treatment method and treating with SDM while taking into account PROs we can provide treatment that the patient can understand. [Conclusion] In treatment aimed at achieving functional remission in RA patients who visit our clinic, we evaluate EQ-5D and RPC by quantifying them, and by making effort to provide treatment that emphasizes PROs, we believe that is possible to understand the patient's daily suffering from multiple perspective and lead to more comprehensive medical care.

P1-089

Establishing a Smooth Introduction of Home-Visit Care for Rheumatoid Arthritis Patients: The Approach of NHO Sagamihara National Hospital

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Conflict of interest: None

[Background] We provide home-visit care for rheumatoid arthritis (RA) patients in cooperation with neighboring clinics. However, managing patients transitioning to home care from other hospitals is often challenging. [Objective] To establish the "Sagamihara Model" for the smooth implementation of home-visit care for RA patients. [Approach] Patients scheduled for home-visit care from other facilities are hospitalized for comprehensive evaluation of RA, comorbidities, medication adjustments, and home environment modifications. [Case 1] A 58-year-old woman with mental retardation had severe hip pain and obesity, making it difficult to sit or change position. After femoral head resection, her pain improved, and she could sit and reposition easily. [Case 2] An 87-year-old woman with dementia was hospitalized due to severe joint pain after a fall. RA exacerbation was successfully treated, pain was reduced and ADL improved, allowing the patient to be discharged and begin home-visit care. [Case 3] A 77-year-old woman with declining ADL, considered for home care due to elderly caregiving needs, underwent a full evaluation during hospitalization. After home environment modifications, home-visit care was initiated. [Conclusion] Our efforts facilitated a smooth transition to home-visit care in these cases.

P1-090

Clinical reality of NSAID use in RA patients

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Conflict of interest: None

[Objective] NSAID use is recommended for RA patients to reduce pain, but should be used as little as necessary and for a short period of time. We conducted a survey to clarify the actual status of NSAID use in clinical practice. [Methods] NSAID use, background, adverse events, and impact on renal function were examined in 56 RA patients who were available for at least 2 years of follow-up. [Results] Sixteen patients (29%) continued regular NSAID use for 2 years (group R), 33 patients (59%) were not prescribed NSAID for 2 years (group N), and 1 patient (6%) in group N experienced peptic ulcer perforation. Comparing the R and N groups, there was a significant difference in age, disease duration, BMI, Hb, serum Alb, and eGFR. No differences were observed in disease activity, MTX use, or b/tsDMARD use. eGFR did not change significantly from in the N group over 2 years, but decreased significantly from 76.0±16.4 to 69.2±14.4 in the R group (P=0.017). [Conclusions] NSAIDs were continuously used for pain relief in patients who were younger, had shorter disease duration, were in good nutritional condition, and had preserved renal function. Careful attention should be paid to peptic ulcers during administration, and it should be noted that renal function decline may occur.

P1-091

Hyper-aged rheumatoid arthritis patients and difficult to treat RA patients in our hospital

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Conflict of interest: None

[Objectives] It was difficult to treat elderly rheumatoid arthritis (RA) patients and difficult-to-treat RA (D2T RA) patients. The aim of this study

was to investigate the situations of hyper-aged RA patients and D2T RA in our hospital. [Methods] 699 RA patients visited our hospital in 2023 and hyper-aged RA patients who were over 90 years old were included. The treatment and disease activities were performed with t-test. D2T RA in hyper-aged RA patients were also investigated. [Results] The number of hyper-aged RA patients were 40 (male 10, female 30 / ACPA positive 14, RF positive 18 / average eGFR 61.4) and whose average age was 92.8 years. The disease activities were DAS28 (ESR) 4.91, SDAI 21.7 and mHAQ0.89 at first visiting. MTX 18, csDMARD 15, bDMARD 7 were used when they visited our hospital. The disease activities were DAS28 (ESR) 2.70 ($P<0.05$), SDAI 13.3 ($P<0.05$) and mHAQ0.89 ($P>0.05$) in 2023. MTX 11, csDMARD 8, bDMARD 19, JAKi 2 were used at last visiting. One patient used more than 2 bDMARD but there was no D2T RA patient. [Conclusion] The disease activity of hyper-aged RA were very high and much MTX were used at first but it was difficult to control them. Much bDMARD were used and their disease activity was controlled and there was no D2T RA patient. mHAQ was almost same.

P1-092

Cases of Suspected Preclinical Rheumatoid Arthritis and Treatment

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Conflict of interest: None

[Objective] To clarify whether rheumatoid arthritis (RA) can be diagnosed at an early stage in daily clinical practice and to determine effective treatments in such cases. [Methods] We extracted cases of suspected very early RA (preclinical RA) at our hospital between 2020 and 2024, analyzed the course of symptoms, and considered treatment methods. [Results] A total of 16 patients (14 women and 2 men) were included in the study. All were positive for anti-CCP antibodies, and all except one was positive for rheumatoid factor (RF). No joint swelling was observed at the initial visit. Ultrasound (US) did not detect synovitis in 10 cases, and slight synovial thickening was observed in some parts of the wrist or finger joints in 6 cases. Six of the 16 patients were started with methotrexate because arthritic findings were confirmed by MRI and US, and two of them were referred to receive biologic therapy. The remaining 10 patients are under observation without use of disease-modifying antirheumatic drugs. [Conclusion] Patients positive for RF and anti-CCP antibody with joint symptoms should be monitored carefully. Early detection of arthritis onset by imaging examination is important. Treatment should be started on onset of arthritis in compliance with the RA treatment guidelines.

P1-093

Investigation of drug therapy for very elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To analyze the treatment of very elderly rheumatoid arthritis (RA) patients aged 85 years or older in our department. [Methods] RA patients aged 85 years or older who visited our outpatient clinic in the past 5 years were analyzed for treatment details, outcome, etc. [Results] Twenty-two patients were 85 years of age or older at the time of their first visit, 5 males and 17 females, ranging in age from 85 to 95 years, with an average age of 87.6 years. Six patients were untreated RA patients, and the remaining 16 patients were on some kind of drug therapy. The main components were biologic agents (BIO) in 6 cases, JAK inhibitors in 1 case, and methotrexate (MTX) in 4 cases. Nine patients were currently on treatment, 7 patients were transferred to another physician, 4 patients died, and 2 patients were unknown. Of the 6 patients who were untreated at the time of initial diagnosis, 2 were started on anti-rheumatic drugs, and the remaining 4 patients were followed up with glucocorticoids and anti-inflammatory analgesics. [Conclusion] Treatment of RA in the very elderly is often not easy for a variety of reasons. However, we believe that the use of BIO and JAK inhibitors is necessary for patients with high disease activity.

P1-094

Pregnancy care of rheumatoid arthritis patients in clinic

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Conflict of interest: None

Purpose: RA affects women of childbearing age, requiring careful management during pregnancy. Treatment plans must balance disease control with fetal safety, especially regarding medication and vaccinations. Clinicians must understand these guidelines and collaborate with pediatricians and gynecologists. **Case:** 1: A woman in her 30s with seropositive RA needed to suppress RA activity before conception. Treatment with PS-Lwas insufficient, requiring more aggressive therapy. 2: A woman in her 30s undergoing artificial insemination, positive for SS-A antibodies, this patient lacked sufficient preventive measures for fetal complications, such as congenital heart block, despite successful conception. 3: A woman in her 30s developing RA in late pregnancy, RA developed in the third trimester, raising questions about appropriate treatment levels while ensuring fetal safety. **Discussion:** Managing RA during pregnancy requires low disease activity while ensuring maternal and fetal health. Medications such as certolizumab pegol and sulfasalazine, known for their relative safety, are recommended. Multidisciplinary collaboration is key, and shared decision-making (SDM) involving patients and partners is crucial. Need for further real-world evidence to inform personalized care in clinical practice.

P1-095

A survey of the progression from the initiation to discontinuation of glucocorticoids (GCs) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] To investigate the continuation rate of GC from the progress of drug treatment in early RA patients. [Subjects] RA patients who were visiting as of April 2024, who had not been treated since onset, and who were able to be followed up for more than one year from the first visit. [Method] The medical records of the patients were used to investigate the use of MTX, GC, and BIO preparations at the time of the first visit, 1 month, 12 months, and the last visit. In addition, a logistic analysis was performed on the patient factors at the time of the first visit regarding the introduction of GC administration. [Results] The patients were 140 cases (mean age 59.3 years, 29 men), the median period from onset to first visit was 0.5 years, and the median observation period was 74 months. GC use was observed in 52 patients (37%) one month after the initial consultation, and the GC continuation rates at 12 months and the last observation date were 77% and 44%, respectively. Seronegativity and DAS28-CRP at the initial visit were independent risk factors for GC initiation. [Conclusion] The latest RA treatment guidelines also state that GC use in RA patients should be tapered and discontinued but many patients who have once started GC are unable to discontinue it even at 12 months.

P1-096

Comparison of drug costs between biologics and JAK inhibitors in RA patients

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Conflict of interest: None

[Objective] In our clinic, we are increasingly introducing biological agents (bio) and JAK inhibitors (JAK) to patients with rheumatoid arthritis (RA). We investigated the use of bio/JAK and the actual drug costs for each patient. [Method] As of August 2024, there were 103 RA patients who had been using bio/JAK, with an average age of 66.7 years. The drugs used were bio in 51 cases and JAK in 52 cases. We compared the drug costs per month. [Results] The breakdown of biologic use was as follows: 26 original biologics (etanercept 3, adalimumab 2, tocilizumab 13, abata-

cept 3, golimumab 1), 25 biosimilars (BS) (etanercept 22, adalimumab 3), and 52 JAK (tofacitinib 6, baricitinib 19, upadacitinib 12, filgotinib 12, peficitinib 3). The average drug cost (yen) per month was 78,760.3 for all original biologics, and 61,424.2 for tocilizumab, which was cheaper than other drugs. 41,676.7 for BS, which was used often by patients with high out-of-pocket expenses. 74,973 for all JAKs, which was used often at half doses. Conclusion: In cases where bio were used, the use of tocilizumab and BS was on the rise. In cases where JAK was used, the number of cases where treatment could be maintained with half-dose administration was increasing, which is expected to reduce the burden of drug costs.

P1-097

A Case of Anti-CCP Antibody Positive Paroxysmal Arthritis: Capturing Ultrasound Findings During Both Flare and Non-Flare States Within 24 Hours

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Conflict of interest: None

[Case] A 61-year-old woman presented with recurrent joint pain and swelling. Two months earlier, she experienced right wrist pain and swelling, which resolved in 2 days. Two weeks later, similar symptoms occurred in her right shoulder and left wrist, resolving in 3 days. Three days before presentation, she developed left elbow pain, which disappeared in 2 days. At her initial visit, physical exam and ultrasound (US) showed no arthritis. [Course after Initial Visit] Twenty-one hours after her first visit, she developed sudden swelling and pain in her right second finger and left wrist. She returned 23 hours later with swelling and tenderness. US showed synovitis and tenosynovitis in the right second metacarpophalangeal joint, left wrist, and extensor tendons. Tests showed anti-CCP antibody (ACPA) of 154.2 U/mL. X-rays showed erosion in the right trapezium. She received triamcinolone, prednisolone 10 mg/day for 3 days, and methotrexate (MTX) 6 mg/week. No flares occurred over 4 months. [Clinical Significance] This case captured flare and non-flare US findings. Paroxysmal arthritis with ACPA positivity and erosions prompted early MTX, preventing further episodes. This raises the question of whether paroxysmal arthritis is an atypical form of RA, pre-RA, or palindromic rheumatism.

P1-098

Characteristics of Sarcopenia Obesity in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To investigate sarcopenia obesity in rheumatoid arthritis (RA) patients. [Methods] Between March 2021 and December 2022, 328 rheumatoid arthritis patients who participated in a prospective cohort study on frailty (Fairy study) were included. Patient background, DAS28-CRP, HAQ-DI, Locomo25 were investigated. Obesity was defined from body fat percentage, and patients were divided into 4 groups: normal, obese, sarcopenia, and sarcopenia-obese. [Results] Of the total 328 patients, 119 (36.3%) were in the normal group, 155 (47.3%) were in the obese group, 31 (9.4%) were in the sarcopenia group, and 23 (9.5%) were in the sarcopenia-obese group. Mean age was 62/62/69/68 years, and DAS28-CRP was 1.82/1.93/2.03/2.21 in the normal/obese/sarcopenia/obese groups. BMI was 20.4/24.6/17.6/21.4 kg/m^2 in the sarcopenia obese group. HAQ-DI was 0.23/0.40/0.42/1.04, and locomotor 25 was 11.0/16.8/16.4/26.0, both significantly higher in the sarcopenia-obese group than in all groups. [Conclusion] Of 328 RA patients, 54 (16.5%) had sarcopenia, and 9.5% were sarcopenia obesity. BMI in the sarcopenia-obese group was not significantly different from that in the normal group, and HAQ-DI and Locomo25 was significantly higher in the sarcopenia-obese group than in the other groups.

P1-100

Survey of blood levels and dosage satisfaction in patients who switched from original to generic tacrolimus

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Conflict of interest: None

Purpose: Tacrolimus (Tac) is recommended for therapeutic drug monitoring (TDM) when switching to generics, as absorption differences may affect autoimmune disease control. Generics offer easier pills taking and lower costs, but patient satisfaction during these switches has not been thoroughly examined. This study investigates blood level changes and satisfaction when switching from original to generic TAC. **Method:** From December 2023 to July 2024, physicians guided patients in switching to generic TAC. Patients aged 18 and older who agreed to the switch were included. Changes in blood levels, satisfaction, swallowing ease, and economic burden were assessed using the Visual Analogue Scale. Prograf costs 390 yen, while Tac "Towa" costs 153 yen. **Results:** A total of 34 patients participated, including 18 with rheumatoid arthritis, 5 with systemic lupus erythematosus, and 11 with other deseases. No significant differences were observed in TAC blood levels. However, swallowability VAS average scores were 65 for the original versus 74 for the generic, and overall satisfaction scores were 57 versus 74 ($p < 0.05$). The economic burden was less for generics, with VAS median of 50 versus 64. **Conclusion:** Switching to generic TAC improved administration ease and patient satisfaction regarding costs.

P1-101

A retrospective study of the use of herbal medicines for joint symptoms at a Kampo specialtyhospital

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Conflict of interest: None

[Objectives] Our hospital is rheumatology specialty facility certified by the Japan Rheumatology Association, and has been certified as a Kampo specialty facility by the Japan Society of Oriental Medicine in 1977. In this study, we conducted a retrospective study on the status of Kampo prescriptions by Kampo specialists at our hospital for patients with joint symptoms. [Methods] We extracted cases of Kampo medicines prescribed for joint symptoms at our hospital from April 1, 2023 to March 31, 2024, and investigated the contents of the Kampo prescription, concomitant medications, age, gender, disease name, etc. [Results] The common diseases for which Kampo medicines were prescribed for joint symptoms were osteoarthritis, rheumatoid arthritis (RA), collagen diseases other than RA, osteoporosis, shoulder periarthritis, and spinal diseases. The common Kampo medicines were Boiogi-to, Etsupikajutsuto, Sokeikaketsuto. Kampo prescriptions for RA patients are often started before the introduction of Western medicine. [Conclusion] This study indicated that in the hospital which provides integrated medical care combining Eastern and Western medicine there is a wide range of options for treatment depending on the patient´s disease and joint symptoms.

P1-102

Reduction and Stoppage of DMARDs in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The development of DMARs made life and functional prognosis better. Patients with rheumatoid arthritis got live longer. The population of over 80 years old is increasing in our town and accounts for 12.16% of the total population which is higher than Niigata Prefecture's 11.81%. The proportion of rheumatoid arthritis patients over 80 years old exceeds 13% in our hospital. We often reduce or discontinue DMARs In daily medical treatment because of the elder patient's reduced physical function and comorbidities. By identifying trends based on the reasons and content of changes, treatment strategies adapted to the aging population can be developed. [Methods] We investigated the reasons for and contents of changes in cases in which DMARDs were changed, reduced in dose, or discontinued in elder patients treated at our hospital. [Results] The reasons for the change were often physical, such as a decline in phyasicl function or comorbidities. However, there were also social reasons, such as worsening economic conditions due to bereavement and admission to a nursing home with drug restrictions. [Conclusion] In order to provide the appropriate treatment, it is necessary to not only understand the general health condition but also living environment, and treat the patient holistically.

P1-103

Bone marrow suppression after gold aurothiomalate administration in a patient with rheumatoid arthritis

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Conflict of interest: None

[Case] A 57-year-old male with RA on MTX + IGU + TCZ s.c., experienced increased disease activity after MTX discontinuation due to fatigue. LEF was added, and TCZ was switched to ETN-BS, but it was ineffective. SAR was started, but disease activity remained high, and PSL 10 mg was added. The patient was then hospitalized with pyothorax. SAR was discontinued, and drainage was required even after discharge. LEF was resumed and SASP was added, but disease activity remained high with TJC (28) 11, SJC (28) 17, and CRP 11.47 mg/dL. Due to a heightened susceptibility to infection, GST was started, administering 10 mg and 25 mg on October 26 and November 5, respectively. On November 19, the patient was admitted to the hospital due to multiple stomatitis, leukopenia and anemia. Suspecting a drug adverse event, GST, LEF, and SASP were discontinued. G-CSF, antibiotics, and cholestyramine were administered. His myelosuppression improved. However, due to worsening RA, PSL was increased to 15 mg. [Discussion] LEF had been used for several years, and SASP was resumed without similar events, suggesting GST as the likely contributor. However, doubts remain given that GST was administered only twice. [Conclusion] GST may cause myelosuppression even shortly after initiation, and close monitoring is advised.

P1-104

A case of age-onset rheumatoid arthritis (RA) developed with rheumatic polymyalgia (PMR)-like symptoms in which tacrolimus was successful

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Conflict of interest: None

Case: An 82-year-old man. An elderly man with diabetes. Pain in both shoulders appeared from April X year. The pain gradually worsened, and the pain joints expanded. In May, there was an exacerbation of CRP. The diagnosis PMR was made and 20 mg of prednin (PSL) was started on the same day. His symptoms did not improve, and he was referred to our hospital. Pain in both shoulders and knees was observed, and symptoms of stiffness in both hands were observed. Blood tests showed high levels of CRP and a positive level of rheumatoid factor (RF). A hand-contrast MRI was performed. Since the findings were consistent with synovitis, the diagnosis was changed from PMR to RA. In addition to PSL 20 mg, Tac was added. Symptoms began to improve, and CRP was found in blood tests. Due to the pain, he was unable to move on his own, but his pain improved, so he began tapering off his PSL. Discussion: A case in which a patient was treated with PSL for PMR, but the diagnosis was changed to RA. Due to pain and high CRP levels, PSL reduction was not possible, but with the Tac, symptoms improved quickly and PSL was gradually reduced. DMARDs are usually said to have no immediate effect, but this was a case where symptoms could be quickly improved by adding them to PSL that has been used.

P1-105

Comparative study of JAK Inhibitor retention rates for difficult-to-treat RA (D2TRA) and non-D2TRA

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Conflict of interest: None

[Objectives] To compare the retention rates of D2TRA and non-D2TRA JAK inhibitors in clinical practice. [Methods] We divided RA patients treated with JAK inhibitors at our institution from May 2014 to July 2023 into D2TRA and non-D2TRA groups and compared the retention rates of the two groups. [Results] A total of 257 patients (TOF 40, BAR 123, PEF 7, FIL 30, UPA 57) were treated with JAK inhibitors. Of these, 51 patients were in the D2TRA group and 206 patients were in the non-D2TRA group. In comparison of patient backgrounds, the D2TRA group was significantly younger than the non-D2TRA group ($p=0.016$), and had a higher RF positivity rate ($p<0.001$) and anti-CCP antibody positivity rate ($p<0.001$). Between the two groups, drug retention rates and cumulative discontinuation rates due to adverse events did not differ, but cumulative discontinuation rates due to lack of efficacy were significantly higher in the D2TRA group ($p=0.025$). That trend was observed in the pan-JAK inhibitor group, including TOF, BAR, and PEF ($p=0.016$), but not in the selective JAK1 inhibitor group, including FIL and UPA. [Conclusion] The discontinuation rate of JAK inhibitors due to lack of efficacy is high in D2TRA, but this trend may not be seen with selective JAK1 inhibitors.

P1-106

Possibility of early initiation and early dose reduction of JAK inhibitors for rheumatoid arthritis

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Conflict of interest: None

[Objectives] This study aimed to determine whether early introduction of a JAK inhibitor in rheumatoid arthritis (RA) patients can effectively control disease activity and facilitate dose reduction. [Methods] We enrolled 181 patients with inadequately controlled RA (132 women, 49 men; average age 75.2 years). Patients received various JAK inhibitors: 21 TOF, 45 BAR, 9 PEF, 15 UPA, and 91 FIL. Treatment commenced at a normal dose, with active dose reduction if disease activity reached low levels. We performed multivariate analysis on 61 patients who reduced their dosage compared to 120 who maintained normal dosing. [Results] Shorter intervals from RA onset to treatment initiation and no prior biological agent use were associated with successful dose reduction. In those starting within 6 months, the Clinical Disease Activity Index (CDAI) improved from 13.5 to 3.8 after 3 months; in those starting later, improvement was from 13.2 to 5.2. Notably, 48% of the early treatment group reduced their dose versus 23% of the later group. [Conclusion] Early JAK inhibitor initiation within 6 months of RA onset significantly improves disease activity and increases the likelihood of dose reduction, underscoring the need for prompt intervention in RA management.

P1-107

A prospective study of treatment outcomes in RA patients who required a switch between tsDMARDs

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Conflict of interest: None

[Objectives] Although the efficacy and safety of various targeted synthetic DMARDs (tsDMARDs) for rheumatoid arthritis (RA) are considered to be broadly equivalent, reports on the outcomes of switching from one tsDMARD to another remain limited. The aim of this study was to evaluate the efficacy of switching tsDMARDs in order to determine an optimal treatment strategy. [Methods] We analysed 67 RA patients who switched tsDMARDs due to poor disease control between 2017 and 2024. For patients who switched, we assessed the proportion who achieved a good or moderate response according to EULAR response criteria 6 months after switching, with DAS28-CRP improvement indicating a positive response. [Results] Of the 44 patients who switched due to inadequate disease control, 64.4% showed improvement in disease activity. The breakdown of improvement by switched type was as follows TOF→BAR, 42.9% (10 cases); TOF→PEF, 100% (1 case); TOF→UPA, 100% (3 cases); BAR→UPA, 75.0% (39 cases); BAR→FIL, 50% (6 cases); PEF→BAR, 0% (1 case); PEF→UPA, 100% (3 cases); PEF→FIL, 0% (2 cases) and FIL→TOF, 100% (1 case). [Conclusion] Switching between tsDMARDs resulted in a reduction in disease activity. Further research is warranted to elucidate the impact of different tsDMARD choices on treatment outcomes.

P1-108

Ultrasonographic evaluation of JAK inhibitor and TNF antagonist therapy in BIO-JAK naïve patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] To evaluate the clinical efficacy of JAK inhibitor (JAK) and TNF antagonist (TCZ) therapy in patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used JAK and TNF treated 22 and 45 RA patients. We evaluated the improvement of gray scale (GS) and power doppler (PD) score from baseline to week 52. [Results] In the patients receiving JAK (n=22) and TNF (n=45), the mean age was 55.4 vs 52.4 years old (p=0.509), disease duration was 7.9 vs 5.6 years (p=0.543), the mean MTX dose was 8.2 vs 10.2 mg/w (p=0.178), the rate of MTX administration was 73% vs 82% (p=0.369), DAS28-ESR was 5.20 vs 4.65 (p=0.025), GS score was 27.0 vs 17.9 (p=0.051) and PD score was 18.2 vs 11.3 (p=0.141). The respective changes in GS and PD score after 4 weeks were as follows: GS: -9.2 vs -4.8 (p=0.201) and -10.4 vs -3.5 (p=0.030). The respective changes in GS and PD score after 12 weeks were as follows: -14.3 vs -6.8 (p=0.070 and -12.5 vs -5.6 (p=0.058). The respective changes in GS and PD score after 24 weeks were as follows: -17.0 vs -9.5 (p=0.115) and -15.1 vs -7.6 (p=0.013). [Conclusion] The present study suggest that JAK inhibitors have an early and strong anti-inflammatory effect on synovitis.

P1-109

Safety analysis of JAK inhibitors in real-world clinical trials: including subgroup analysis of patients aged 65 years or older and those with risk factors for cardiovascular events

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Conflict of interest: None

[Objectives] This study analyzed the administration of JAK inhibitors and the occurrence of side effects in clinical practice. [Methods] 31 patients were treated with tofacitinib, 191 with baricitinib, 143 with upadacitinib, and 42 with filgotinib, for a total of 406 patients. In addition, a subgroup analysis was performed on 242 patients with risk factors for cardiovascular events (age 65 or older, smoking history, diabetes, obesity, hypertension). [Results] There were 4 cases of MACE with an incidence rate of 0.4/100 person-years. There were 15 cases of malignant tumors, and pre-administration screening combining CT and gastrointestinal examinations significantly reduced the incidence of malignant tumors within one year of JAK inhibitor administration (p<0.0001). There was 35 cases of herpes zoster, 5.5/100 person-years. There were two deaths during JAK inhibitor administration, one sudden death and one fatal myocardial infarction. Both patients had a history of steroid administration of 30 mg/day or more of prednisolone equivalent. [Conclusion] It was suggested that the occurrence of side effects can be reduced by thoroughly evaluating risk factors, including malignant tumor screening, before administration and avoiding administration to at-risk patients.

P1-110

Treatment Trends in Rheumatoid Arthritis following 1st JAK Inhibitor Failure

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Conflict of interest: None

[Objective] To evaluate treatment trends, including JAK rotation, in RA patients who experienced failure with 1st JAK inhibitor. [Methods] This was a single-center, retrospective cohort study. RA patients with a history of JAK inhibitor use were included in the analysis. [Results] All 120 patients included. The median age was 69 years, the median disease duration was 55 months, and 71 (59%) had a history of b/tsDMARDs use. The median duration of JAK inhibitor exposure was 22 months. At the last follow-up, 108 (84%) remained on JAK treatment: 1st JAK in 66 (55%), 2nd in 26, 3rd in 8, and 4th in 1. The retention rate for the 1st JAK inhibitor was 87% for Upadacitinib (13/15; median exposure: 27 months), 80% for Filgotinib (10/12; 12 months), and 53% for Baricitinib (39/74; 13 months). 1st JAK failure occurred in 54 cases, primarily due to inefficacy. Of these, 42 patients switched to 2nd JAK inhibitor. The retention rate for the 2nd JAK inhibitor was 88% for Filgotinib (7/8; 14 months), 74% for Upadacitinib (14/19; 9 months), and 36% for Baricitinib (5/14; 20 months). [Conclusions] More than half of RA patients with a history of JAK inhibitor use continued 1st JAK treatment. JAK rotation was more common than switching to other bDMARDs following 1st JAK failure in our clinical settings.

P1-111

Use of JAK inhibitor (JAKi)s and prevention of pneumocystis pneumonia (PCP) and herpes zoster (HZ) in our hospital

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Conflict of interest: None

[Background] Treatment of RA has advanced markedly in the last 20+ years. We now have a variety of weapons in our arsenal. In Japan, MTX was approved in 1999. In 2003, first biologics became available, bringing the total to 9. In 2013, the first JAKi were approved, we now have 5 available. In our hospital, among the 5 JAKi, Baricitinib (BAR: B), Upadacitinib (UPA: U), and Filgotinib (FIL: F) are used in the majority of patients. In this issue we summarized use of the 3. [Methods] Data were compiled based on a retrospective review of medical records. [Results] BAR was introduced to 126 patients, UPA to 102, and FIL to 98. The starting dose was 15 mg in more than 95% of UPA patients, but about half of BARI and

FIL patients were started at half dose due to concerns about renal function and risk due to advanced age. Continuation rates at 12 months were similar (B 69.8%, U 75.5%, F 71.5%), but at 24 months, were highest for UPA (B 60.3%, U 73.6%, F 60.2%). The incidence of adverse events was the same. Of all 3 formulations, PCP prophylaxis was provided in more than 70%, and Singrix vaccination for HZ prophylaxis was in more than 20%. [Discussion] The high retention rate of UPA may be attributed not only to its high efficacy, but also to the fact that it is initiated at a sufficient dose.

P1-112

A study of the efficacy and continuation rate of dose reduction of JAK inhibitors in elderly rheumatoid arthritis patients without impaired renal function: the ANSWER cohort study

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Conflict of interest: None

[Objectives] This study aims to examine the effects and continuation rates of JAK inhibitors when administered at a reduced dose to elderly rheumatoid arthritis (RA) patients without renal impairment. [Methods] We focused on 296 RA patients aged 65 and older with an eGFR of 60 mL/min/1.73 m^2 or higher who started JAK inhibitors. For those who continued treatment for six months, we performed propensity score matching between 166 patients on full-dose group and 39 patients on reduced-dose group. After matching, each group had 33 patients, and we compared CRP, CDAI, mHAQ, MMP-3, glucocorticoid dosage, and MTX dosage six months post-treatment initiation, as well as baseline changes in CRP, CDAI, mHAQ, and MMP-3. We also analyzed reasons for discontinuation for those who stopped treatment within six months. [Results] Among patients who continued treatment, the reduced-dose group had significantly higher CRP levels but no significant differences in CDAI, mHAQ, MMP-3, glucocorticoid, or MTX dosages. Additionally, there were no significant differences in baseline changes. The reduced-dose group had a higher proportion of discontinuations due to adverse events compared to the full-dose group. [Conclusion] JAK inhibitors should generally be administered at the standard prescribed dose.

P1-113

Upadacitinib Therapy-associated Virus-associated Hemophagocytic Syndrome: A Case Report

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Conflict of interest: None

A 63-year-old man with rheumatoid arthritis (RA), initially managed successfully with methotrexate and adalimumab, experienced a flare-up in October 2023. Despite a change in bDMARDs, symptoms persisted, prompting a switch to upadacitinib in January 2024, which restored remission. In July 2024, he presented with fever and malaise. Lab results revealed pancytopenia, elevated LDH, and high ferritin levels, all suggesting hemophagocytic syndrome (HPS). EBV DNA was detected, with a significantly high C7-HRP. Bone marrow and skin biopsies showed no malignancy. He was diagnosed with secondary HPS due to viral infection and treated with ganciclovir, leading to marked improvement and discharge on day 24. While reactivation of herpes zoster is known with JAK inhibitors (e.g., upadacitinib), reports of HPS linked to other herpesviruses like EBV are limited. This case highlights the need to consider viral reactivation in patients on JAK inhibitors who develop HPS symptoms, enhancing clinical vigilance and response.

P1-114

Comparative Study of Short-Term Outcomes of AVANTA and INTEGRA MCP Joint Arthroplasty

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Conflict of interest: None

[Objectives] AVANTA has shown a high rate of early postoperative failure, prompting us to evaluate the short-term outcomes of AVANTA and INTEGRA prostheses. [Methods] From June 2005 to March 2024, MCP joint arthroplasties using either AVANTA or INTEGRA were performed in our hospital, followed by postoperative rehabilitation with preoperative and 6-month postoperative finger extension and flexion angles evaluated. [Results] The AVANTA group (Group A) included 59 patients 72 hands, 236 fingers, while the INTEGRA group (Group I) included 22 patients 22 hands, 64 fingers. The average preoperative MP joint range of motion was as follows: Group A and I: extension -33.6°/-55.2°, flexion 69.6°/84.3°, range of motion 36.0°/ 29.0°, with Group I showing a significantly greater tendency toward flexion, though no significant difference in total range of motion was observed. Postoperatively, Group A and I: extension -7.1°/-8.8°, flexion 63.6°/71°, range of motion 56.6°/ 62.2°, with no significant differences. [Conclusion]: The study results indicate that INTEGRA prostheses achieved a similar range of motion to AVANTA, with no early postoperative failures observed. However, further investigation with long-term follow-up and a larger sample size is required.

P1-115

A case of functional reconstruction for severe Jaccoud deformity in both hands

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Conflict of interest: None

A 36-year-old woman, who developed SLE at the age of 23. The thumb and fingers in both hands were severely deformed, and she was unable to spread her fingers or play rock-paper-scissors or wash her face. On the right hand, Swanson implant was able to insert only at the 2nd MPj, however fusion had to done at the 3rd, 4th and 5th MPjs, due to severe myostatic contracture of the flexor digitorum profundus. On the left hand, the operation was divided into two stages. First, on the thumb, suspensionplasty (Thompson) at the CMj and fusion at the MP joint were performed. Two weeks later, Swanson implant arthroplasty was performed at the 2nd thru 5th MPjs, and modified Thompson-Littler method was performed at the 5th PIPj. After the operation, the patient was greatly satisfied with the appearance of the hand and the number of ADL that the patient was able to do without help increased. For further postoperative improvement, the operation should be performed before severe dislocation and joint contracture occur in the thumb and fingers.

P1-116

Non-union and Plate Breakage in a Distal Radial Shaft Fracture After Sauve-Kapandji Procedure in a Patient with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Distal radial shaft fractures post-Sauve-Kapandji (SK) surgery are rare, and instances of plate failure post-fixation are undocumented. This report evaluates factors in plate failure after SK surgery. [Case] An 84-year-old female with rheumatoid arthritis (RA), diagnosed in X-19 and managed with methotrexate 4 mg/week, underwent right SK surgery in X-13, achieving bone fusion. In March X, she sustained a distal radial shaft fracture due to a fall. Open reduction and plate fixation were performed, followed by two weeks of forearm splinting and non-weight-bearing restrictions. Due to solitary living, right-hand use was occasionally unavoidable. Progressive bone resorption developed, and in late July, after twisting a bottle cap, she experienced severe wrist pain. Radiography confirmed plate breakage, necessitating revision surgery with iliac grafting and teriparatide therapy. [Discussion] In patients with RA, bone resorption may be augmented by inflammatory cytokines, even in non-articular regions. In this case, local inflammatory responses and osteoporosis likely contributed to non-union. [Conclusion] Osteoporosis and localized inflammation may impede fracture healing in RA, with accelerated resorption intensifying mechanical stress on plates, leading to failure.

P1-117

Reconstruction of hand and wrist deformities in Blau syndrome: A case report

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Conflict of interest: None

We herein report a case of Blau syndrome in which hand and wrist deformities were reconstructed to improve functional ability. A 58-year-old woman was diagnosed with Blau syndrome at the age of 50 years, but it was suspected that the symptoms had begun in her 10s. Medical examination by a qualified hand surgeon at the age of 51 years revealed ulnar drift, adduction contracture of the thumb, and buttonhole (BH) deformity of the ring finger of her right hand and erosive deformity of the distal radioulnar joint and BH deformity of the middle and ring fingers of her left hand. Although she initially declined to undergo surgical treatment due to family circumstances, she agreed for tendon reconstruction after her extensor tendon ruptured at the age of 55 years. After satisfactory surgery, she agreed for surgical reconstruction of the BH deformity of her middle and ring fingers of the left hand 4 months later, partial arthrodesis of the carpus and ulnar-head resection of the right wrist at the age of 56 years, and reconstruction of the BH deformity of her ring finger of the right hand. In our experience, surgical reconstruction should be performed timely before osseocartilaginous deformity progression in Blau syndrome.

P1-118

Report of surgical treatment of 3 patients with RA with wrist joint dysfunction

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Conflict of interest: None

In the treatment of rheumatoid arthritis (RA), wrist dysfunction is an important factor that directly impacts daily activities, making early functional improvement essential. Therefore, in cases with significant functional impairment, early surgical intervention should also be considered. Here, we report on three cases of RA patients with monoarthritis limited to the wrist joint who required early surgical treatment after pharmacological intervention. All cases were referred to our hospital with monoarthritis of the wrist. MRI images revealed synovitis in the wrist and extensive edema in the carpal bones. Methotrexate (MTX) therapy was initiated immediately. Although blood tests showed negative inflammatory markers three months after treatment initiation, local symptoms in the wrist showed minimal improvement, leading to wrist surgery. Postoperative outcomes were favorable in all cases, with confirmed pain improvement. In cases of RA presenting with monoarthritis, even when pharmacological treatment results in negative inflammatory markers in biochemical tests, some cases still exhibit persistent local arthritis. For such cases, rather than continuing conservative treatment indefinitely, active consideration of surgical intervention may be beneficial.

P1-119

Study of SAPHO Syndrome with Refractory Skull and Jaw Osteitis

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Conflict of interest: None

We report three cases of SAPHO syndrome with refractory aseptic osteitis of the skull and jaw. **Case 1:** A 20-year-old woman with no acne or palmoplantar pustulosis experienced left-sided temporal pain and fever for 7 years. MRI showed left temporal dura mater thickening and bone scintigraphy revealed the involvement of the left temporal bone, sternoclavicular joints, and right sacroiliac joint. She was diagnosed with SAPHO syndrome, and her symptoms improved with tofacitinib. **Case 2:** A 34-year-old woman with acne but no pustulosis experienced right mandibular pain and swelling for three years. Despite tooth extraction, her condition worsened, and CT showed bone resorption in the mandible. Bone scintigraphy confirmed SAPHO syndrome, and her symptoms improved with baricitinib and denosumab. **Case 3:** A 69-year-old man experienced mandibular pain for over 10 years. CT showed diffuse bone sclerosis and resorption. Bone scintigraphy revealed the involvement of both mandibles and the sternoclavicular joint. He was diagnosed with SAPHO syndrome, and treatment with denosumab, prednisolone, and tacrolimus improved his condition. **Clinical Significance:** Bone scintigraphy may be useful for diagnosing multiple aseptic osteonecrosis, including asymptomatic cases caused by SAPHO syndrome.

P1-120

Examination of clinical features and treatment of patients with sternoclavicular arthritis

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Conflict of interest: None

[Objectives] Sternoclavicular arthritis (SCJ) is a characteristic joint symptom of SAPHO syndrome and palmoplantar pustular arthritis (PAO). but there are also cases where skin symptoms are not clear and cases are associated with rheumatoid arthritis, although it is less frequent. [Methods] We analyzed the clinical course and imaging findings (MRI, CT and Ultrasonography) of 14 patients with sternoclavicular arthritis (SCJ). [Methods] Average age 68±12, male/female2/12, anterior chest pain due to SCJ arthritis was measured on the VAS scale. MRI, CT, joint ultrasonography findings and post-treatment changes were measured. [Results] Eight cases of palmoplantar pustular arthritis (PAO). There were 2 cases of SAPHO syndrome, 3 cases with axial-spondyloarthritis, 1 case of rheumatoid arthritis, and 1 case of unknown cause. In PAO, subjective symptoms were significantly improved by anti-IL-23 antibody preparations (risankizumab). Patients with spondyloarthritis were dramatically improved by anti-IL-17 preparations (secukinumab). We also found cases in which JAK inhibitors (upadacitinib), anti-TNF inhibitors (golimumab), and MTX were effective. [Conclusion] The pathophysiology of SJC is diverse, and it is important to search for the cause and select a drug.

P1-121

Clinical Characteristics of Spondyloarthritis Patients with Coexisting Interstitial Lung Disease

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Conflict of interest: None

[Background] Spondyloarthritis (SpA) can be complicated by interstitial lung disease (ILD), potentially affecting treatment approaches, though details remain unclear. [Objective] To elucidate clinical characteristics of SpA patients with concurrent ILD. [Methods] We studied 552 SpA patients (293 male/259 female) with >1 year follow-up since April 2015 at our hospital. A retrospective chart review was conducted for ILD cases. [Results] Mean age at initial visit was 52.3 years. SpA cases included: PsA 437, PAO 91, AS 16, others 12. ILD was present in 14 cases (3.2%): 6 collagen disease-associated (43%), 4 drug-induced (28.5%), and 4 unknown cause (28.5%). Collagen diseases comprised RA (3), SSc (2), and SjS (1). Drug-induced cases were from MTX (3) and TNF inhibitors (1). The MTX-ILD cases developed within months, showed pre-symptomatic KL-6 elevation, and occurred in males >70 years with diabetes and ACPA positivity. [Discussion and Conclusion] With nearly half of ILD cases linked to collagen diseases, screening is essential when ILD develops. MTX-ILD cases shared risk factors reported in RA (elderly age, diabetes), suggesting careful MTX administration in SpA. Male gender, ACPA positivity, and early KL-6 elevation were common features.

P1-122

Extremities arthritis in palmoplantar pustulosis osteoarthritis

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Conflict of interest: None

Palmoplantar osteoarthritis (PAO) most commonly involves the anterior thoracic region, but is occasionally associated with arthritis of the extremities. [Objectives] To investigate arthritis of the extremities in patients with PAO. [Methods] Twelve patients with PAO attending our department were studied. [Results] All patients were female, mean age 59 years, and had PAO for a mean of 7.5 years. At the time of initial examination, 66.7% had pain in the anterior chest, 25% in the spine, 8.3% in the pelvis, and 33.3% (2 shoulder, 2 knee, 1 hip, and 1 ankle) in the extremities. Three patients were treated with SASP, five with MTX, and three with biologics (guselkumab, adalimumab, risankizumab), with a mean BASDAI of 1.58 at last follow-up. Two patients had persistent limb arthritis, one had persistent arthritis and had undergone bilateral TKA 10 years after onset and left THA 14 years, with persistent right hip arthritis to date. [Conclusion] It has been reported that arthritis of the extremities occurs in approximately 30% of patients with osteoarthritis, but only two cases we were able to negotiate resulted in joint replacement surgery. In the rare cases of persistent arthritis, bone destruction may occur, and it is necessary to consider treatment methods to control arthritis.

P1-123

Treatment results for inflammatory lower back pain 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.

P1-124

A Case of Protein-Losing Enteropathy Associated with Systemic Lupus Erythematosus identified Following the Onset of Superior Mesenteric Artery Thrombosis

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Conflict of interest: None

About six weeks prior to X Day, 51-year-old male developed diarrhea and severe abdominal pain. Four weeks prior, the abdominal pain worsened and he was hospitalized at the previous hospital. CT scans revealed a thrombus at the root of the SMA, considered the cause of the abdominal pain, and he was treated with fasting. It was also found that he had hypoalbuminemia, hypocomplementemia, and tested positive for antinuclear, anti-Sm, and anti-RNP antibodies. He was referred to our department on X Day and admitted. He had neither nephrotic syndrome nor liver cirrhosis, and Tc-HSA scintigraphy demonstrated accumulation throughout his intestine, leading to a diagnosis of PLE, and treatment with PSL and IVCY was started. He didn't meet the criteria for APS, so the thrombosis was attributed to PLE and clopidogrel and pitavastatin were also started since he had arterial thrombosis. Over the course of treatment, the pain improved and serum albumin levels increased. Seven months after admission, we confirmed the thrombosis have resolved. It is known that many cases of PLE present with thrombotic complications, with both venous and arterial thromboses potentially occurring. In cases of thrombosis in SLE patients, it is essential to consider the possible coexistence of PLE, as well as APS.

P1-125

A Case of Diffuse Large B-cell Lymphoma Presenting as Protein-Losing Enteropathy during Treatment for Systemic Lupus Erythematosus

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Conflict of interest: None

Case: A 38-year-old woman. She developed proteinuria at the age of 13, and few years later she was diagnosed with systemic lupus erythematosus (SLE) on the basis of butterfly erythema, Raynaud's phenomenon and positive anti-dsDNA antibodies. Renal pathology revealed lupus nephritis (type IV+V). She was maintained in remission with prednisolone, tacrolimus and mycophenolate mofetil. Six months before admission, she developed iron deficiency anemia and abdominal pain, with her symptoms progressively worsening. Suspecting lupus enteritis, she was hospitalized after contrast-enhanced CT showed small bowel wall edema. She was diagnosis with protein-losing enteropathy (PLE) secondary to SLE as evidenced by hypoalbuminemia, white villi on endoscopy and protein leak scintigraphy. High-dose glucocorticoids and cyclophosphamide pulses were initiated. After two months of treatment, persistent hypoalbuminemia and unresolved bowel edema prompted a small bowel biopsy, which confirmed the diagnosis of diffuse large B-cell lymphoma (DLBCL). Her symptoms improved with R-CHOP therapy. Clinical significance: The presentation of DLBCL with PLE is extremely rare. SLE is a risk factor for DLBCL, and if PLE associated with SLE failed to respond to treatment, DLBCL should be considered.

P1-126

A case of diverticulitis and peritonitis that was difficult to differentiate from intestinal lupus

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Conflict of interest: None

66-year-old female She developed systemic lupus erythematosus (SLE) in 1996 with the manifestations of thrombocytopenia, pericarditis, and nephritis. Remission induction was attempted with cyclophosphamide and tacrolimus for nephritis, but renal function worsened. Hemodialysis was initiated in 2014. Most recently, disease activity, including anti-dsDNA antibodies and complement, had settled down with 3 mg of tacrolimus. Two days before admission, she came to the hospital because of recurrent abdominal pain upon defecation, bloody stools, and vomiting. She was suspected to have ischemic enterocolitis and was admitted to the hospital. After admission, the abdominal pain worsened, and shock vitals and signs of peritoneal irritation appeared. A contrast-enhanced CT scan showed edema of the transverse to descending colon and increased lipid intensity. Exploratory laparotomy revealed stool protruding through the intestine to the mesenteric side. After cleaning the abdominal cavity, rectal amputation and stoma construction were performed. In patients with SLE, it is important to differentiate between generalized acute abdomen and intestinal lupus, but sometimes an invasive procedure may be necessary to make the diagnosis. We report the course of this case with a review of the literature.

P1-127

A Case of Systemic Lupus Erythematosus (SLE) Complicated by Manganese Poisoning-Related Parkinsonism Due to Intrahepatic Portosystemic Shunt

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Conflict of interest: None

A 49-year-old woman developed right finger joint pain in June of year X and tested positive for antinuclear antibodies at a titer of 160 at a local clinic. She was referred to our department but showed no other symptoms, so she was placed under observation. In spring of year X+2, she experienced persistent fatigue and returned for follow-up in August. Based on the 2019 SLE classification criteria, she met the diagnostic threshold with elevated ANA, leukopenia, arthralgia, oral ulcers, and decreased serum C3, totaling 14 points. Treatment with prednisolone 20 mg/day and hydroxychloroquine was initiated, leading to symptom improvement. However, on September 16, she was admitted for severe fatigue and difficulty moving. Brain MRI revealed high T1-weighted signals in the bilateral globus pallidus and substantia nigra, initially suggestive of hepatic encephalopathy, which was ruled out. Elevated serum manganese levels indicated manganese poisoning due to an intrahepatic portosystemic shunt. After referral to neurology, she was diagnosed with manganese poisoning-related parkinsonism. Chelation therapy resolved her fatigue, normalized serum manganese, and significantly reduced MRI signal abnormalities. This rare case is reported with a review of the literature.

P1-128

An autopsy case of systemic lupus erythematosus in which the evaluation of disease activity was difficult due to complications of liver cirrhosis

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Conflict of interest: None

[Case] A 65-year-old woman was diagnosed with SLE based on the presence of antinuclear and anti-Sm antibodies, pancytopenia, and hypocomplementemia. Despite receiving treatment with glucocorticoids, hydroxychloroquine, tacrolimus, and belimumab, her symptoms did not improve sufficiently, and she newly developed impaired consciousness and ascites. An analysis of the cerebrospinal and ascitic fluid ruled out central nervous system manifestations and serositis related to SLE. However, abdominal ultrasonography revealed hepatic atrophy and portal vein thrombosis. She was treated with anticoagulants, but she developed a perforated gastric ulcer which led to her death. The autopsy revealed the acute peritonitis due to perforation of a cytomegalovirus-associated gastric ulcer, which was identified as the immediate cause of death. Additionally, the autopsy also revealed the histopathological diagnosis of liver cirrhosis and portal vein thrombosis. [Discussion] The autopsy showed that the cause of the liver cirrhosis was alcoholic and that the portal congestion led to the portal vein thrombosis. Since liver cirrhosis and SLE cause similar clinical manifestations, we should take care to accurately evaluate the disease activity of SLE in patients with SLE complicated by liver cirrhosis.

P1-129

A case of prominent liver damage during treatment of systemic lupus erythematosus

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Conflict of interest: None

(Case) A 50-year-old-female was referred to our hospital due to a fever. Before X-15 years, she was diagnosed with systemic lupus erythematosus (SLE) and had been treated with glucocorticoids (GC) until X-10 years. In August X, she was referred to our hospital due to fever and fatigue. She had 39°C and dry mouth, multiple lymphadenoma. Laboratory data showed leukocytopenia, ANA 320x (homo), anti-DNA Ab 16 IU/mL, anti-Sm Ab positive, and hypocomplementemia, fulfilling the classification criteria for SLE. She was treated with PSL 20 mg. After one week, she was admitted to our hospital for examination due to elevated AST 694 U/L, ALT 247 U/L, and CRP 1.5 mg/dL to discriminate for macrophage activation syndrome and other disease (day 0). On admission, serum levels ferritin 3138 ng/mL and sIl-2R 854 U/mL. Liver biopsy was performed on day 6. Pathology showed lymphocytic infiltrate in portal area, but no hemophagocytic evidence. She was diagnosed with lupus hepatitis. PSL was increased to 35 mg and HCQ was added. She was discharged on day 35 after liver enzymes improved. (Clinical significance) Elevated liver enzymes in patients with SLE is reported to be about 50%, considered to cause by multiple pathological conditions. Liver enzyme abnormalities in SLE should be considered for liver biopsy.

P1-130

A case of systemic lupus erythematosus (SLE) caused by dilated cardiomyopathy (DCM)-like myocarditis

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Conflict of interest: None

[Case] 29-year-old male [Chief complaint] dyspnea [Medical history] He had a fever in February, and in March, cough appeared. In April, he went to a local doctor because of dyspnea. Progress] He had positive for antinuclear antibodies and anti-dsDNA antibodies. Hypocomplementemia were observed, and a diagnosis of SLE was made. There was no CK-MB elevation. The pericardial effusion was relieved by steroid pulse, and prednisolone and mycophenolate mofetil started. His blood counts improved and proteinuria decreased. However, he had ventricular tachycardia and cardiac echocardiography showed no improvement in cardiac ejection fraction (EF). Because a delayed linear contrast image was observed in the middle myocardium, DCM was suspected. Cardioprotective drugs were started. Because of improvement in EF, it showed that he did not have idiopathic DCM but DCM-like myocarditis caused by SLE. [Clinical Significance] There are few reports of acute myocarditis as the initial manifestation of SLE, and the negative CK-MB test results made it difficult to detect myocarditis. We report this case as a valuable example of a patient who was thought to have only pericarditis, but who was detected with a longitudinal cardiac Echo, which could point out the presence of potential myocarditis.

P1-131

A case of Libman Sacks endocarditis complicated by SLE and APS diagnosed and followed up by transthoracic echocardiography

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Conflict of interest: None

[Case] A 31-year-old woman developed SLE in her late teens and was treated with immunosuppressive therapy. Transthoracic echocardiography (TTE) in early August X (year) revealed vegetation adherent to the anterior and posterior apex of the mitral valve and mild mitral regurgitation (MR). Blood cultures were negative, and were determined to be noninfectious vegetation, leading to a diagnosis of Libman Sacks endocarditis. In May X+1, a renal biopsy revealed APS nephropathy and lupus nephritis type III, and the patient was started on warfarin and intensified treatment for SLE with mycophenolate mofetil and increased doses of glucocorticoids. TTE at the same period showed no significant change in vegetation, and MR was worsening. Subsequently, the SLE went into remission, and at TTE in September X+2, the vegetation disappeared and MR was almost improved. [Discussion] Libman Sacks endocarditis is a rare cardiac complication in patients with SLE and a risk factor for cerebral infarction and valvular heart disease. Although the detection rate of Libman Sacks endocarditis is low in TTE, in this case, TTE made the diagnosis, and the patient was followed up with periodic TTE for resolution of the vegetation and improvement of MR. We consider this case valuable, and we report it here.

P1-132

A case of systemic lupus erythematosus complicated by macrophage activation syndrome that led to irreversible cerebral edema and death after a half-day course

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Conflict of interest: None

A 29-year-old woman. Arthralgia appeared, and the following month she was admitted to her previous doctor for a close examination of fever, headache, chills, arthralgia, erythema in the cheeks, and loss of appetite. Suspecting collagen disease, she was transferred to our hospital and diagnosed with systemic lupus erythematosus (SLE). Blood tests suggested the possibility of macrophage activation syndrome (MAS), so she was given remission induction therapy, and her condition quickly improved. The patient's symptoms were stable thereafter, but on the 11th day of the illness, she developed fever again, and from the 12th day of the illness, her level of consciousness and blood pressure decreased, which was thought to be a relapse of MAS. On the morning CT scan of the 13th day, cerebral edema was mild, but on the noon CT scan of the same day, cerebral edema had progressed markedly, and MRA showed poor visualization of all the main arteries of the brain. Despite intensive treatment, the patient died on the 28th day. Although there have been scattered reports of MAS secondary to SLE, it is rare for a patient to develop irreversible disease in as little as half a day. It is important to recognize that there have been cases of fulminant disease in MAS secondary to SLE.

P1-133

A Case of Systemic Lupus Erythematosus Complicated by Catastrophic Antiphospholipid Syndrome (CAPS) Leading to Multiple Organ Failure

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Conflict of interest: None

A 74-year-old female with left hemiplegia from a right putaminal hemorrhage 12 years ago was independent in bathing and toileting before this illness. In June of Year X, she experienced loss of appetite and was diagnosed with dehydration at a local clinic in July. Two days later, she developed a fever, necessitating emergency hospitalization. Upon admission, she exhibited altered consciousness and became unable to take oral nutrition. Central venous nutrition was initiated, but renal function worsened, leading to her transfer to our facility for further evaluation. A 50 mm thrombus was found at the tip of her central venous catheter. She presented with livedo reticularis in both legs and blackening of the left fourth toe. Laboratory tests showed ANA 1:160, positive anti-dsDNA, decreased complement levels, and positivity for anti-cardiolipin and anti-cardiolipin β2GP1 antibodies. Diagnosed with CAPS due to SLE, she began glucocorticoids and heparin therapy. After initial improvement, consciousness declined again. Plasmapheresis was initiated, but she died from organ failure on day nine. Autopsy confirmed lupus nephritis. CAPS is characterized by systemic inflammation and microthrombi leading to organ dysfunction, underscoring the need for early intervention.

P1-134

A case of systemic lupus erythematosus (SLE) in a very elderly man with nephritis, hemophagocytic syndrome, and NPSLE as initial symptoms

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Conflict of interest: None

Background: SLE is prevalent in young women, but late-onset SLE is increasing. However, SLE in veryelderly men is extremely rare. Case: An 82-year-old man whose eldest son was being treated for SLE had been suffering from general fatigue for the past 12 months. He was admitted to the previous hospital one month ago due to anorexia. After admission, fever and difficulty communicating appeared. He was consulted to the immunology department of the same hospital because of pancytopenia and hypocomplementemia, and was transferred to our department. Anti-dsDNA antibody levels were 116.6 IU/mL, and he was diagnosed as SLE with nephritis based on abnormal urinalysis, hemophagocytic syndrome based on elevated ferritin levels and abnormal coagulation, and NPSLE based on elevated levels of cerebrospinal fluid IL-6. Steroid pulse therapy was administered on the second day, and his general fatigue, levels of consciousness, pancytopenia, and abnormal urinalysis improved. Clinical importance: Skin symptoms and high levels of anti-dsDNA antibodies are rare in late-onset SLE patients. In our case, typical serological findings allowed early diagnosis.

P1-135

A case of sensorineural hearing loss associated with Raynaud's phenomenon successfully treated with Celexipag

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Conflict of interest: None

(Case presentation) 36-year-old female. She was referred to our department after complaining of photosensitivity, oral ulcers, Raynaud's symptoms and systemic fatigue for X-17 years. Antinuclear antibodies (ANA) were 1:40, anti-DNA antibodies and anti-phospholipid antibodies were all negative, and no definitive diagnosis was made. In April X-6, she was admitted to the hospital because of a temperature rise to 37°C and general malaise and pain. Although ANA was elevated at 1:80, anti-DNA antibodies were negative and there was no complement depletion. For Raynaud's symptoms, she was started on sarpogrelate hydrochloride 100 mg/day and beraprost sodium 80 μg/day. Around July of X-6, she began to experience ear pain and sensorineural hearing loss. In X, fingertip scars and scleroderma was noted, leading to discontinuation of beraprost sodium and initiation of bosentan 125 mg/day, which was then discontinued due to persistent fever. She was then started on selexipag 0.4 mg/day, which resulted in a significant improvement in Raynaud's symptoms and hearing (mean hearing level: before selexipag introduction 66.2/64.7dB → after selexipag introduction 31.9/32.2dB). (Conclusion) We have experienced a case where selexipag was effective in hearing impairment associated with Raynaud's symptoms.

P1-136

A case of pericarditis associated with scleroderma responding to tocilizumab

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Conflict of interest: None

An 81-year-old woman visited to clinic 4 months ago because of anorexia and shortness of breath. She was referred to previous hospital because of pleural effusion and anemia. She was judged to have fluid retention due to anemia, and diuretics and blood transfusion were administered. This improved the pleural effusion, but pericardial fluid remained. She was referred to our hospital because two months ago she noticed stiffness of the hands and anti-RNA polymerase III antibody positivity was revealed. Subsequently, pericardiocentesis was performed, and inflammatory pericardial fluid was observed, leading to a diagnosis of pericarditis due to scleroderma. Massive pericardial fluid were targeted for treatment, but colchicine and mycophenolate mofetil (MMF) did not stop the increase of pericardial fluid. Therefore, tocilizumab (TCZ) infusion was administered and pericardial fluid decreased. Pericardial effusion in scleroderma is relatively common but is often asymptomatic, and large amounts of pericardial effusion are rare. This patient was at high risk for scleroderma renal crisis, so the treatment strategy was to avoid steroid therapy, and TCZ was effective. We report this case because we believe that experience in treating rare medical conditions should be shared.

P1-137

A case of anti-Th/To antibody-positive systemic sclerosis with interstitial pneumonia, treated with intravenous cyclophosphamide pulse therapy

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Conflict of interest: None

Case: A 68-year-old woman visited to local clinics because of chest discomfort in May, 2023. And then she was introduced to respiratory medicine, diagnosed as interstitial pneumonia. As a result of a close examination, she was pointed out usual interstitial pneumonia with partial organizing pneumonia. And antinuclear antibodies and anti Th/To antibodies were positive. She was followed up and finally introduced to our department in June, 2024, appeared with severe pain in the lower limbs, which made it difficult to visit the hospital. She complained of cough and dyspnea with dermatosclerosis of the fingers, high level of KL-6 (5113 U/mL), low level of %FVC (75.5%) and %DLCO (57.4%). MRI showed high intensity of T2-weighted images in the crural muscles. We diagnosed anti-Th/To antibody-positive systemic sclerosis with interstitial pneumonia. After the treatment with nintedanib and three courses of IVCY, level of KL-6 improved to 4770 U/mL, and her respiratory symptoms and X-ray findings also improved. We will continue up to 6 courses of IVCY. **Discussion:** Anti-Th/To antibody complicated with interstitial pneumonia and pulmonary hypertension, may become to be often severe and poor prognosis. In this case, we successfully treated withnintedanib and IVCY.

P1-138

Evaluation of Skin Thickening Changes in Systemic Sclerosis Using Skin Ultrasound Before and After Rituximab Administration

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Conflict of interest: None

[Objectives] Systemic sclerosis (SSc) is characterized by progressive fibrosis affecting skin and organs. While rituximab (RTX) has shown efficacy against skin sclerosis, mRSS relies on subjective assessment. Skin ultrasound (Skin-US) offers an objective, non-invasive method for skin thickness measurement. This study used Skin-US to evaluate RTX-induced changes in skin thickening in SSc patients. [Methods] Four SSc patients initiating RTX treatment were included. Skin thickness was measured using Skin-US at baseline, one week, 2-3 weeks, and three months. Measurement sites were the second fingers and dorsum of the hands, assessing epidermal/dermal and subcutaneous layers. mRSS was also used. [Results] A significant reduction in subcutaneous thickness was observed one week after RTX (baseline: 2.115±0.295 mm, one week: 1.998±0.276 mm, p=0.0097), sustained through three months. No change was noted in epidermal/dermal thickness (baseline: 0.347±0.040 mm, one week: 0.341± 0.053 mm, p=0.692). mRSS showed improvement in three patients after 2-3 weeks, with one patient unchanged. [Conclusion] Skin-US provides an objective tool for evaluating skin thickening in SSc, potentially detecting earlier changes than mRSS and suggesting its utility in monitoring therapeutic effects.

P1-139

Systemic sclerosis developed with limb edema after COVID-19 vaccination and was successfully treated with rituximab: A case report

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Conflict of interest: None

A 51-year-old woman with a history of type 2 diabetes mellitus noticed left axillary lymphadenopathy after receiving the COVID-19 vaccine. Approximately 3 weeks later, high grade fever developed, and a blood test performed showed a high CRP level and elevated ferritin. Symptoms alleviated with symptomatic treatment, but 6 weeks after vaccination, fever relapsed, and she was admitted to our hospital. CT scan revealed multiple lymph node swelling up to 26 mm in diameter. Left inguinal lymph node biopsy was performed for diagnosis. During hospitalization, the fever improved, and blood tests showed improvement in the inflammatory response. She was discharged and histopathological diagnosis revealed no malignant findings. Three months after vaccination, edema in the peripheral limbs and arthralgia appeared. No obvious findings were found in the search for the cause, and she was relieved with symptomatic treatment. However, she noticed difficulty in gripping her hands, and the skin sclerosis gradually spread from the fingers to the upper arms. With the positivity for anti-RNA polymerase III antibody, she was diagnosed with systemic sclerosis. Rituximab was started and the skin sclerosis improved with no worsening after 2 years of maintenance treatment.

P1-140

Clinical Characteristics by Graded Administration of Nintedanib at our hospital

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Conflict of interest: None

[Objectives] Although nintedanib can inhibit the decline of respiratory functions, it is sometimes discontinued for adverse events such as diarrhea. This study aims to clarify how graded administration of nintedanib affects clinical characteristics at our hospital. [Methods] We conducted a retrospective study of patients with CTD-ILD who started nintedanib between Oct 2020 and Sep 2024. 1) Background, 2) retention rate, and 3) respiratory functions were examined in the graded administration group. [Results] 1) The study included 75 patients. Among them, 45 were in the graded administration group and 30 in the non-graded group. The proportion of SSc-ILD was higher in the former group (25/45 vs. 10/30, p=0.0029).

2) The retention rate was higher (p=0.0328) and the duration of treatment was longer (p=0.0242) in the graded-administration group. 3) The rate of decrease in %VC per month did not differ between the two groups (-0.486 vs -0.412, p=0.4070). [Conclusion] The graded administration of nintedanib might induce better retention rate in patients with CTD.

P1-141

A retrospective study of systemic sclerosis patients treated with rituximab at our hospital

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Conflict of interest: None

[Objectives] To clarify the clinical characteristics suitable for RTX therapy and the effectiveness of RTX maintenance therapy for SSc, we reviewed the patient characteristics and clinical course of SSc patients treated with RTX at our hospital. [Methods] Eight SSc patients treated with RTX were included in this study. Skin lesions were assessed by mRSS, and lung lesions were assessed by HRCT and FVC before and after RTX therapy (week 24 and 48). [Results] The mean age of SSc onset was 46.3 years. The median time from onset to RTX therapy was 20.5 months. The median follow-up period of RTX therapy was 59.3 weeks. Before RTX therapy, the severity of skin lesions was mild in 2, moderate in 4, and severe in 2 patients. Six patients had interstitial lung diseases, and severity was mild in 4 and moderate in 2. At week 24, mRSS had improved in 7 of 8 patients. HRCT improved in 2 of 5 patients. At week 48, mRSS improved in 4 of 6 patients. HRCT improved in 2 of 3 patients. FVC improved in 1 of 4 patients. [Conclusion] The present study suggests that RTX therapy may be effective not only for skin lesions, but also for lung lesions in SSc patients. And RTX maintenance therapy may be necessary, because some patients improved for the first time at week 48.

P1-142

A case of pulmonary hypertension complicated by systemic sclerosis with good outcome after switching from inhaled iloprost to inhaled treprost

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Conflict of interest: None

[Patient] 60s year-old Female. [Present illness] In her 40s, she was diagnosed with systemic sclerosis (SSc) based on skin sclerosis and Raynaud's phenomenon. She developed dyspnea, and right heart catheterization (RHC) revealed mean pulmonary arterial pressure (mPAP) of 40 mmHg and wedge pressure (PCWP) of 4 mmHg. She was diagnosed with pulmonary hypertension (PH) with SSc. In her 50s, she began treatment with inhaled iloprost (ILO), riociguat, and macitentan, resulting in hemodynamic stability. She was hospitalized to change her treatment due to concerns about stable drug supply. [Clinical Course] At baseline, RHC showed mPAP at 37 mmHg and PAWP at 10 mmHg. treprostinil (TRE) was initiated at the minimum dose, reaching the maximum dose by day 58. Follow-up RHC showed mPAP at 32 mmHg and PAWP at 6 mmHg. During hospitalization, there were no signs of worsening right heart failure. [Clinical Significance] Due to its unique administration route, transitioning from ILO inhalation to oral medication is often difficult. In this case, a switch to TRE inhalation was achieved under hemodynamic monitoring. TRE inhalation is approved for PH associated with interstitial lung disease and appears to be a useful alternative for treating PH with connective tissue diseases.

P1-143

Intravenous immunoglobulin therapy significantly improved refractory gastrointestinal symptoms associated with systemic sclerosis: A case report

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Conflict of interest: None

This presentation focuses on the efficacy of intravenous immunoglobulin therapy (IVIg) for refractory gastrointestinal symptoms associated with systemic sclerosis (SSc). A 45-year-old female was referred to our department in 2021 with generalized skin sclerosis and interstitial pneumonia. A skin biopsy confirmed the diagnosis of SSc, revealing swelling and degeneration of collagen fibers in the dermis. She subsequently developed refractory pseudo-obstruction and secondary pneumatosis cystoides intestinalis. She underwent steroid and cyclophosphamide therapy combined with probiotics, prokinetic agents, herbal medicines, and erythromycin. Despite these treatments, her condition did not improve. As a result, by 2023, she was unable to eat orally, and her body weight had dropped from 54 kg to 26 kg. However, after receiving three courses of IVIG, her ability to eat orally gradually recovered, and by March 2024, her body weight had improved to 43 kg. The pharmacological mechanisms of IVIg in SSc patients are thought to involve modulation of fibroblast activity or neutralization of autoantibodies, although they are not fully understood. Therefore, further evidence is needed to establish IVIg as a potential new treatment for SSc patients suffering from severe disease complications.

P1-144

A case of anti-nuclear matrix protein 2 (NXP2) antibody-positive dermatomyositis with generalized edema, dysphagia, and thrombotic microangiopathy

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Conflict of interest: None

[Case Presentation] A 22-year-old man presented with myalgia and muscle weakness over two months. Heliotrope rash, Gottron's papules, high creatine kinase (CK) levels, positive anti-NXP2 antibodies, electromyography and muscle biopsy confirmed the diagnosis of dermatomyositis (DM) without interstitial lung disease or malignancy. Prednisolone (PSL) and tacrolimus (TAC) improved symptoms. After two weeks, limb weakness, dysphagia, generalized subcutaneous edema and diarrhea appeared. CK levels increased, suggesting myositis relapse. Moreover, anemia with schistocytes, thrombocytopenia, undetectable haptoglobin and normal ADAMTS13 activity indicated thrombotic microangiopathy (TMA) complicating DM. Discontinuation of TAC/trimethoprim-sulfamethoxazole, and methylprednisolone pulse (MP) therapy concomitant cyclophosphamide induced initial improvement. However, symptoms deteriorated again after PSL reduction. MP therapy was repeated with mycophenolate mofetil, achieving disease remission. [Clinical Significance] Significant subcutaneous edema in DM patient may be associated with severe myositis, especially with anti-NXP2 antibodies. TMA may indicate DM progression and manifest as diarrhea. Recognizing non-disease specific indicators of worsening DM is important.

P1-145

Interstitial lung disease as an initial episode of anti-SRP antibody-positive immune-mediated necrotizing myopathy: two cases

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Conflict of interest: None

[Case 1] A 63-year-old female was admitted to our hospital because of dyspnea and cough for 2 months due to deterioration of interstitial lung disease (ILD) that was first diagnosed along with increased serum levels of CK and KL-6 14 months ago. Muscle weakness was not observed. Muscle biopsy from right thigh muscle, where indicated high intensity signal in

MRI, resulted in the diagnosis of immune-mediated necrotizing myopathy (IMNM). In addition, positive for anti-SRP antibody (SRP) was found. She was simultaneously diagnosed with breast cancer, which was treated surgically first, while having no deterioration of ILD. [Case 2] A 55-year-old female with 3-month history of muscle weakness, indicated increased serum CK levels and ILD, was admitted to our hospital. Positive results for SRP and histology by muscle biopsy led to the diagnosis of SRP-positive IMNM. She was refractory for prednisolone, tacrolimus, and intravenous immunoglobulin, and subsequently had worsened muscular involvement and ILD. Cyclosporine and cyclophosphamide following methylprednisolone were intravenously administered, leading to remission. [Conclusion] Muscle biopsy was useful for determining the therapeutic strategy based on the diagnosis of SRP-positive IMNM, despite ILD being principal manifestation.

P1-146

Clinical features of polymyositis/dermatomyositis-associated interstitial pneumonia coexisted with hypersensitivity pneumonitis

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Conflict of interest: None

[Objectives] In interstitial pneumonias (IPs), recently it has been found that chronic hypersensitivity pneumonitis (CHP) is frequently present. In this study, we investigated the clinical characteristics of cases IP associated with polymyositis/dermatomyositis (PM/DM), in which HP was considered to be complicated. [Methods] We analyzed PM/DM-IP patients at our hospital from April 2014 to October 2024. Those with suspected HP based on social history, imaging, and pathology findings were selected. [Results] Among all 14 cases, four cases were extracted. Bird antigens were the suspected exposure in all, with one case also involving chemicals. CK, ESR, and KL-6 were 524.5 U/L, 15 mm/hr, and 1326.5 U/mL, respectively. Anti-ARS and anti-Ro-52 antibodies were found in 3/4 cases. CT showed ground-glass opacities in all, reticular opacities in 3/4, and centrilobular nodules and mosaic attenuation in 2/4. Immunosuppressive therapy including glucocorticoids and tacrolimus and antigen avoidance improved symptoms. During a median follow-up of 59.5 months, 3/4 patients were managed without rehospitalization. [Conclusion] A subgroup of PM/DM-IP patients may have coexistent HP findings, requiring both immunosuppressive therapy and antigen avoidance.

P1-147

A case where type 2 respiratory failure acts as a catalyst for the diagnosis of inflammatory myopathies associated with anti-mitochondrial antibodies, following recurrent exacerbations of chronic heart failure

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Conflict of interest: None

[Case Report] A 74-year-old female was taken to the hospital. Six years ago, she was incidentally noted elevated CK levels. Four years ago, she was diagnosed with mitral valve regurgitation, tricuspid valve regurgitation, atrial fibrillation. The antinuclear antibody pattern was 640 times positive for centromere. Two years ago, she experienced leg edema, which led to adjustments in her medication for chronic heart failure. One year ago, she was hospitalized due to worsening heart failure and she was unable to wean off vasopressors, leading to her referral to our hospital. The surgery for valvular disease and atrial fibrillation was performed. Eight months after discharge, she was readmitted due to severe heart failure and CO2 narcosis, requiring ICU management. Serum anti-mitochondrial antibody (AMA) positivity was confirmed. Treatment with immunosuppressant resulted in improvement of serum CK levels. However, respiration and cardiac function did not fully recover. [Discussion] There are no reports of valvular diseases complicated by inflammatory myopathies associated with AMA. It is important to consider the involvement of inflammatory myopathies associated with AMA in cases of heart failure associated with elevated serum CK levels and subacute courses or recurrences.

P1-148

A Case of Anti-MDA5 Antibody-Positive Dermatomyositis with Consciousness Impairment

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Conflict of interest: None

[Case] A 64-year-old woman. [Chief Complaints] Rash, loss of appetite, decreased motivation. [Present History] After contracting COVID-19 in January of Year X, she experienced persistent cough, dyspnea, and loss of appetite. By June, anorexia persisted, and she developed generalized joint pain, and admitted to a previous hospital. She then presented with liver dysfunction, elevated LDH, high ferritin, generalized rash, and a sudden decline in motivation and ADL. On July 4th, she was transferred to our hospital. [Clinical Course] Gottron's sign, myalgia, muscle weakness, joint pain, and mild interstitial pneumonia were observed, suggesting dermatomyositis (DM). She had impaired consciousness (JCS II-10), but cerebrospinal fluid and brain MRI were normal, indicating DM-related consciousness. Steroid pulse therapy was started, and later anti-MDA5 antibody (Ab) was detected. Intravenous cyclophosphamide pulse therapy and tacrolimus were administered, improving both skin symptoms and consciousness (JCS I-2). Cyclophosphamide was stopped due to side effects, and rituximab was added as anti-MDA5 antibody titers and ferritin worsened. [Clinical Significance] Consciousness impairment in anti-MDA5 Ab-positive DM is rare, and few cases have been reported. So this case is valuable to report.

P1-149

A case of anti EJ antibody positive dermatomyositis with repeated ileus

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Conflict of interest: None

[Clinical Course] A 54-year-old female. She had polyarthralgia, Gottron's sign and heliotrope rash, and was diagnosed with anti-EJ antibody-positive dermatomyositis. All scleroderma autoantibodies were negative. The disease was controlled by using various immunosuppressants in addition to prednisolone (PSL), but from around X-6 year, She often had ileus and acute kidney injury due to dehydration. During the course of the disease, myositis repeatedly flared up and interstitial pneumonia worsened, making it difficult to reduce the dose of tacrolimus and PSL, so rituximab (RTX) was introduced in X year. Afterwards, it was possible to discontinue tacrolimus without any recurrence of myositis, but ileus flare-up occurred repeatedly. [Discussion] We experienced a case of anti-EJ antibody-positive dermatomyositis accompanied by treatment-resistant interstitial pneumonia and repeated episodes of ileus. It is well known that scleroderma causes ileus due to decreased intestinal peristalsis, but all scleroderma autoantibodies were negative, and the diagnostic criteria for mixed connective tissue disease were not met. We report this as a valuable case in which dermatomyositis was managed with RTX, but ileus was difficult to control.

P1-150

A case of anti-Zo antibody-positive dermatomyositis with organizing pneumonia (OP)-like findings after cryobiopsy for progressive interstitial pneumonia

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Conflict of interest: None

A 50-year-old male with a pulmonary nodule noted on CT in year X-1, monitored by his primary physician, began experiencing exertional dyspnea, bilateral shoulder pain, and finger rashes in July of year X. Follow-up CT that month revealed new ground-glass opacities, and blood tests showed elevated KL-6, with negative results for myositis antibodies (anti-ARS, anti-MDA5, anti-TIF1-γ, and anti-Mi-2). Referred to our department in September, he showed elevated aldolase, CRP, and worsening NSIP-like interstitial shadows on CT. Pulmonary function tests revealed restrictive impairment, with %VC at 74.5%. Anti-Zo antibody was positive on A-CUBE and ELISA. Finger skin biopsy revealed basal cell liquefaction, single-cell necrosis, and lymphocytic infiltration, confirming dermatomyositis. Following cryobiopsy, which showed patchy organizing fibrosis and lymphocyte infiltration suggesting OP, mPSL pulse therapy was initiated, followed by PSL at 0.6 mg/kg/day. Outpatient management with Tac was started while tapering PSL. Anti-Zo antibody positivity in anti-synthetase syndrome is rare, and further studies are needed to determine if OP patterns in such cases differ from other anti-synthetase syndrome.

P1-151

A case of anti-SRP antibody-positive polymyositis complicated with neuromyelitis optica spectrum disorder

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Conflict of interest: None

The patient was a 52-year-old woman. She was diagnosed with neuromyelitis optica spectrum disorder (NMOSD) 6 years ago due to left visual disturbance, high signal and contrast enhancement of the optic nerve on MRI (STIR) and anti-aquaporin4 antibody positivity. She received methylprednisolone pulse, followed prednisolone (PSL) 40 mg. From the time PSL was reduced to 10 mg, serum CK level elevated to approximately 700 U/L. Due to recurrent numbness of the left lower limb, satralizumab was added three years ago. Myalgia in the bilateral thighs appeared in year X-1 and muscle weakness in year X. Serum CK elevated, and anti-SRP antibodies detected. MRI showed high-signal areas in the right triceps and bilateral adductor muscles. Electromyography showed fibrillation potential. Muscle biopsy showed fiber size variability without necrosis, leading to a diagnosis of polymyositis (PM). PSL was increased to 55 mg, showing a favorable response. Common rheumatic diseases associated with NMOSD are systemic lupus erythematosus and Sjögren's syndrome, with only 11 cases of NMOSD and inflammatory myopathy. Most cases presented with both diseases simultaneously. We report a case of PM developing five years after the onset of NMOSD and its clinical features, together with a review of the literature.

P1-152

Clinical characteristics of two patients with new-onset and two patients with relapsed anti-signal recognition particle (SRP)-positive immune-mediated necrotizing myopathy: A case series report

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Conflict of interest: None

We present 4 cases with anti-signal recognition particle (SRP)-positive immune-mediated necrotizing myopathy (IMNM), including 2 relapsed cases identified by the re-elevation of creatine kinase (CK) levels and mild muscle weakness. Dysphagia was observed in one patient with new-onset and one patient with relapsed. All patients were treated with high-dose glucocorticoids (GC) and immunosuppressants (1 methotrexate, 3 tacrolimus). One new-onset case and one relapsed case were also treated with intravenous immunoglobulin (IVIg). Although muscle weakness did not improve within a month in any cases, CK levels decreased in all cases. The CK levels of relapsed cases were more rapidly decreased to within the normal range than that of new-onset cases (duration from the start of GC therapy to time CK levels decreased to within the normal range, 1 week and 5 weeks vs. 3 weeks and 13 weeks). As previously reported, anti-SRP-positive IMNM revealed refractory to immunosuppressive therapy and, on occasion, required IVIg.

P1-153

An autopsy case of anti-PL-7 antibody-positive dermatomyositis with interstitial pneumonia complicated by refractory pericarditis

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Conflict of interest: None

[Case] 86-year-old woman was admitted to our hospital due to fever and dyspnea in July. Nine years ago, she was diagnosed with dermatomyositis based on interstitial pneumonia, Gottron's sign and a positive test for anti-PL-7 antibody. In addition, early esophageal cancer was detected and resected endoscopically. The activity of interstitial pneumonia controlled by immunosuppressive (IS) therapy, but it progressed slowly over time. Pericardial effusion was slightly observed after the onset of the disease, and increased in May. It revealed exudative without the evidence of infection and malignancy, and was thought to be due to pericarditis associated with dermatomyositis. In July, after admission, we diagnosed with acute exacerbation of pericarditis and intensified of IS therapy. While adjusting of IS drugs, interstitial pneumonia worsened acutely. Although we increased the dose of GC and added intravenous cyclophosphamide therapy, the interstitial pneumonia did not improve, and she died of respiratory failure. Autopsy findings showed a large amount of pericardial effusion. [Discussion] There is a report suggesting that anti-PL-7 antibody-positive dermatomyositis is often complicated by pericarditis, but the number of reported cases is limited.

P1-154

Efficacy of rituximab for elderly-onset refractory anti-HMGCR antibody-positive immune-mediated necrotizing myopathy: a case report

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Conflict of interest: None

[Case summary] An 87-year-old female with no significant medical history presented with gait disturbance that began one month prior. She was admitted due to an elevated CK level (19,774 U/L). During hospitalization, she developed dysarthria, dysphagia, and muscle weakness, leading to aspiration pneumonia. She exhibited a heliotrope rash, although there were no other skin lesions. Neurological examinations showed proximal dominant muscle weakness with myalgia. Laboratory findings showed continuous high CK level (19,519 U/L) and positive myositis-specific autoantibodies for anti-HMGCR, SS-A/Ro52, titin, and dsDNA antibodies. PET-CT indicated pneumonia and myositis with no interstitial pneumonia and malignancy. An MRI revealed abnormal signals in the biceps, leading to a biopsy confirming anti-HMGCR positive immune-mediated necrotizing myopathy (IMNM). Because intravenous methylprednisolone and immunoglobulin with tacrolimus and methotrexate didn't show enough efficacy, we initiated rituximab (RTX) on the 20th day after ethical committee approval. 4 doses of RTX improved CK levels to 300 U/L range and muscle strength with no relapse and complications. [Clinical Significance] RTX therapy may be effective and safe for treating refractory anti-HMGCR positive IMNM in elderly patients.

P1-155

A case of dermatomyositis (DM) with anti-NXP-2 antibody accompanied by complications due to severe core and limb muscle weakness

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Conflict of interest: None

Cases of DM with anti-NXP-2 antibody are reported to have severe muscle weakness and dysphagia. Here we report such a case who required multiple surgeries because of complications but recovering without flare. A 42-year-old man was suffered from bilateral upper arm pain and muscle weakness in his thighs from 2 months before. Because of the gait difficulty, he decided to visit the clinic nearby. Since Gottron's papules, heliotrope rash and elevated CK were found, he was referred to our hospital. Further evaluation revealed elevated serum aldolase and LDH levels and anti-NXP-2 antibody positive. Electromyography and muscle biopsy supported the diagnosis as DM. No malignancy was detected. Pulse therapy of glucocorticoid and tacrolimus were introduced, but drug-induced TMA occurred. His muscle weakness resulted in choking due to aspiration and a tracheotomy was needed to prevent this event. Furthermore, the weakness of core strength caused constipation and elevation of intraabdominal pressure, which resulted in intestinal perforation. Regardless of the emergent surgery, long-term antibiotic therapy was required. The disease activity of DM was stabilized and limb strength was improved enough to start walking exercise with support, but dysphagia was still and a gastrostomy was needed.

P1-156

A case of treatment-resistant anti-MDA5 antibody-positive dermatomyositis with marked subcutaneous and mediastinal emphysema that could be treated conservatively with multimodal therapy including tofacitinib

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Conflict of interest: None

(Case) 60s male (Case presentation) For 14 years, he had been suffering from Raynaud's phenomenon and had been followed up. One year earlier, he was admitted to our hospital. After admission, he was found to be positive for anti-MDA5 antibody. A Computed tomography revealed progressive interstitial pneumonia, and a diagnosis of anti-MDA5 antibody-positive dermatomyositis was made. (Clinical course) He began treatment with a triple combination of prednisolone, tacrolimus, and cyclophosphamide pulses, but was refractory to therapy. In the same year, subcutaneous and mediastinal emphysema appeared and rapidly expanded, and it spread to the whole body. He was highly immunosuppressed, therefore plasma exchange and tofacitinib 20 mg/day were added first. In June, there was a decrease in disease activity and subcutaneous and mediastinal emphysema improved. (Clinical Significance) We experienced a case of interstitial pneumonia caused by treatment-resistant anti-MDA5 antibody-positive dermatomyositis which improved with multidisciplinary treatment. Subcutaneous and mediastinal emphysema caused by interstitial pneumonia has been reported as a poor prognostic factor. We report this case in the hope that it will be helpful in the treatment of patients with similar conditions in the future.

P1-157

A case of anti-MDA5 antibody-positive dermatomyositis and interstitial pneumonia that relapsed 7 years after induction of remission

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Conflict of interest: None

A 57-year-old woman was referred to our hospital in September X-7 due to arthralgia, and painful skin rash on both fingers. Gottron's sign and reverse Gottron's sign were noted. A few days later, she developed shortness of breath, and a chest CT showed reticular and linear shadows on the dorsal surfaces of the bilateral lower lobes. Methylprednisolone pulse, followed by PSL 60 mg, cyclosporine, and intravenous cyclophosphamide (IVCY) were initiated, and she tested positive for anti-MDA5 antibodies. During treatment, infectious side effects occurred, but all were cured. The antibody titer showed a decreasing trend, and she was discharged from the hospital. In August X, there was a sharp increase in antibody titer, along with fatigue and a skin rash on her fingers. A chest CT scan showed linear shadows in the bilateral lower lobes. After hospitalization, PSL 1 mg/kg, tacrolimus, and IVCY were introduced. She was treated cautiously on an outpatient basis. Clinical Significance: This disease can be managed with early and aggressive immunosuppressive therapy. It has been reported that relapses can occur even after long-term stabilization, often preceded by elevated antibody titer. This case highlights the importance of regular follow-up to detect early signs of relapse.

P1-158

A case of sertraline-induced rhabdomyolysis necessitating differential diagnosis from lipid storage myopathy in pathology

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Conflict of interest: None

Case: Female in her 30s with depression, familial hypercholesterolemia, on pitavastatin 2 mg, sertraline 100 mg. Presented with elevated CPK for 3 years. Endocrine exams normal; no skin or muscle symptoms noted. Two months before presentation, developed lower leg and then upper arm muscle pain, leading to referral. Physical Exam: MMT deltoid, biceps 4/4; iliopsoas, quadriceps 4/4. **Lab Findings:** Negative for antinuclear, myositis-associated, and specific autoantibodies. Labs: AST 66 U/L, LDH 319 U/L, CPK 1863 U/L, ALD 8.1 U/L, LDL 112 mg/dL. CT showed no ILD; PET-CT showed no malignancy, but diffuse muscle uptake in pectoralis major, biceps, trapezius, erector spinae, transverse abdominis, gluteus medius, semimembranosus, piriformis, etc. **Course:** Muscle biopsy showed lipid deposits, suggesting lipid storage myopathy. No inflammatory changes in fibers. Genetic tests normal. CPK rise coincided with sertraline start; due to sertraline-induced rhabdomyolysis reports, meds adjusted. After stopping sertraline, CPK fell to 296 U/L in 2 months, then normalized. Discussion: This case required differentiation from polymyositis and lipid storage myopathy. With few reports on sertraline-induced myopathy/rhabdomyolysis, we present this case.

P1-159

A Case of Anti-ARS Antibody Syndrome Showing Improved Treatment Response Following Breast Implant Removal

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Conflict of interest: None

[Case Summary] A 57-year-old woman had breast implants placed around October 20XX. On September 28th, 20XX-1, she was hospitalized for pneumonia, which was unresponsive to antibiotics. Anti-ARS antibodies were detected, and she was transferred to our hospital on October 11th.

Elevated serum CK levels, high STIR signals in thigh muscles on MRI, myogenic changes on electromyography, and interstitial pneumonia confirmed anti-ARS antibody syndrome. Steroid pulse therapy with PSL (50 mg/day) and TAC began on day 2, but there was minimal improvement in pneumonia, and CK levels remained high. IVCY was added on day 14, and another pulse was given on day 29, switching PSL to betamethasone (BTM). Improvement was mild. Considering the implant's role as an adjuvant, it was removed on day 45. Intraoperative findings showed rupture and leakage of the right implant, possibly contributing to the refractory condition. After surgery, BTM was tapered, and TAC and IVCY continued, leading to CK normalization by February 20XX. [Clinical Significance] This case shows improvement in refractory anti-ARS antibody syndrome after implant removal, suggesting implants' role as adjuvants. We discuss mechanisms and features of adjuvant-induced autoimmune diseases.

P1-160

A case of tracheomediastinal fistula complicating anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

[Case] A 33-year-old man presented with a back rash, joint and muscle pain, hoarseness. Gottron's sign, multiple skin ulcers, and progressive interstitial lung disease on CT led to a diagnosis of clinically amyopathic dermatomyositis (DM). Glucocorticoid pulse therapy, tacrolimus, and intravenous cyclophosphamide were initiated. Anti-MDA5 antibody was positive. Due to increased lung opacity on X-ray, tofacitinib was introduced. Subsequently, CT showed mediastinal emphysema, and bronchoscopy revealed ulcers on the right vocal cord, small tracheal ulcers, and a tracheomediastinal fistula (TMF). Furthermore, Aspergillus was detected by the culture of brushing from the edge of the fistula. Despite bacterial mediastinitis during percutaneous drainage of mediastinum, multidisciplinary care was successful. [Discussion] Tracheal ulcers are rare in DM, and their pathogenesis is poorly understood. In this case, the tracheal ulcers were probably related to skin ulcers. However, detection of Aspergillus suggested that the infection contributed to the fistula formation. Immunosuppressive therapy and antifungal treatment were effective. In anti-MDA5 antibody-positive DM with TMF, it is important to consider the possibility of infection and to perform prompt evaluation and treatment.

P1-161

The case of cytomegalovirus pneumonia complicated by anti-MDA5 antibody-positive dermatomyositis and summer-type hypersensitivity pneumonitis

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Conflict of interest: None

Case 69-year-old woman. She was diagnosed with anti-MDA5 antibody-positive dermatomyositis and rapidly progressive interstitial pneumonia (RP-ILD) in X-5 years. She was in remission, but in August X-1, ground-glass opacity (GGO) appeared. She was diagnosed as summer-typehypersensitivity pneumonitis (HP). In May of X year, anti-MDA5 antibody titer was increased. Her dose of PSL was increased to 30 mg/day, the shadows improved with a decrease in anti-MDA5 antibody titer. In July of the same year, She was hospitalizedue to dyspnea. The number of cytomegalovirus (CMV) antigen-positive cells was 464, and CMV-PCR of bronchoalveolar lavage fluid (BALF) was positive, so She was diagnosed with CMV pneumonia. Since there was no re-elevation of anti-MDA5 antibody titer, a relapse of RP-ILD was ruled out. Since She taked moderate dose of PSL, the lymphocyte ratio of BALF was <20%, and the CD4/CD8 ratio was 1.15, a relapse of HP was also considered to be negative. After intravenous ganciclovir infusion, her dyspnea was improved. CMV antigenemia tested negative, and she was discharged on day 36 of hospitalization. conclusion We have experienced the case of CMV pneumonia differentiated from the primary disease or relapse of summer HP during treatment of anti-MDA5 antibody-positive dermatomyositis.

P1-162

MDA5 antibody-positive dermatomyositis with rapidly progressive interstitial lung disease that responded to plasma exchange and tofacitinib

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Conflict of interest: None

MDA5 Ab-positive CADM with RP-ILD is treated with m-PSL pulse, TAC and IVCY, but opportunistic infections can be a problem. PE and TOF may allow early PSL reduction. Case 1: A 62-year-old man presented with cough and dyspnea. He had ILD, heliotrope rash, and positive MDA5 Ab. m-PSL pulse, IVCY, and TAC were started. He was intubated, VV-ECMO and 7 times of PE were performed due to worsening of his condition. PSL was reduced, ferritin was elevated again, and mediastinal emphysema worsened, so TAC was changed to TOF 10 mg. PSL was finished after 11 months. Case 2: A 63-year-old woman had cough and dyspnea on exertion. She had ILD and MDA5 Ab. She was received PE, TAC and IVCY after m-PSL pulse. Ferritin increased as withdrawal PSL, TAC was changed to TOF. Respiratory status did not worsen, and PSL was finished. Case 3: A 59-year-old woman presented with rash on the fingers and elbows. ILD was progressive. TAC was changed to TOF. Her respiratory status was stabilized and PSL was reduced. High ferritin level is a risk factor for RP-ILD with CADM and cytokine storm is involved in exacerbation. MDA-5 Ab, removal of inflammatory cytokines by selective PE and administration of TOF to suppress type 1 IFN allowed us to manage the disease and reduce the dose of PSL. SePE may be effective.

P1-163

A case series of 10 patients with immune-mediated necrotizing myopathy

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Conflict of interest: None

[Objectives] Immune-mediated necrotizing myopathy (IMNM) is an idiopathic inflammatory myopathy with severe muscle impairment and muscle fiber necrosis, proposed in 2003. This study aims to characterise the clinical features and prognosis of IMNM. [Methods] We retrospectively reviewed 10 patients with IMNM admitted to the Department of Clinical immunology at Osaka University Hospital from January 2012 to August 2024. [Results] Eight cases were diagnosed by muscle biopsy, while two cases without biopsy were diagnosed based on clinical findings and positive for anti-SRP antibodies. Six patients were positive for anti-SRP antibodies, one for anti-HMGCR antibodies, and three were negative for both antibodies. MRI was performed in all cases, with findings of myositis in seven cases. All patients received glucocorticoids Rituximab was used in six cases, other immunosuppressants in eight cases, and IVIG in four cases. Muscle symptoms improved in all cases, with normalization of CK levels in a median of two months. CK levels re-elevated in three cases after six months. [Conclusion] Although IMNM is known to have a poor prognosis for muscle weakness, combination of immunosuppressive therapy improved symptoms in all patients.

P1-164

A Case of Anti-MDA5 Antibody Positive Dermatomyositis Diagnosed Following the Exacerbation of Arthritis and Ulcers on the Dorsal Hands during the Treatment of Rheumatoid Arthritis

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Conflict of interest: None

Patient: A 66-year-old female. **Chief Complaint:** Worsening joint pain. **Medical History:** In year X-1, the patient developed finger joint pain. Laboratory tests revealed a rheumatoid factor of 201 IU/mL and anti-citrullinated peptide antibodies at 477.6 U/mL, leading to a diagnosis of rheumatoid arthritis. She was treated with methotrexate at 6 mg/week. In year X, due to worsening joint pain, she was referred to our hospital. **Examination:** Ultrasound showed synovitis. Crusting was noted on the dorsal MCP joints, with erythema and nail pain. Gottron's papules were observed on the elbows and upper arms. Blood tests indicated elevated transaminases and a ferritin level of 1380 ng/mL, suggesting dermatomyositis. **Diagnosis and Treatment:** Testing revealed high anti-MDA5 antibodies (index 4400), and a chest CT confirmed interstitial pneumonia, leading to a diagnosis of anti-MDA5 antibody positive dermatomyositis. Treatment was initiated with prednisone at 1 mg/kg, tacrolimus, and intravenous cyclophosphamide. The patient improved in skin findings and laboratory results, with no worsening of interstitial pneumonia. **Clinical Significance:** When rheumatoid arthritis patients symptoms worsen, contradictory findings necessitate reassessment for alternative diagnoses like dermatomyositis.

P1-165

A case of anti-ARS antibody syndrome (anti-PL-12) complicated by pericarditis

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Conflict of interest: None

[Case] A 75-year-old woman was admitted to our hospital with a 3-day history of dyspnea. 8 months prior to admission, she noticed skin irritation on the lateral aspects of her bilateral digits. Additionally, she had experienced fatigue for the past 3-months and polyarthralgia for 1 month. 2 weeks prior to admission, she developed a persistent low-grade fever. 9 days before her admission, chest CT showed findings of interstitial lung disease in the left lung. Due to worsening dyspnea over the course of 3 days, she presented to our hospital. Follow-up chest CT demonstrated bilateral pleural and pericardial effusions along with interstitial lung disease. Those did not improve with antibiotics and diuretics. Laboratory findings on admission revealed a positive anti-aminoacyl tRNA synthetase (anti-ARS) antibody (PL-12). The mechanic's hands were observed on the lateral aspects of her bilateral digits, and we diagnosed anti-ARS antibody syndrome. She was started on prednisolone (60 mg/day) and tacrolimus, which resulted in the resolution of the pleural and pericardial effusions. While pericarditis has been previously reported in patients positive for anti-Jo-1 and anti-PL-7 antibodies, this is the first documented case of pericarditis in a patient with anti-PL-12 antibody positivity.

P1-166

Anti-Jo-1 antibody positive dermatomyositis presenting with steroid-resistant, rapidly progressive interstitial pneumonia successfully treated with multidrug immunosuppression and plasma exchange therapy: a case report

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Conflict of interest: None

[Case] A 64-year-old woman was admitted to the previous hospital with a diagnosis of pneumonia. She had skin symptoms such as Gottron's sign, so she was transferred to our department. Blood tests showed severe inflammation (CRP 13.65 mg/dl) and increased myogenic enzymes and interstitial pneumonia markers (CK 2258 U/l, KL-6 1285 U/ml). Also, anti-Jo-1 antibodies were strongly positive. Based on these results, MRI and CT images, we diagnosed her with dermatomyositis and interstitial pneumonia associated with anti-ARS antibody syndrome. Treatment with mPSL 500 mg/day was started, but the interstitial pneumonia rapidly progressed. Because of severe respiratory failure, multidrug immunosuppressive therapies with IVCY and Tac 4 mg/day were administered from the 3rd day. However, the next day, invasive mechanical ventilation was required, so plasma exchanges were performed. These multidisciplinary treatments were successful, and the patient recovered with no respiratory failure. [Clinical Significance] Even in cases of interstitial pneumonia with anti-ARS antibody syndrome, if the patient has steroid-resistant and rapidly progressive interstitial pneumonia, multidrug immunosuppression and plasma exchange therapy should be recommended in accordance with anti-MDA5 antibody positive cases.

P1-167

A 7 Case series of Remission Induction Therapy with JAK Inhibitor for ILD in MDA5 Antibody Dermatomyositis

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Conflict of interest: None

[Objectives] Remission induction therapy for ILD in Anti-MDA5+DM is mainly a multidrug combination therapy, and there are not many reports of cases using JAK-i. [Methods] We retrospectively evaluated the clinical characteristics and outcomes of patients with primary CADM, positive for anti-MDA5+, using JAK-i during remission induction, between June 2019 and October 2024. [Results] We surveyed 7 patients (1 male, 6 females) in this study. The mean age was 57.9, MDA5 antibody titer was 2853.3 IU/mL, ferritin was 768.5 ng/ml, and KL-6 was 863.4 U/ml. The mean disease duration was 1.5 months. 1 patient had Rapidly progressive ILD, and 6 patients had lung lesions localized to the lung bases. We used high-dose GC, and JAK-i for all patients during remission induction. We also used TAC for 4 patients during maintenance therapy. 1 patient died during induction remission, and the survival rate was 85% at 72 weeks. Mean GC dose was 15 mg and 1.5 mg, and mean MDA5 antibody titer was 972.5 IU/ml and 312.6 IU/mL at 12 and 72 weeks. No serious adverse events were occured in surviving patients. [Conclusion] We suggest that we can treat with JAK-i for remission induction in patients with ILD in Anti-MDA5+ DM, a short disease duration and localized pulmonary involvement.

P1-168

A case of dermatomyositis presenting with acute interstitial nephritis with fever by tacrolimus and valaciclovir: Case Report and Review of the Literature

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Conflict of interest: None

Elevation of myogenic enzymes and exacerbation of interstitial pneumonia were observed during treatment of dermatomyositis with positive anti-PL-7 antibody with prednisolone 10 mg/day and tacrolimus 3 mg/day. Remission induction therapy using high-dose steroids and intravenous cyclophosphamide was started. During remission induction therapy, reactivation of cytomegalovirus was observed, and valganciclovir was administered concurrently. Approximately three months after the start of remission induction therapy, intermittent fever and increases in inflammatory responses were observed, and renal function declined at the same time. A renal biopsy revealed interstitial nephritis, and drug-induced interstitial nephritis associated with the concomitant use of tacrolimus and valganciclovir was suspected. The fever was strongly suspected to be due to interstitial nephritis based on the patient's course. Interstitial nephritis can be accompanied by nonspecific symptoms such as fever and joint pain, and is important as a differential diagnosis for unknown fever accompanied by renal impairment. It has been pointed out that the combination of calci-

neurin inhibitors and antiviral drugs may increase renal toxicity, and we will discuss the course of this case with a literature review.

P1-169

A case of anti-ARS antibody-positive dermatomyositis and interstitial pneumonia with preceding joint symptoms and successful response to baricitinib

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Conflict of interest: None

A 57-year-old woman presented with joint pain and swelling and was diagnosed with RS3PE syndrome. PSL was initiated, but joint symptoms recurred when PSL was reduced to 8 mg. After the introduction of tocilizumab, her symptoms improved, and PSL was reduced; however, she discontinued her follow-up visits. Four years after the onset, she presented with a fever of around 38°C, recurrence of joint symptoms, elevated muscle enzyme levels (CK 2963 IU/ml), and interstitial shadows, leading to her referral to our department. RF and anti-CCP antibodies were negative. Based on the presence of Gottron's sign/papules, myalgia, arthralgia, elevated CK and inflammatory markers, positive anti-ARS antibodies, and interstitial pneumonia, she was diagnosed with anti-ARS antibody-positive dermatomyositis (ARS DM). PSL 30 mg and an immunosuppressant led to improvements in her rash, muscle symptoms, and lung lesions; however, when PSL was tapered to 4 mg, her joint symptoms recurred. Since immunosuppressants were insufficiently effective, treatment was switched to baricitinib (BAR), resulting in a rapid improvement and further PSL tapering. ARS DM responds well to PSL; however, it often relapses, making it difficult to taper PSL. BAR has been suggested as a potential option for maintenance therapy.

P1-170

A case of psoriatic arthritis complicated by anti-ARS antibody positive dermatomyositis successfully treated with upadacitinib

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Conflict of interest: None

[Case] A 65-year-old woman presented 14 years ago with bilateral upper arm muscle weakness, arthralgia, and dry cough. She was diagnosed with dermatomyositis (DM) and interstitial lung disease (ILD) 12 years ago and was treated with prednisolone (PSL). Nine years ago, while taking PSL 5 mg/day, she developed arthritis in both hands and was prescribed additional treatment with tacrolimus (TAC). Eight years ago, she developed erythema, and a skin biopsy confirmed a diagnosis of psoriasis. Seven years ago, due to worsening of ILD, her PSL dose was increased to 20 mg/day. During the tapering of PSL, her psoriasis worsened and TAC was switched to cyclosporine (CS). However, her skin rash persisted. Six months ago, while taking 5 mg/day of PSL, her DM worsened, and she developed arthritis in the DIP joints, leading to a diagnosis of psoriatic arthritis (PsA). Treatment with upadacitinib (UPA) was initiated in place of CS, resulting in improvements within 4 weeks: PASI score decreased from 5.6 to 2.2, DAPSA score from 14 to 10, and CK levels from 350 to 208 U/mL. [Clinical Significance] The roles of JAK1 and TYK2 in the pathogenesis of DM and PsA have been reported. In this case, UPA was effective for both diseases, suggesting its potential utility in managing not only PsA but also DM.

P1-171

A case of myositis diagnosed by non-specific systemic symptoms, followed by skin and lung lesions and various autoantibodies

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Conflict of interest: None

[Case] A 37-year-old woman had been experiencing fever and joint pain since early month. Blood test showed CRP 4.08 mg/dL, CPK 59 U/L, ANA 80x (Speckled 80x, Cytoplasmic 40x), and anti-SS-A antibody 523 U/mL. There was tenderness in both shoulders and hands, and thighs, but there was no pain the upper arms and skin rash. Joint ultrasound showed synovitis in both hand, and whole-body CT showed no gross lesions. Analgesics were started, but they were ineffective, so PSL 15 mg (=PSL 0.25 mg/kg) was started. The joint pain improved, and PSL was gradually tapered. CRP rose again with PSL 10 mg, and similar symptoms recurred, so the dose was increased to PSL 25 mg. After three months, periungual erythema and NFB appeared, and CT showed reticular shadows in both lower lung fields. Anti-ARS antibodies rose to 177, suggesting dermatomyositis. At that time, CPK was 90 U/L and aldolase was 10.8 U/L. Thigh MRI showed myositis, electromyogram showed myogenic changes, anti-PL-12 antibodies, and various other autoantibodies were positive, leading to a diagnosis of myositis. [Conclusion] In this case, CPK did not consistently rise. We report this case because the series of events and diagnostic process were very instructive.

P1-172

Two cases of anti-TIF1-γ antibody-positive dermatomyositis with impaired swallowing function who were successfully treated with immunosuppressants and swallowing rehabilitation

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Conflict of interest: None

[Cases] Case 1: 65 F. In 20XX, she had a red rash on her eyelids and ears. She difficulty used her hands, couldn't lift her arms, and difficulty stepped the stairs. She was referred to our hospital. After admission, she was diagnosed with dermatomyositis (TIF1-gamma (γ)+DM). She didn't swallowed, so she didn't eat or take oral medication, and used tube feeding. She improved after receiving immunosuppressants (IMSs) and swallowing rehabilitation. She was weaned from tube feeding, and was discharged. Case 2: 88 F. In 20XX, she had erythema on her face. She had pain in her shoulders and hands, and didn't lift them. She didn't swallowed, so she visited a doctor, where DM was suspected, and was referred to our hospital. After admission, she was diagnosed with TIF1-γ+DM. She didn't swallowed, so she didn't eat or take oral medication, and used tube feeding. She improved after receiving after treatment with IMSs and swallowing rehabilitation. She was transferred to another hospital, and weaned off tube feeding and discharged. [Clinical Significance] Dysphagia due to DM can be difficult to treat. Treatment isn't established. We report two cases in which the patient was able to be weaned off tube feeding through a combination of IMSs and swallowing rehabilitation.

P1-173

Anti-HMGCR antibody-positive immune-mediated necrotizing myopathy developed after more than 20 years of statin use: a case report

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Conflict of interest: None

[Objectives] We report a case of anti-HMGCR antibody-positive IMNM that developed after more than 20 years of statin use. [Case] 69 years old. Male. Three months before admission, he became aware of fatigue on exertion. Two months ago, he developed difficulty in standing up from a sitting position. He was referred to our hospital one month ago because of high AST/ALT levels. He was referred back to the Department of

Rheumatology due to high CK levels, and was admitted to the hospital. He had a history of statin use, CK: more than 10,000 U/L, muscle weakness predominantly in proximal muscles, and MRI, EMG, and muscle biopsy were performed, leading to the diagnosis of IMNM. Anti-HMGCR antibodies were positive. The patient was treated with high-dose glucocorticoid pulse, high-capacity steroids, MTX, and IVIg. [Discussion] According to the literature, more than half of patients with positive anti-HMGCR antibodies have a history of statin use, and the older the patient, the higher the rate. In general, the onset of the disease usually occurs within 2~3 years after the patient starts taking statins, but as in the present case, the onset of the disease may occur after 20 years or more, so even long-term users should be included in the differential if clinically suspected.

P1-174

Two cases of interstitial lung disease (ILD) with anti-ARS antibodies under long-term observation without treatment

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Conflict of interest: None

Case 1: A 65-year-old-man. A chest CT revealed ground-glass opacities in the bilateral lower lobe subpleural regions during a health check. Blood tests showed positive anti-ARS antibodies. He had no subjective symptoms. Physical examination reveald no abnormal findings in the skin, muscles, or joints. During the period of observation without treatment, he experienced temporary increases in shadowing, followed by spontaneous improvement. Five years have passed without treatment. Case 2: A 57-year-old man. During postoperative follow-up for renal cell carcinoma, a localized infiltrative shadow was noted in the left lower lobe on chest CT. Bronchoscopic lung biopsy confirmed the diagnosis of organizing pneumonia. Blood tests revealed positive anti-ARS antibodies. He had no subjective symptoms. Physical examination revealed no abnormal findings. During the observation period without treatment, the shadow extended to the other side but completely resolved after one year. A few months later, shadows reappeared in both lower lobes. Six years have passed without treatment. Clinical significance: If worsening of shadows but there are no subjective symptoms or functional decline, anti-ARS antibodies-positive ILD may be observed withiout treatment.

P1-175

The case of mediastinal and intestinal pneumatosis observed during the course of anti-TIF1-gamma antibody-positive dermatomyositis

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Conflict of interest: None

[Case] 75-year-old woman [Chief Complaint] Dysphagia [Current Medical History] September 20XX-1, she developed facial erythema, and around February 20XX, she developed skin rashes on her hands and felt fatigued. She was suspected of dermatomyositis, and from March 19 she felt dysphagia. [Clinical Course] She was diagnosed with dermatomyositis with facial erythema, heliotrope rash, Gottron's sign, and muscle weakness, as well as anti-TIF1-γ antibody and elevations of CK and aldolase. On the other hand, a nodular shadow was detected in the lung on the CT scan, which diagnosed lung adenocarcinoma, stage IIIA. On April 16, lung resection was performed. From May 7th, prednisolone was administered. After treatment, muscle weakness was improved, and CK also decreased. Tacrolimus was added on May 23rd, and she was recovering well. However, on May 27th, CRP increased, and CT showed the mediastinal and intestinal pneumatosis with free air, so we administered oxygen, targeting PaO2 of 100 mmHg from May 31st. After oxygen administration, the mediastinal pneumatosis had disappeared and the intestinal pneumatosis had almost disappeared. [Discussion] We report on the possibility that oxygen administration is effective in pneumatosis associated with dermatomyositis, with some literature review.

P1-176

A case of anti-MDA-5 antibody-positive dermatomyositis treated with three-drug combination therapy, which progressed slowly and underwent plasma exchange and IVIg therapy

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Conflict of interest: None

[Case] 65 years old, female [History] She was referred to our department with erythema on her fingers, buttocks on August 2. At the initial examination, Gottron's sign, reverse Gottron's sign, and heliotrope rash on the fingers were observed, and the titer of anti-MDA5 antibody was 4385, so we diagnosed her with dermatomyositis. HRCT of the chest showed minor enhancement of interstitial shadows, and we started steroid pulse (mPSL 1000 mg/day), TAC 3 mg/day, and IVCY 500 mg/m2. HRCT of the 17th day showed progression of interstitial pneumonia, and respiratory function tests showed deterioration. Also, hypogammaglobulinemia due to plasma exchange therapy was observed, so IVIg therapy was given as the most severe myositis. However, HRCT showed mild progression. Although intensification of treatment was considered, lung lesions progressed slowly and we decided to continue IVCY. HRCT on the 70th day showed no apparent deterioration and she is now being treated with IVCY under PSL 25 mg/day and TAC 8 mg/day. [Discussion] This is a case of anti-MDA5 antibody-positive dermatomyositis with slow progression of interstitial pneumonia despite plasma exchange in addition to triple therapy. We report the course of treatment and future treatment options, with some discussion of the literature.

P1-177

The efficacy of mepolizumab dose reduction in patients with eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objective] The aim of this study was to clarify the efficacy of mepolizumab dose reduction in patients with eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] This retrospective study included 8 of 11 patients with EGPA treated with mepolizumab (MPZ), excluding 3 patients with no data at glucocorticoid initiation. Prednisolone (PSL) dose, eosinophil count and relapses were assessed before and after starting MPZ and before and after dose reduction. [Results] Five patients were female and the mean initial dose of PSL was 35 mg/day. Seven patients initially received MPZ 300 mg every 4 weeks and one patient received 100 mg every 4 weeks. After a mean of 4 months, MPZ was reduced to 100 mg in 7 patients on 300 mg. The mean eosinophil count decreased from 3054/μL at MPZ initiation to 15/μL at dose reduction and 50/μL at the last observation. The mean dose of PSL also decreased from 20 mg/day to 11 mg/day and 4 mg/day. Although 0.06 relapses per person-year (PY) were observed during the total observation period of 36 PY before MPZ, no relapses were observed during 19 PY after MPZ initiation. [Conclusion] PSL dose was further reduced after MPZ dose reduction without relapse in patients with EGPA. This study suggests that MPZ dose reduction is beneficial in patients with EGPA.

P1-178

Evaluation of the efficacy biological therapy for eosinophilic granulomatosis with polyangiitis in our department

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Conflict of interest: None

[Objectives] The effectiveness of biological therapy for eosinophilic granulomatosis with polyangiitis (EGPA) was evaluated in our department. [Methods] From April 2019 to October 2024, we extracted cases of EGPA treated in our department from the medical records. All ten cases of

EGPA received biological agents, with nine cases being treated with mepolizumab (MEPO) and two cases with rituximab (RTX). [Results] In the remission induction therapy, all cases received glucocorticoids (GC), with seven cases received methylprednisolone pulse therapy. Four cases received cyclophosphamide pulse therapy, and three cases received intravenous immunoglobulin therapy. The biological agents were introduced nine cases of MEPO and two cases of RTX. Both cases selected for RTX had MPO-ANCA positive renal impairment. Seven patients who started MEPO within fifty days of diagnosis, the median starting dose of PSL was 35 mg/day, successfully reduced to a median of 5 mg/day after six months and to 4.5 mg/day after one year. Treatment improved sensory impairment in four cases, and lung ground-glass opacities in one case. No adverse events related to MEPO were observed, and all cases continued treatment without relapses or deaths. [Conclusion] MEPO can be a promising option for induction therapy for EGPA.

P1-179

Early induction of mepolizumab in eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

[Objectives] Biologics have fewer adverse events than glucocorticoids (GC) and can promote reduction of GC dose, which determines long-term prognosis, but their use has not been clearly established in collagen diseases other than rheumatoid arthritis. Therefore, we investigated the effect of GC sparing and factors promoting GC sparing in patients initiating mepolizumab (MEP), a biologic agent indicated for eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] Thirteen patients [8 females, age 65.2 (±17.1) years, BVAS 8.38 (±2.60), GC 30.85 (±15.37) mg, time from treatment initiation to MEP induction 12.77 (±7.505) days] in whom MEP was started for induction remission were evaluated for BVAS and GC changes at 104 weeks. The BVAS and GC changes at 104 weeks were evaluated. [Results] At 104 weeks, BVAS improved significantly and GC use decreased. In addition, the group that could discontinue GC had a higher BVAS at the start than the continuation group, both of which were receiving either gammaglobulin or cyclophosphamide. [Conclusion] It is significant to introduce biologic agents, which are highly selective drugs, early and to try to reduce GC dose to improve long-term prognosis.

P1-180

A Study of the Efficacy of Mepolizumab in Patients with EGPA at our Hospital

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Conflict of interest: None

[Background/Objectives] Mepolizumab is indicated for EGPA patients who have had inadequate response to existing therapy. We investigated the efficacy of MPL in patients with EGPA in our hospital and the effect of reducing the dose of glucocorticoids (GC) and immunosuppressive drugs. [Methods] Twelve EGPA patients with MPL at our hospital were compared regarding affected organs at the time of induction, GC dosage, concomitant use of immunosuppressive agents, reason for induction, use of GC and immunosuppressive agents after induction, and adverse events. [Results] Systemic symptoms were observed in all patients, and upper respiratory tract lesions and peripheral nerve lesions were observed in more than half of the patients. The mean GC dose at induction was 20.6 ± 17.8 mg/day, 4 patients received tacrolimus (Tac) and 2 patients received azathioprine. After MPL induction, PSL could be reduced in 11 patients except for one patient with inadequate response, and PSL could be discontinued in 7 of them. No adverse events were observed at this time. [Conclusion] In addition to the efficacy of GC in reducing the dose as previously reported, remission was maintained with MPL alone in 7/11 patients at our hospital, and in some cases, the interval between MPL administration could be extended.

P1-181

Clinical characteristics of 3 cases treated with Mepolizumab for peripheral neuropathy due to eosinophilic granulomatosis with polyangiitis

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Conflict of interest: Yes

[Objectives] Numbness and paralysis of limbs due to peripheral neuropathy are characteristic of eosinophilic granulomatosis with polyangiitis (EGPA) and significantly reduce the quality of life of patients. We analyzed to clarify the clinical characteristics of EGPA patients treated with Mepolizumab (MPZ). [Methods] We investigated the clinical characteristics of 3 female patients diagnosed with EGPA in our department in 2024. [Results] In all cases, patients developed EGPA after the onset of bronchial asthma, and had generalized pain and numbness in the extremities. All of their treatment was initiated with oral glucocorticoid (GC) and/or high-dose GC pulse therapy. In the two cases treatment with MPZ within 2 weeks of onset, peripheral neuropathy improved dramatically. Intravenous immunoglobulin therapy was performed in 2 patients due to neuropathy, with no response in 1 patient and improvement in the other patient. One case treated with MPZ 8 years after onset showed little improvement. [Conclusion] In all cases, GC alone was insufficient in response, but early use of MPZ may improve peripheral neuropathy.

P1-182

Significance of Early Introduction of Mepolizumab for Eosinophilic Granulomatosis with Polyangiitis (EGPA) in Our Institution

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Conflict of interest: None

[Objectives] This study examines the significance of early mepolizumab (MEP) introduction in eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] EGPA patients prescribed MEP between December 1, 2022, and August 31, 2024, were identified. They were grouped into early (E), where MEP was started within 1 month of diagnosis, and late (L), where MEP was initiated after 1 month. The time to achieve glucocorticoid (GC)-free status was compared retrospectively. [Results] Of 27 cases, 7 were in group E and 20 in group L. At MEP initiation, the median age (years), ANCA-positive rate, eosinophil count (cells/μL), disease duration (days), prednisolone dose (mg), and immunosuppressant use (rate) were as follows for E and L: 74/54, 1 (14%)/12 (60%), 423/5378, 4/2001, 50/6, and 1 (14%)/11 (55%). The duration of MEP therapy was 428 days in group E and 1420 in group L. No patients required re-induction of remission. Among 19 GC-free patients, 6 (86%) were from group E and 13 (65%) from group L. The time to GC-free status was significantly shorter in group E (234 days) than in group L (779 days) (p=0.001). [Conclusion] MEP is effective in remission induction for EGPA. Early MEP introduction, within 1 month of diagnosis, shortened the time to GC-free, supporting its benefit in early treatment.

P1-183

Mepolizumab Use in patients with Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: Yes

[Objectives] To evaluate the real-world efficacy of mepolizumab for eosinophilic granulomatosis with polyangiitis (EGPA). [Methods] A retrospective study was conducted on EGPA patients at St. Luke's International

Hospital treated with mepolizumab (MEPO) for over a year or who had discontinued treatment. Data on drug retention and disease relapse were analyzed using the Kaplan-Meier method, and changes in glucocorticoid use were assessed with the Wilcoxon signed-rank test. [Results] A total of 25 patients were identified, with a median age of 61 years; 11 were male. Ten patients (40%) had a Five-Factor Score (1996) of >0, and 7 (28%) were ANCA-positive. MEPO retention rates were high. Median prednisolone dose significantly decreased from 9 mg/day (range: 5-20) at initiation to 2.75 mg/day (range: 1-4.25) by month 3. Median doses at 6, 9, 12, 18, and 24 months visit were 2, 0.75, 0, 0, and 0 mg/day, respectively. At the final visit, with a median of 1,387 days, the glucocorticoid dose was 0 mg/day (range: 0-1.25). The rate of patients in remission between 18 and 24 months with prednisolone less than or equal to 4, 2.5, and 0 mg/day at month 24 were 85, 75, and 70%, respectively. [Conclusion] In this EGPA cohort, mepolizumab demonstrated high retention and effective steroid-sparing effect.

P1-184

Clinical Characteristics of Patients with EGPA Treated with Mepolizumab in a Community Hospital in Japan

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Conflict of interest: None

[Objective] Mepolizumab (MEPO) was approved in Japan in 2018 for EGPA patients. Since then, efficacy data for Japanese EGPA patients has been accumulating. This study reports the clinical characteristics of EGPA patients who received MEPO at our department and the changes in steroid dosages. [Methods] We retrospectively reviewed EGPA patients treated with MEPO at our department between May 1, 2019, and April 30, 2024. We analyzed age, gender, organ involvement, steroid dosages, and the organ involvement and steroid dosage at the final observation. [Results] 12 patients (6 women, 50%) were included, with an average age of 62 years and a median disease duration of 3.5 months. 10 patients (83%) had neurological symptoms, and all 12 had asthma or sinusitis. The average prednisone (PSL) dose at the start of MEPO treatment was 26.7 mg. At the final observation, 10 patients continued MEPO, with a median treatment duration of 13 months and a observation period of 27 months. The final PSL dose averaged 2.4 mg. Six out of 10 patients continuing MEPO achieved steroid-free status, with a median treatment period of 24 months. [Conclusion] This study confirmed that MEPO effectively reduced PSL dosages in EGPA patients at our department. Several patients achieved steroid-free status.

P1-185

Establishing the Japan Collaborative Registry of ANCA-Associated Vasculitis (J-CANVAS): A Descriptive Study of Clinical Characteristics and Patient-reported Outcomes

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Conflict of interest: None

[Objective] To address the heterogeneity of practice in ANCA-associated vasculitis (AAV), we are developing a multicenter registry in Japan. [Methods] Patients with new-onset or severe relapsing AAV diagnosed after January 2017 were followed until March 2024 at 29 sites. In 2024, we conducted a survey on patient-reported outcomes. [Results] As of October 2024, 1,084 patients (637 MPA, 239 GPA, 208 EGPA; median age 73 years) were registered. The most affected organs were lungs (61%), kidneys (61%), nerves (38%), and ENT (29%). After treatment, 80% developed irreversible organ damage, including peripheral neuropathy, kidney dysfunction, lung fibrosis, diabetes, hearing loss, hypertension, muscle weakness, malignancies, cataracts, and osteoporosis. Over 3,210 person-years (PY) of follow-up, there were 61 severe relapses (1.9/100 PY) and 113 deaths (3.5/100 PY). Among 290 patients who participated in the survey, 43% reported fatigue, 58% felt anxiety or stress, and 69% expressed concerns about the future. Additionally, 33% were engaged in work, with a median productivity loss of 20% due to AAV. [Conclusions] In our patients, both vasculitis-related and treatment-related organ damage are frequent, with substantial impacts on their physical, psychological, and social quality of life.

P1-186

Clinical Characteristics of Severe Relapse in ANCA-Associated Vasculitis: Insights from the J-CANVAS Registry

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Conflict of interest: None

[Objectives] To clarify clinical characteristics of severe relapses in ANCA-associated vasculitis (AAV) patients. [Methods] J-CANVAS, a registry of 29 centers in Japan, has tracked AAV patients with new-onset or severe relapse since 2017, with follow-up until March 2024. We included patients with microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA), documenting relapse timing, prednisolone (PSL) dose, and baseline characteristics in relapsing vs. non-relapsing patients. Differences in organ involvement between onset and relapse were examined. Continuous variables were shown as medians [IQR] and categorical data as percentages. [Results] Of 452 patients (MPA: 318, GPA: 134), 41 (9%) had severe relapse. Relapsing patients showed no clear baseline differences from non-relapsing patients. Median time to relapse was 340 days, with 51% relapsing within a year. Median PSL dose at relapse was 10 mg. New major organ involvement emerged in 36% at relapse, including hypertrophic pachymeningitis, hearing loss, vision loss, and alveolar hemorrhage. Median BVAS was lower at relapse than onset (9 vs. 12). [Conclusion] No distinct baseline characteristics were found in severe relapses. Although BVAS was lower at relapse, new major organ involvement may develop, requiring monitoring.

P1-187

Treatment and outcome during induction of remission in microscopic polyangiitis in our department

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Conflict of interest: None

[Objectives] To determine the outcome of microscopic polyangiitis after one year of remission induction therapy. [Methods] After 1 year of retrospective follow-up, remission was defined as BVAS=0, PSL <10 mg, and no relapse. [Results] Twenty-eight cases of microscopic polyangiitis in our department were selected from 2013 to 2024. Compared 14 cases of GC alone, 10 cases with IVCY, and 7 cases with RTX. GC starting dose (median) for each group was 37.5 mg GC alone/47.5 mg with IVCY/45 mg with RTX; median dose after 52 weeks was 8.5 mg GC alone/11.6 mg with IVCY/6.3 mg with RTX; pretreatment BVAS (median) 12.5/16.5/10.0; pretreatment CRP (FFS≧2 in 8 patients with GC alone/8 with IVCY/6 with RTX, FFS (median) in 2 patients with GC alone/2 with IVCY/2 with

RTX, BVAS ≧50% improvement in 14 patients with GC alone/10 with IVCY/5 with RTX, The number of remission cases was 5 with GC alone, 1 with IVCY, and 1 with RTX. Diabetes mellitus was the most common adverse event. Deaths were 1 case of GC alone, 1 case with IVCY, and 1 case with RTX. Relapse or increased dose of GC was required in 3 patients with GC alone, 5 patients with IVCY, and 3 patients with RTX. [Conclusion] In severe cases, IVCY or RTX combination was used, but diabetes resulted in a low remission rate.

P1-188

A comparative study of biomarkers in interstitial nephritis associated with systemic lupus erythematosus and ANCA-associated vasculitis

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) and ANCA-associated vasculitis (AAV) can both cause interstitial nephritis. We measured urinary N-acetyl-β-D-glucosaminidase (NAG) and urinary β2-microglobulin (β2MG) as biomarkers to investigate if differences arise due to varying disease onset patterns. [Methods] We compared pre-biopsy urinary NAG and β2MG levels in 21 SLE patients and 22 AAV patients diagnosed with interstitial nephritis through optical microscopy among 531 renal biopsies conducted at our hospital from January 2006 to October 2022 (384 SLE and 147 AAV cases). [Results] In SLE patients, there were no significant differences in urinary NAG and β2MG based on interstitial nephritis presence. In AAV patients, NAG levels were higher in the interstitial nephritis group, but β2MG showed no significant difference. Between groups, no significant difference was found for NAG, while β2MG was significantly higher in AAV patients. [Conclusion] AAV patients, who experience rapid renal function decline, are more influenced by β2MG levels. In SLE, no significant differences in NAG and β2MG indicate challenges in assessing interstitial nephritis outside of biopsy. Further discussion will include a review of relevant literature.

P1-189

Study on Underlying Pulmonary Lesions in ANCA-Associated Vasculitis

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Conflict of interest: None

[Objective] ANCA-associated vasculitis can cause pulmonary lesions such as alveolar hemorrhage. Conversely, asthma is a risk factor for EGPA, and silica inhalation can induce MPA, indicating that pulmonary lesions can also be secondary to these conditions. [Methods] We reviewed cases at our hospital from December 2004 to September 2024, selecting those who tested positive for ANCA at least once. We focused on cases that were previously ANCA-negative but later converted to positive, examining the underlying pulmonary lesions before conversion. [Results] Among the 21 PR3-ANCA positive cases and 62 MPO-ANCA positive cases (with one overlap), 7 cases (2 PR3-ANCA and 5 MPO-ANCA) were previously ANCA-negative. At the time of ANCA negativity, all cases had chest X-rays, and 6 had CT scans. Interstitial lung disease was observed in 5 cases, and chronic airway inflammation in 2 cases. Other findings included silicosis, emphysema, and post-inflammatory changes, each in one case. Upon ANCA conversion, clinical phenotypes included 3 asymptomatic cases, 1 case of another collagen disease, 2 cases of exacerbated ANCA-associated ILD, and 1 case of MPA. [Conclusion] Underlying pulmonary lesions may be a risk factor for ANCA-associated vasculitis.

P1-190

The usefulness of cardiac MRI in evaluating cardiac involvement in MPO-ANCA-positive and/or ANCA-negative eosinophilic granulomatosis with polyangiitis (EGPA)

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Conflict of interest: None

The prevalence of cardiac involvement is significantly lower in patients (pts) with ANCA-positive (+ve) eosinophilic granulomatosis with polyangiitis (EGPA) than in pts with ANCA-negative (-ve) pts. In recent years, parametric mapping has become a novel method for evaluating myocarditis using cardiac MRI (cMRI). In this study, we compared cases of EGPA in which myocarditis was diagnosed using cMRI from the perspective of ANCA-presence. MPO-ANCA (+ve): 45-year-old male. Eosinophil count was 24,700/μL at onset, elevations in cardiac enzymes and NT-proBNP were seen. CRP was 7.68 mg/dL, MPO-ANCA was 92 U/ml. There was an abnormality in the global extracellular volume fraction (ECV), no abnormalities in T2 mapping was seen. Delayed gadolinium enhancement (LGE) was negative. MPO-ANCA (-ve): 46-year-old female. Eosinophil count was 9300/μL at onset, there was no elevation in cardiac enzymes or NT-proBNP. CRP 13.31 mg/dL, MPO-ANCA 1 U/ml, ECV global elevation was observed, and T2mapping was also abnormal. LGE was observed in the pericardium. The dualism of ANCA-positive and/or ANCA-negative-eosinophilic phenotype is widely accepted. We identified acute myocardial edema using T2 mapping. cMRI might be useful for selecting treatment based on the activity of myocarditis and MPO-ANCA status.

P1-191

Risk Factors for Hepatic Injury following Azathioprine Treatment for ANCA-Associated Vasculitis

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Conflict of interest: None

[object] Azathioprine (AZA) has been used as an immunosuppressive drugs to maintain remission for ANCA-associated vasculitis (AAV) for decades. Hepatic injury is a well-known side effect of AZA. However, few studies have reported on risk factors for AZA hepatotoxicity in patients with AAV. Therefore, the purpose of our study was designed to investigate the risk factors for AZA hepatotoxicity in patients with AAV in our hospital. [method] Our study was a retrospective study and included patients diagnosed with AAV and treated with AZA while attending our hospital between April 2010 and July 2024. “Baseline” was defined as the time of diagnosis. The risk factors were extracted with multivariate logistic regression analysis considering baseline age and gender as covariates. [Result] 23 patients were included 15 females (65.2%) with a median age at onset of 72 years. Multivariate logistic regression analysis showed that the presence of hepatic impairment at baseline (95%CI; 1.1-364.1 odd ratio; 20.4, p=0.04) was a significant predictor for AZA hepatotoxicity. [Conclusions] The risk factor for AZA hepatotoxicity in patients with AAV may be influenced by the presence or absence of liver injury at diagnosis.

P1-192

Umbilical cord-derived mesenchymal stem cells suppress Sjogren’s syndrome pathology

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Conflict of interest: None

[Objectives] Primary Sjögren’s syndrome (pSS) causes dry mouth and

dry eyes. Recently, mesenchymal stem cell transplantation has been shown to improve salivary flow and decrease lymphocytic infiltration of the salivary glands. We aimed to confirm the anti-inflammatory effect of umbilical cord mesenchymal stem cells (MSCs) on the pathogenesis of pSS and to elucidate the mechanism of this effect. [Methods] We evaluated the induction of differentiation and cytokine production of each cell by co-culturing peripheral blood mononuclear cells (PBMCs) from pSS patients with MSCs. $CD4^+$T cells and B cells were isolated from PBMCs and co-cultured with MSCs and the induction of differentiation and inhibition of IgG production of each cell were evaluated. MSCs were also administered to NOD mice to evaluate saliva volume and cellular infiltration of glandular tissue. [Results] Co-culture of PBMCs with MSCs decreased the percentage of IFN-γ^+ and IL-4^+T cells and TNF-α^+ monocytes. Co-culture of $CD4^+$T and B cells with MSCs decreased plasma cells. In NOD mice, MSCs maintained salivary flow and inhibited cellular infiltration. [Conclusion] We showed that MSCs suppress inflammation of various immune cells, and MSCs may improve the pathogenesis of pSS.

P1-193

T follicular helper 1 cells in blood potentially mirror salivary gland-infiltrating T cells in primary Sjögren's syndrome

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Conflict of interest: None

[Objectives] To clarify circulating CD4+ T cell subsets which reflect salivary gland (SG) inflammation, and function of these subsets in pSS. [Methods] 1) Circulating CD4+ T cell subsets were compared between 30 pSS and 20 healthy controls, and clinical correlations were also assessed. 2) Similarity of TCR repertoire between SG T cells and circulating CD4+ T cell subsets was analyzed in pSS. 3) Based on 1) and 2), Tfh1 differentiation factors in the pSS SG environment were examined. 4) Cytokine production and effects on B cell differentiation of Tfh1-squeezed pSS CD4+ T cells were examined in vitro. [Results] 1) In pSS, circulating PD-1+ICOS+ Tfh1 cells were increased and positively correlated with autoantibody titers. 2) Circulating Tfh1 and Th1 cells shared TCR repertoire with SG T cells. 3) TGF-β, IL-12, and CXCR5 were significantly elevated in pSS SG, with TGF-β correlating positively with CXCR5. pSS CD4+ T cells were differentiated into Tfh1 by TCR+TGF-β stimulation. 4) TCR+TGF-β stimulated pSS CD4+ T cells produced increased levels of IL-2, TNF-α, and IL-21, and promoted differentiation of naïve B-cells into CD19+CD38+ B cells. [Conclusion] Circulating Tfh1 cells potentially mirror SG T cells and reflect the inflammatory state of the SG in pSS, driven by TGF-β stimulation with TCR recognition.

P1-194

Differences in menopausal symptoms based on the presence of SS-A antibodies

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Conflict of interest: None

[Objectives] This study aimed to investigate whether menopausal symptoms differ based on the presence of SS-A antibodies. [Methods] We reviewed the records of 23 patients with SS-A positive menopausal syndrome and 64 with SS-A negative menopausal syndrome. We analyzed their initial pain VAS, stiffness VAS, Simplified Menopause Index (SMI), various menopausal symptoms, and the presence of dry mouth and dry eyes. [Results] A significant difference was noted only in the presence of dry mouth ($p<0.05$). SS-A positive patients (Group A) had a higher prevalence of dry mouth than SS-A negative patients (Group B) (A: 47.8%, B: 25%, $p=0.0442$). Among SS-A positive patients, those with dry mouth had higher pain VAS ($p=0.0441$), stiffness VAS ($p=0.0109$), and SMI ($p=0.00265$). [Conclusion] SS-A positive menopausal syndrome symptoms are similar to typical menopause, but there is a higher prevalence of dry mouth, and those with dry mouth experience more severe symptoms. Therefore, more proactive treatments, including hormone replacement therapy (HRT), are needed. While pain and stiffness may also indicate Sjögren's syndrome, we have seen effective HRT cases. If improving patient-reported outcomes (PRO) is the goal, rheumatological care should consider the possibility of menopausal syndrome.

P1-195

A case of primary Sjögren's syndrome complicated by hemophagocytic syndrome

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Conflict of interest: None

[Purpose] We report a case of primary Sjögren's syndrome (SjS) complicated by hemophagocytic syndrome (HPS). [Case] A 33-year-old male from Myanmar was admitted to the gastroenterology department due to fever and loss of appetite. He was treated with antibiotics; however, his fever did not subside, and roxoprofen was administered. A blood test showed a sudden decrease in all blood cell counts and a progressive decline in kidney function. Furthermore, a bone marrow test showed blood cell phagocytosis; thus, he was diagnosed with HPS and transferred to our department. Blood tests revealed a variety of autoantibodies. Minor salivary gland biopsy and scintigraphy findings were consistent with SjS, and the patient was diagnosed with SjS complicated by HPS. After steroid pulse therapy, the patient was treated with prednisolone 40 mg/day as maintenance therapy, and the blood cell count and fever improved. [Discussion] The coexistence of collagen disease and hemophagocytic syndrome is well known; but there are very few reports of HPS complicating primary SjS. Similar to systemic lupus erythematosus, an interferon signature has been reported to be involved in the pathogenesis of SjS, suggesting that common immune dysregulation may be involved in the development of HPS.

P1-196

A case of necrotizing lymphadenitis complicated by hemophagocytic syndrome in the background of Sjögren's syndrome

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Conflict of interest: None

A 55-year-old woman, who was diagnosed with Sjögren's syndrome (SS) at the age of 27, visited our hospital with fever and rush in April, Year X. Since she had rush on her upper arms, abdomen, back, and face, drug eruption was suspected. Although prednisolone (PSL) was initiated, her condition did not improve, leading to hospitalization. She had tender axillary lymph node swelling, and a lymph node biopsy revealed findings consistent with necrotizing lymphadenitis (NL). No other significant findings were observed. Despite restarting 50 mg of PSL, she experienced recurrent fever. Additional steroid-pulse therapy and tacrolimus were also ineffective. Pancytopenia and elevated ferritin levels suggested hemophagocytic syndrome (HPS), which improved with the addition of baricitinib and an increase in the dose of PSL to 100 mg. Since ferritin levels rose again, PSL was switched to betamethasone (BMZ), and cyclophosphamide pulse was added. After switching to BMZ, the fever quickly subsided, and both blood cell counts and ferritin levels improved, leading to the remission. NL generally resolves spontaneously. While there are reports of NL occurring in the context of SS, cases with a refractory course like this one are rare. We will report this case with a review of the relevant literature.

P1-197

Comparison of Salivary Gland Ultrasound Findings in Mikulicz Disease and Sjogren's Syndrome: A Single-Center, Retrospective Observational Study

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Conflict of interest: None

Objective: To compare salivary gland ultrasound findings in Mikulicz Disease (MD) and Sjogren's Syndrome (SS). **Methods:** We conducted a retrospective analysis of patients undergoing salivary gland ultrasound from May 2020 to September 2024, including those meeting IgG4-related MD diagnostic criteria (2008) and ACR/EULAR classification criteria for SS (2016). Ultrasound was performed using an Aplio i700 (Canon) with an 18 MHz linear probe. Grey-scale (GS) findings were categorized from Grades 0 to 3 per OMERACT criteria. Power Doppler (PD) grading evaluated low/no echo areas: Grade 0 indicated none; Grade 1 represented three points or one fusion plus one point; Grade 2 indicated low echo areas <50%; and Grade 3 denoted ≧50%. Maximum diameter of hypo/anechoic areas was classified as <5 mm, 5-10 mm, or >10 mm. **Results:** A total of 10 MD patients and 26 SS patients were analyzed. In the parotid gland, GS grades for MD were 0.0%/10.0%/40.0%/50.0%, while SS grades were 30.8%/46.2%/11.5%/11.5% (p=0.043). PD grades in the parotid gland showed MD at 40.0%/30.0%/20.0%/10.0% vs. SS's 80.8%/19.2%/0.0%/0.0% (p=0.012). **Conclusion:** MD exhibited significantly larger GS and PD grades compared to SS, suggesting SGUS findings may aid in distinguishing these conditions.

P1-198

The significance of rheumatoid factor in IgG4-related disease

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Conflict of interest: None

[Objectives] While rheumatoid factor (RF) is known to bind to the Fc portion of IgG, its association in IgG4-related disease (IgG4RD) remains unclear. This study aimed to investigate the impact of RF in patients with IgG4RD. [Methods] We retrospectively analyzed 35 patients diagnosed with IgG4RD at our department between 2017 and 2024. The cohort was divided into RF-positive and RF-negative groups, and clinical features and relapse rate were compared. [Results] The median age at disease onset was 66 years, with 21 male patients (60%), and 16 patients (46%) were RF-positive, with a median RF level of 28.5 IU/mL. The RF-positive group tended to exhibit higher serum IgG4 levels (841 vs. 370 mg/dL, p=0.07) and higher sIL-2R levels (754 vs. 571 U/mL, p=0.06) compared to the RF-negative group. However, there were no significant differences in the number of affected organs or the relapse rate between RF-positive and RF-negative groups. [Conclusion] IgG4RD cases with positive RF exhibited a trend toward higher serum IgG4 and sIL-2R levels, suggesting that RF may reflect immunological activity in IgG4RD. However, RF has minimal direct impact on the clinical course. Further studies are necessary to elucidate the role of RF in the pathophysiology of IgG4RD.

P1-199

Usefulness of Monitoring Serum IgG4 Level as a Predictor of Relapse in IgG4-Related Disease

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Conflict of interest: None

[Objectives] To examine the usefulness of monitoring serum IgG4 level as predictor of relapse in IgG4-related disease (IgG4-RD), we investigate the relationship between serum IgG4 level and clinical course after treatment. [Methods] We analyzed 99 patients diagnosed IgG4-RD from 2008 in our facility. We compared between the relapse and non-relapse groups about laboratory data and clinical course analyzed from their medical records retrospectively. [Results] Forty-four patients were followed up for more than one year after treatment. Relapse was observed in 17 (39%) of the patients during follow-up (median 18 months, range 12-30 months). Compared to the non-relapse group, the relapse group had more organ involvements and higher serum IgG4 levels before treatment significantly. Serum IgG4 levels decreased in all patients after treatment, and 28 of 44 patients normalized (<135 mg/dl). The normalization rate of serum IgG4 levels was higher in the non-relapse group than in the relapse group, especially between 3 and 18 months of treatment. [Conclusion] Serum IgG4 levels decreased with treatment in all IgG4-RD patients. We suggested that the normalization of serum IgG4 levels during the 18 months of treatment may reduce the risk of relapse.

P1-200

Use of colchicine and its problems in patients with Behcet's disease

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Conflict of interest: None

[Objectives] Colchicine (COL) is used in the treatment of Behçet's disease (BD). In this study, we investigated the use of COL in BD patients and examined problems with COL. [Methods] Clinical data, COL and its adverse events were retrospectively extracted from the medical records of BD patients and analyzed. [Results] There were 233 BD patients (89 men). 194 patients (83.6%) had a history of COL administration. At the end of the observation period, 128 cases (55.2%) were continuing cases of COL. When examining each clinical symptom, COL was continued in 51 cases (47.7%) for eye lesions, 128 cases (55.4%) for stomatitis, 85 cases (56.7%) for erythema nodosum, 93 cases (54.1%) for genital ulcers, 10 cases (90.9 %) for epididymitis, 98 cases (60.1%) for arthralgia, and 23 cases (52.2%) for fever. The reasons for discontinuing COL were adverse events in 32 patients, remission in 19 patients, try to conceive in 12 patients, and immunosuppressive therapy in 9 patients. COL was used in combination with CyA in 12 patients, and CK elevation was observed in five patients and liver damage in three patients. [Conclusion] The results of the use of COL in BD patients have been clarified. Adverse events occurred at a high rate when combined with CyA, so caution is required when using the combination.

P1-201

Characteristics of patients with lupus anticoagulant-positive Behçet's disease

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Conflict of interest: None

[Objectives] Behçet's disease (BD) is at high risk for thrombus formation, and endothelial dysfunction has been suggested to be involved. There have been occasional reports of BD patients testing positive for antiphospholipid antibodies (aPL), which are involved in thrombus formation. In this study, we investigated BD patients who tested positive for aPL. [Methods] We retrospectively extracted and analyzed disease type, thrombosis, and aPL from the medical records of BD patients. [Results] aPL was measured in 47 cases. The reason for measuring aPL was to examine vascular BD in 14 cases and for screening in 33 cases. In this study, aCL antibodies and anti-β2-GPI antibodies were all negative. LA was positive in 6 of 38 cases. Three cases of DVT (50.0%) (one with pulmonary embolism) were observed in the LA positive group, and six cases of DVT (18.8%) (four with pulmonary embolism) were observed in the LA negative group. No thrombophlebitis was observed in the LA positive group, but six cases were observed in the LA negative group. Three of 14 cases (21.4%) of vascular BD were LA positive. [Conclusion] Our results suggest that LA may be involved in some of the thrombosis tendencies in BD. We also found that LA-positive BD patients exist regardless of whether they have vascular lesions.

P1-202

A Case of Vasculitis in Behcet's Disease Initially Suspected to be Buerger's Disease

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Conflict of interest: None

[Case] A 27-year-old male patient. [History of Present Illness] Two years ago, he was diagnosed with thrombophlebitis after presenting with the redness in both lower limbs. Around the same time, he was diagnosed with uveoretinitis. Four months ago, skin ulcers appeared on his right toes, leading to his admission to our hospital. [Past Medical History] T2DM [Smoking History] 20 cigarettes/day for 7 years [Physical Examination] Stomatitis and multiple skin ulcers on the right toes were observed. [Imaging Findings] CT revealed multiple nodules in both lungs, suggestive of pulmonary infarction. Angiography demonstrated peripheral arterial occlusions in the limbs, with corkscrew-like collateral blood vessels. [Clinical Course] Buerger's disease was initially suspected, and vasodilators was initiated, but the response was poor. These findings led us to consider the lesions as manifestations of vascular Behçet's disease. In addition to colchicine, we administered mPSL, followed by PSL, and infliximab. The skin ulcers improved, and the lung lesions showed signs of shrinking. [Clinical Importance] Differentiating between Buerger's disease and vascular Behçet's disease is crucial when assessing the causes of peripheral vascular stenosis and skin ulcers.

P1-203

Clinical features of Behcet's Disease in the Koto-Toyosu Hospital

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Conflict of interest: None

[Objectives] To elucidate the characteristics of Behçet's disease (BD) in our hospital. [Methods] Between July 1st and September 30th, 2024, 21 (4.3%) BD patients visited at our division and 3 (14.3%) were men. The median age at this survey was 52 year-old (y/o) (IQR: 41, 58), and the median age at the onset was 30 y/o (IQR: 18, 40.5). [Results] The lesions of BD in the Japanese criteria were as below; oral and skin lesions: each 21 (100%), genital: 19 (90.5%), arthritis: 18 (85.7%), ocular: 10 (47.6%). 9 patients (42.9%) with special lesions, intestinal: 6 (28.6%), neurological and vascular: each 2 (9.5%), and only 1 patient had both intestinal and vascular lesions. The median stage severity classification was 4 (IQR: 2, 4), and the median BDCAF was 2 (IQR: 1.5, 3.5). The treatment options were as below; colchicine: 13 patients (61.9%), NSAIDs: 9 (42.9%), GC: 5 (23.8%), CyA: 2 (9.5%), TNFα inhibitors: 2 (9.5%), APR: 2 (9.5%), AZP: 1 (4.8%), and 5-ASA: 1 (4.8%). The median PSL-conversion was 0 mg/d (IQR: 0, 2.5). [Conclusion] The male patients were fewer than previously reported. BD patients attending our hospital had low disease activity indices.

P1-204

Severe inferior vena cava thrombosis in a patient with vascular Behcet's disease responded to infliximab

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Conflict of interest: None

[Background] Behcet's disease (BD) is associated with a variety of vascular diseases, and inferior vena cava (IVC) thrombosis is one of the most devastating abnormalities for which standard treatment has not yet been established. [Patient] A 22-year-old woman presented with polyarticular pain and painful erythema on both lower legs. She visited a clinic and was prescribed antibiotics, which resulted in no improvement, and visited our hospital. We diagnosed her as BD since she had multiple aphthous ulcers in the mouth, erythema nodosum, and genital ulcers. Despite the treatment with colchicine, her oral ulcers recurred. Since she developed right hip pain, an MRI and enhanced CT scan were performed, which showed persistent thrombus in the right external iliac vein to IVC. She was treated with 40 mg of prednisolone, infliximab, and apixaban for deep vein thrombosis (DVT). After the treatment, hip pain rapidly improved, and the thrombus also shrank significantly. [Conclusion] Immunosuppressive therapy is considered to be an effective treatment option for severe DVT in BD, and one possible reason for this was the modifying effect on vascular endothelial damage caused by excessive neutrophil activation, which is one of the pathological conditions of thrombosis formation in vascular BD.

P1-205

A Case of Behçet's Disease Involving Large Arterial Lesions Detected Through Vessel Wall Thickening Without Aneurysm Formation

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Conflict of interest: None

[Case] A 46-year-old woman presented with recurrent oral ulcers since her teenage years, along with episodes of fever and back pain starting in her 30s. Five days before consulting, she experienced a high fever and back pain. Three days before consulting, she developed oral ulcers, rashes, and joint pain. She was initially diagnosed with pyelonephritis and treated with antibiotics, which did not improve. An enhanced CT scan revealed thickening of the abdominal aorta and common iliac artery walls, along with increased fat density around the inferior vena cava. Physical examination revealed oral ulcers, folliculitis-like rashes, arthritis, and genital ulcers. Laboratory tests showed elevated CRP levels, but autoantibody tests were negative. No ocular lesions were noted, and HLA-B51 and A26 were negative. Given the arterial and venous involvement, she was diagnosed with Behçet's disease (BD) complicated by vascular involvement. Glucocorticoid (GC) pulse therapy, high-dose GC, colchicine, and cyclophosphamide were introduced, leading to disease remission. [Discussion] Large vessel involvement in BD often presents as aneurysms. However, this case only showed inflammatory changes, highlighting the importance of early diagnosis in preventing further complications.

P1-206

This case study demonstrates the efficacy of a JAK inhibitor in the treatment of Behçet's disease with myelodysplastic syndrome and trisomy 8

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Conflict of interest: None

The patient is a 76-year-old male who was diagnosed with myelodysplastic syndrome (MDS) following leukocytopenia seven years ago. His MDS was identified as trisomy 8-positive and classified as low risk in IPSS-R, being stable in white blood cell counts. From that time, an autoinflammatory disease was considered due to his history of fever and joint pain. In year X-4, the presence of an ulcer and stomatitis, in addition to HLA A26, led to the diagnosis of intestinal Bechet disease (BD) associated with trisomy 8. He was treated with colchicine and prednisolone, but did not improve. Subsequently, he was administered two TNFα inhibitors, however, the CRP levels remained elevated, and he exhibited multiple ulcers and erosions in the gastrointestinal tract. Because the efficacy of JAKi has been demonstrated in autoinflammatory diseases that have been part of MDS, he was treated with upadacitinib, a JAKi, which improved his

symptoms and CRP levels. It has been reported that patients with MDS and trisomy 8 often present with symptoms similar to BD, particularly intestinal lesions, which are often challenging to treat. In this case, upadacitinib demonstrated efficacy in the treatment of refractory BD, in which two TNFαinhibitors proved to be JAKi may treat trisomy 8-positive BD.

P1-207

A 15-year-old female with Lipschütz Ulcer after Subclinical Infection with SARS-CoV2

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Conflict of interest: None

Patients with recurrent vulvar ulcers are often referred to the rheumatologist suspected of Behçet's disease (BD), but acute vulvar ulcers, known as Lipschütz ulcers, are rarely seen. A 15-year-old female. She had been in contact with a patient with fever two weeks prior to the onset of symptoms. On the day of onset, she had a pain in the genital area and was prescribed valacyclovir. On the 3rd day, a vulvar ulcer appeared and rapidly worsened. She developed a fever on the 4th day, and on the 9th day, she was admitted to our hospital with suspected BD and vulvar cellulitis. Swelling of the labia majora and five deep ulcers measuring up to 2 cm were noted on the labia majora and minora. Blood tests showed neutrophil-predominant leukocytosis, high CRP and D-dimer. Lumipulse SARS-CoV-2 Ag was negative, but SARS-CoV2 anti-spike protein-IgG on the 19th day of illness was high at 11,400 AU/ml. Thus she was diagnosed with Lipschütz ulcerdeveloped after asymptomatic infection with SARS-CoV-2. Prednisolone (PSL) 1 mg/kg was started. The ulcer improved, and PSL was gradually tapered over 20 days. There has been no recurrence. In adolescent females with rapidly exacerbating vulvar ulcers, Lipschütz ulcers should be considered.

P1-208

A Case of MTX-LPD Initially Suspected as Chronic Progressive Neuro-Behçet's Disease

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Conflict of interest: None

[Case] 56-year-old male [Chief Complaint] Unsteadiness [Present Illness] The patient, treated for Behçet's disease from 43-year-old with prednisolone, infliximab, and methotrexate (MTX), noticed decreased walking speed in the fall of year X-1 and unsteadiness from February of year X. By April, his walking worsened, requiring support. Brain MRI was unremarkable, but neurological exams showed limb and truncal ataxia and cerebellar dysarthria. Cerebrospinal fluid (CSF) showed mild protein elevation and pleocytosis. Suspecting chronic neuro-Behçet's disease, CSF IL-6 was measured and found normal. Autoantibody tests for autoimmune or paraneoplastic syndromes were negative. Steroid pulse therapy had no effect. During hospitalization, a positive cytomegalovirus (CMV) antigen prompted a torso CT, revealing lymphadenopathy. Biopsy confirmed malignant lymphoma (OI-LPD). MTX was stopped, suspecting paraneoplastic cerebellar degeneration from MTX-related lymphoproliferative disorder (MTX-LPD), and chemotherapy led to symptom improvement. [Discussion] Despite focusing on cerebellar symptoms with CSF and brain imaging, torso evaluation was delayed until CMV positivity. For patients on MTX, MTX-LPD should be considered, and torso evaluation is important even if symptoms are neurological.

P1-209

Remission of trisomy 8 associated refractory intestinal Behçet's-like disease and myelodysplastic syndrome with high-dose infliximab

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Conflict of interest: None

[Introduction] Myelodysplastic syndrome (MDS) with trisomy 8 is occasionally complicated by an intestinal Behçet's disease-like phenotype. Although TNF inhibitors, colchicine and azacitidine are thought to be partially effective, the condition is often refractory, and the optimal treatment remains to be elucidated. [Case Presentation] The patient is a 78-year-old female with a 15-year history of thrombocytopenia. She presented to our department 1.5 years ago with periodic fever, intestinal ulcers, arthralgia, and erythema. Trisomy 8 was detected in her bone marrow, and she was later diagnosed with MDS. She was treated with prednisolone and 6 mg/kg of infliximab (IFX), but suffered relapses upon prednisolone tapering. IFX was switched to tocilizumab, tofacitinib, and adalimumab, all with little effect. High-dose IFX (10 mg/kg every 4 weeks) was initiated 7 months ago, and her symptoms improved. 4 months ago, IFX was suspended for bacteremia, and she experienced ileocecal ulcers and aseptic liver abscess. A recurrence of intestinal Behçet's-like disease was suspected, and IFX was reinitiated. [Clinical Significance] High-dose IFX may be effective against trisomy 8 associated intestinal Behçet's-like disease, but further studies need to be conducted to test its efficacy and safety.

P1-210

A case of Behcets disease presenting extensive subcutaneous panniculitis on PET-CTimages, like "subcutaneous panniculitis-like T-cell lymphoma"

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Conflict of interest: None

(case) A 28-year-old female patient with a history of recurrent oral ulcers since childhood. She was hospitalized with a fever that persisted for a week, refractory to antibiotics. After admission, she began complaining of severe pain in the upper limbs, trunk, and thighs, where the skin looks normal except painful erythemas on the both lower legs. PET-CT revealed subcutaneous FDG accumulation in the painful but normal-appearing skin area, suggesting the presence of panniculitis, which was later confirmed by deep skin biopsy. With diagnosis of Behcet's disease, she was treated by colchicine and NSAIDs, with transient remission. One week later, as she had massive melena, colonoscopy was performed showing ileocecal ulcer consistent with intestinal Behcet's disease. Thirty mg of PSL was enough to relieve all the symptoms, and the dose of PSL was reduced to 12.5 mg without relapse. (Clinical Significance) This case was atypical in that the erythema nodosum was not predominantly on the lower legs but distributed throughout the body, and in that the disease flared up after a short period of recovery by colchicine. Combined with the characteristic FDG uptake findings, differential diagnosis from subcutaneous panniculitis-like T-cell lymphoma was necessary.

P1-211

A case of intestinal Behcet's disease that developed in old age

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Conflict of interest: None

Behcet's disease is a refractory systemic inflammatory disease. The most common age at onset is reported to be between 30 and 40 years old. Intestinal Behcet's disease is a condition classified as a special type of Behcet's disease. It is said to appear 4.5 to 6 years after the appearance of the first symptom. We experienced a case of an elderly male who developed intestinal Behcet's disease with multiple ulcerative lesions in the entire digestive tract from the mouth to the rectum, without skin or eye symptoms or vulvar ulcers, about 2 years after the appearance of refractory aphthous stomatitis. The case was an 80-year-old man who had been suffering from recurrent stomatitis for about two years before the onset of

the disease. In early July 2024, his stomatitis worsened, and he also developed anorexia, diarrhea, and abdominal pain. After being hospitalized and undergoing an upper and lower gastrointestinal endoscopy, multiple ulcers were found in the pharynx, epiglottis, esophagus, stomach, duodenum, bauchin valve, entire colon, and anus, and the patient was diagnosed with intestinal Behcet's disease based on the nature of the gastrointestinal lesions and the clinical course.

P1-212

A case of 2-year-old girl with an anti-aquaporin 4 and anti-SS-A/Ro antibody-positive neuromyelitis optica spectrum disorder well controlled by mycophenolate mofetil

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Conflict of interest: None

[Background] Juvenile-onset neuromyelitis optica spectrum disorders (NMOSD) are rare and the knowledge of therapeutic strategies is limited. [Case] A 2-year-old girl, she had a history of immune thrombocytopenia. She had left abducens nerve palsy and ataxic gait, and was tentatively diagnosed with encephalitis. One month after the discontinuation of steroid, fever and claudication were occurred. She had bilateral conjunctival hyperemia and dilated nail bed vessels in both fingers. ANA titers of 1:640 (speckled pattern), anti-SS-A/Ro antibody 12770 U/ml, MRI showed abnormal signals at the knee of corpus callosum and posterior part of right optic nerve bulb, but no spinal cord lesions. Anti-aquaporin 4 antibody was positive, thus, we finally diagnosed her with NMOSD. A biopsy of the small salivary glands of the lips was performed, but no evidence of Sjögren's syndrome. She was treated with systemic corticosteroids and mycophenolate mofetil (MMF), and her symptoms rapidly improved. After discontinuation of steroids, no relapse have been observed with MMF alone. We performed whole exome sequencing, but no diagnostic variants have been found. [Conclusion] MMF could be effective drug for preventing the relapse of juvenile-onset NMOSD. A similar case series is required.

P1-213

Antineutrophil cytoplasmic antibodies (ANCA) in patients with relapsing polychondritis (RP)

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Conflict of interest: None

[Objectives] Relapsing polychondritis (RP) is a chronic and recurrent inflammatory disease of cartilage tissue throughout the body. There is no specific test for diagnosis. The diagnosis is made comprehensively based on clinical and imaging findings and biopsies of the lesions. There is no serological marker for diagnosis. We report the relationship between RP and anti-neutrophil cytoplasmic antibodies (ANCA). [Methods] Among RP patients who visited our hospital between October 2004 and April 2023, We looked at 56 people who were treated. [Results] All patients with RP met the classification criteria for Damiani and Levine. There were five ANCA-positive cases, which was a transient increase in the early stages of diagnosis. Two patients were positive for PR3-ANCA, two for p-ANCA, and one for MPO-ANCA. None of whom met the classification criteria for ANCA-associated vasculitis. [Conclusion] Since ANCA may be positive in RP, it is necessary to comprehensively judge pathological diagnosis for differentiation.

P1-214

Two Cases of TAFRO Syndrome Associated with Autoimmune Diseases (SLE and Sjögren's Syndrome)

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Conflict of interest: None

[Introduction] The diagnostic criteria of TAFRO syndrome requires excluding other autoimmune diseases. [Case 1] A 23-year-old woman presented with one month of erythema and 2 week of dyspnea on exertion. She developed anasarca, splenomegaly, and nephrotic syndrome with hematuria. Laboratory test showed thrombocytopenia, hypocomplementemia, and positive antinuclear and anti-DNA antibodies. Renal biopsy revealed lupus nephritis (ISN/RPS IV (G)-A), and bone marrow biopsy showed reticulin fibrosis. We diagnosed TAFRO syndrome associated with SLE. She responded well to glucocorticoids and biologics. [Case 2] A 62-year-old woman with rheumatoid arthritis and Sjögren's syndrome was admitted due to chronic subdural hematoma and thrombocytopenia. She developed persistent fever, anasarca, lymphadenopathy, hepatosplenomegaly, and acute renal impairment in 2 weeks. Bone marrow biopsy revealed reticulin fibrosis, and lymph node biopsy indicated plasma cell-type Castleman disease. Remission induction was initiated with glucocorticoids and biologics, then we added cyclosporine due to persistent cytopenias. [Discussion] This case series suggests that some cases of TAFRO syndrome may coexist with or manifest as a serious condition of autoimmune diseases.

P1-215

Clinical characteristics of TAFRO syndrome in our hospital

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Conflict of interest: None

[Objectives] TAFRO syndrome is characterized by thrombocytopenia, anasarca, fever, renal insufficiency, and organomegaly. Recently, TAFRO syndrome has been proposed as a clinical manifestation of iMCD-TAFRO, which the lymph node histopathology isn't consistent with iMCD or other comorbidities. [Methods] We examined patients with TAFRO syndrome, who admitted to our hospital between Jan 2017 and Oct 2024. Clinical symptoms, laboratory data, and the course of treatment were examined between patients with iMCD-TAFRO and TAFRO syndrome except for iMCD-TAFRO. [Results] 5 patients (60.6±10.2 years old, 4 males/1 female) were evaluated. iMCD-TAFRO group has 3 patients, which had mixed type of lymph node histopathology in one case. iMCD-TAFRO group had higher CRP (17.81 vs 3.39 mg/dL), lower platelet count (2.8 vs 6.3 $\times 10^4/\mu L$), lower total IgG (1396.3 vs 3694.5 mg/dL), and higher severity classification score (8.67 vs 4.50 points). All patients received steroid therapy and additional drugs (cyclosporine in 5, tacrolimus in 3, tocilizumab in 1, and rituximab in 1). Calcineurin inhibitors were effective in all patients. [Conclusion] TAFRO syndrome can be severe with a rapid course, and iMCD-TAFRO group tends to be more severely affected, suggesting the importance of early diagnosis and treatment.

P1-216

Baseline Characteristics of Patients Enrolled in the FIBRONEER-ILD Trial of Nerandomilast (BI 1015550) Including Those with Systemic Autoimmune Rheumatic Disease ILD (encore presentation)

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Conflict of interest: Yes

[Objectives] Nerandomilast (BI 1015550), an oral preferential inhibitor of phosphodiesterase 4B (PDE4B), is being evaluated in a 52-week, randomized Phase 3 trial in progressive pulmonary fibrosis (PPF), which includes patients with systemic autoimmune rheumatic disease associated interstitial lung disease (SARD-ILD). We report baseline characteristics of patients in the FIBRONEER-ILD trial, including those with SARD-ILD. [Methods] Patients aged ≥ 18 years with pulmonary fibrosis (other than idiopathic pulmonary fibrosis) who met criteria for progression were randomized to nerandomilast 9 mg, 18 mg, or placebo twice daily. Baseline characteristics were collected prior to randomization. Primary endpoint is absolute change from baseline in forced vital capacity (FVC, mL) at Week 52. [Results] Overall, 1782 patients were screened and 1178 randomized. In the 1176 treated patients, mean age was 66 years, 56% were male, 43% were receiving antifibrotic therapy and mean FVC was 70% predicted. A subgroup of 323 (27%) patients had SARD-ILD. In the subgroup, mean age was 64 years, 35% were male, 34% were receiving nintedanib and mean FVC was 72% predicted. [Conclusion] The trial will provide insights into the efficacy and safety of nerandomilast in patients with PPF, including those with SARD-ILD.

P1-217

Investigation of the efficacy and safety of anti-rheumatic drugs for rheumatoid arthritis complicated by interstitial lung disease and the effect of these treatments on changes in respiratory function

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Conflict of interest: None

[Objective] To evaluate the pulmonary function test and the extent of interstitial lung disease (ILD) lesions in rheumatoid arthritis (RA)-ILD with and without a history of ILD exacerbations. [Methods] We selected 46 RA-ILD patients (mean 70.9 years old) who had pulmonary function tests and HRCT (high-resolution CT) between 2023 and 2024. ILD exacerbation was defined by the start or increase of glucocorticoid (GC) due to worsening imaging. We semiquantified HRCT findings. [Results] ILD worsened in 29 of 46 patients with RA-ILD, and there were no significant differences in age, sex, anti-CCP antibody positivity, or smoking history between ILD exacerbations and non-exacerbations. Methotrexate (MTX) was given to 41.4% when ILD worsened, and 41.2% of non-worsened cases with a mean duration of 428 weeks. RA-ILD patients with ILD exacerbations had more upper lobe lesions than those without exacerbations (58.6% vs. 35.3%, p=0.127) and numerically more extensive lesions by HRCT. The mean %FVC (standard deviation) after ILD exacerbations was 97.2% (17.9), which was similar to the cases of the non-worsened group. [Conclusion] MTX was not associated with ILD exacerbations. Patients with ILD exacerbations tended to have extensive ILD involvement but maintained pulmonary function.

P1-218

Long-Term Clinical Course and Risk Factors for Relapse of Methotrexate-Related Lymphoproliferative Disease (MTX-LPD)

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Conflict of interest: None

[Objectives] Methotrexate (MTX)-associated lymphoproliferative disease (LPD) is a serious complication of rheumatoid arthritis (RA), but there is insufficient information about the long-term prognosis. In this study, we investigated the long-term prognosis of MTX-LPD, especially the risk factors for relapse. [Methods] We retrospectively evaluated the clinical background, the course of LPD and RA treatment after onset, and RA disease activity in 49 patients with MTX-LPD who had been diagnosed at our hospital from 2000 to 2017. [Results] Among 49 patients, 38 patients achieved complete response (CR)/partial response (PR) to first-onset LPD (31 patients with spontaneous regression after discontinuation of MTX and 7 patients with chemotherapy). Of the 38 patients, 10 (26.3%) subsequently relapsed within 10 years, with a median time from initial LPD to relapse of 84 weeks, including 2 patients who relapsed more than 5 years later. The significant risk factors for relapse were the same biologic as at the time of initial LPD (p=0.031), and there were no significant differences in the presence or absence of chemotherapy for first onset. [Conclusion] Relapse of MTX-LPD can occur even more than 5 years after the initial onset, so careful decision making is required for the re-use of biologics.

P1-219

Efficacy and safety of nintedanib for lung disease in connective tissue disease in our hospital

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Conflict of interest: None

[Objective] Interstitial pneumonia (IP) with connective tissue disease (CTD) is an important organ lesion that affects prognosis. There is still little clinical evidence of nintedanib (NTB), so we investigated its efficacy and safety in our hospital. [Method] 9 patients with CTD who started NTB from April 2019 to April 2024 and underwent respiratory function tests were included. They were divided into two groups: %FVC >70% and <70%, and into two groups: disease duration >3 years and <3 years. We retrospectively analyzed their respiratory function and diarrhea. [Results] The mean age was 66.4±15.4 years, and 55.6% (N=5) were female. The mean initial dose of NTB was 222±83.3 mg. 6 of 9 patients had diarrhea. In the %FVC >70% and the %FVC <70% groups, ΔFVC was -0.003±0.006 L vs +0.065±0.002L (p=0.12) at 24 weeks, and -0.423±0.497L vs -0.001± 0.140L (p=0.07) at 52 weeks. In the disease duration >3 years and the disease duration <3 In years groups, ΔFVC was +0.056±0.101L vs -0.025± 0.164L (p=0.81) at 24 weeks and -0.220±0.448L vs -0.045±0.157L (p= 0.65) at 52 weeks, so in cases with normal FVC and early onset, FVC tended to be maintained. [Conclusion] It was suggested that respiratory function may be preserved if NTB is introduced early before FVC declines in IP with CTD patients.

P1-220

Clinical features of acute exacerbation of interstitial pneumonia in patients with systemic sclerosis

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Conflict of interest: None

[Objectives] Systemic sclerosis (SSc) is often complicated by interstitial pneumonia (IP), but acute exacerbations (AE) are rare and few clinical reports have been published. In this study, we examined the clinical features of cases from our hospital. [Methods] We retrospectively extracted AE cases from 2011 to 2023 and compared the clinical backgrounds and laboratory data with non-AE cases from 2023. We also examined treatments and mortality rates in AE group. [Results] The AE group included 8 cases, while the non-AE group had 48 cases. There were no significant differences in sex or age. The AE group had significantly higher CRP (8.73 vs. 0.21 mg/dL, p<0.01), WBC (14,387 vs. 6,075/μL, p<0.01), LD (357 vs. 232 U/L, p<0.01), and KL-6 (3,973 vs. 812 U/mL, p<0.01). There was also a tendency for higher anti-centromere antibody positivity in the AE

group (5/8 vs. 13/48 cases, P=0.0954). All AE cases received steroids, and two received immunosuppressants, with a mortality rate of 37.5%. [Conclusion] In the AE group, CRP, WBC, LD, and KL-6 were elevated, suggesting a strong inflammatory response and lung tissue damage. Although IP with positive anti-centromere antibodies is often mild, this study showed a tendency for it to be more prevalent in the AE group, so caution is required.

P1-221

Pursuing suppression of methotrexate-associated lymphoproliferative disease by reducing the dose of MTX every other week in Japanese rheumatoid arthritis patients

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Conflict of interest: None

Objective: Methotrexate (MTX)-associated lymphoproliferative disorder (LPD) often affects elderly rheumatoid arthritis (RA) patients. Spontaneous regression after stopping MTX shows tumor shrinkage within two weeks, with increased lymphocyte counts. Thus, longer MTX dosing intervals may reduce LPD risk. This study aims to verify if biweekly MTX is a practical dose reduction. **Methods:** We analyzed 24 RA patients at our hospital using biweekly MTX for various reasons, assessing RA activity and lymphocyte changes after reduction. **Results:** There were 10 males and 14 females, average age 74.3 ± 6.1 years, and average disease duration 19.4 ± 22.1 years. Biweekly doses: 4 mg in 17 cases, 6 mg in 6, 8 mg in 1. Before reduction, most were in remission/low activity. After reduction, 4 cases flared, needing adjustments; 4 maintained remission and stopped MTX; 15 continued. Lymphocyte counts rose from 1281 ± 491 to 1445 ± 538. **Conclusion:** Elderly patients may have a reduced metabolism, and biweekly MTX administration appears to be a realistic method of dose reduction after remission. Flare-ups occurred, but similar results might happen with weekly reduction. Biweekly administration increases lymphocyte counts, which may make MTX-LPD less likely to develop.

P1-222

Primary Cardiac Diffuse Large B-Cell Lymphoma in an Elderly Patient with Rheumatoid Arthritis on Methotrexate: A Case Report

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Conflict of interest: None

An 89-year-old woman with a 14-year history of rheumatoid arthritis (RA), seropositive for anti-citrullinated peptide antibodies and rheumatoid factor, presented with progressive chest and back pain, cough, wheezing, and worsening orthopnea over two weeks. Physical examination revealed tachycardia, low oxygen saturation (SpO_2 91% on room air), significant bilateral lower extremity pitting edema without superficial lymphadenopathy, breath sounds abnormalities, or heart murmurs. Imaging studies, including echocardiography and contrast-enhanced CT, identified a primary cardiac lesion with a 20 mm myocardial mass displaying heterogeneity and irregular borders, along with significant pericardial effusion causing cardiac tamponade. Cytology of the pericardial effusion confirmed diffuse large B-cell lymphoma (DLBCL). EBER testing was negative. Discontinuation of methotrexate and sulfasalazine, along with chemotherapy, led to remission. This case highlights the rare occurrence of primary cardiac DLBCL in RA patients on immunosuppressive therapy and provides insight into clinical presentations, diagnostic challenges, and treatment outcomes for immunodeficiency-associated lymphoproliferative disorders.

P1-223

A case of LPD-arising in immune deficiency/ dysregulation (LPD-IDD) discovered with fever and back pain, which required differentiation from lymph node and lung metastasis of adrenal cancer

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Conflict of interest: None

A 60-year-old woman developed rheumatoid arthritis in 28 years ago, and was treated with DMARs and bDMARDs including MTX 8 mg/week. 9 years ago, the dose was increased to 12 mg/week of MTX. In July, she had a fever and severe back pain. An abdominal CT scan showed a mass shadow on the right adrenal gland. PET-CT showed a 30-mm-sized right adrenal mass with hyperintensity of FDG, a 30-mm-sized intraperitoneal lymph node, a small nodule of the left adrenal gland, and multiple small nodules in the bilateral lung fields. The biopsy was negative for EBER and showed necrosis, but possibility of LPD-IDD was pointed out. Blood tests showed WBC 2200 /μL, LDH 198 U/L, and sIL-2R 1353 U/mL. Suspecting LPD-IDD, MTX was discontinued on August 16. The hematologist decided to follow up the patient without treatment. CT scan on September 16 showed that the bilateral adrenal masses had disappeared. A blood test on October 31 showed sIL-2R 272 U/mL within normal range. On CT scan in next June, the nodular shadows of both lungs disappeared, and only the para-aortic lymph node remained 6.5 mm in size. [Clinical Significance] LPD-IDD should be considered as one of the differentials of acute low back pain during MTX administration, and imaging and histological diagnosis should be performed.

P1-224

Thrombotic microangiopathy following pulsed steroid therapy to treat with acute interstitial pneumonia caused by rheumatoid arthritis

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Conflict of interest: None

[Case] 81-year-old woman. [Chief Complaint] Shortness of breath. [History of Present Illness] Patient had been visiting our clinic for rheumatoid arthritis (RA) with interstitial lung disease (ILD) since X-10, and was switched from abatacept and tacrolimus to upadacitinib in May X. On August 3, X, nausea, joint pain and slight fever were observed, upadacitinib was discontinued as acute enteritis. On August 13, she was admitted to treat new Ground-glass opacity over both lungs and hypoxemia. [Clinical Course] Pneumocystis pneumonia was ruled out because of negative βD-glucan in serum, then methylprednisolone pulse, meropenem, and levofloxacin were induced. On August 16, anuria, thrombocytopenia, anemia, elevated LDH, decreaddsed haptoglobin, and fragmented red blood cells in the peripheral blood were observed. On suspicion of thrombotic microangiopathy (TMA), we performed hemodialysis and plasma exchange, but the patient died on August 19. [Discussion] While the blood test was negative for ADAMTS13 antibodies and deacreasing activity, the renal pathology was consistent with TMA. Based on the poor response to antimicrobial agents, we diagnosed acute exacerbation of RA-ILD and secondary TMA due to RA, that is a relatively rere cause warth reporting (Fujimura Y. Intern Med. 2010; 49(1): 7-15).

P1-225

The reality and challenges of screening and follow-up of collagen disease-associated interstitial lung disease (CTD-ILD)

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Conflict of interest: None

Objective Collagen disease is frequently complicated by interstitial lung disease. Appropriate follow-up and intervention is necessary. Screening and follow-up for interstitial lung disease in patients with collagen disease attending our hospital are left to the decision of the physician, and no standardized evaluation. To develop follow-up recommendations that investigate and standardize the actual conditions of screening and follow-up in order to understand the disease status of interstitial lung disease and support appropriate interventions. Results Patients with CTD-ILD at our hospital were selected and stratified according to the recommended protocol for testing according to risk and severity. We evaluated the cases in which the interval between examinations by the physician in charge was shorter, appropriate, or longer than the recommended protocol. Conclusion Differences in follow-up intervals were shown between cases relying on the setting of screening intervals by the attending physician and cases with established protocols. In the future, we will establish screening and follow-up methods and recommend the timing of anti-inflammatory and anti-fibrosis treatment to each attending physician to verify whether appropriate therapeutic intervention was performed.

P1-226

Infectious Diseases after Rituximab Administration in Patients with Rheumatic Diseases

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Conflict of interest: None

Objectives: The contribution of rituximab (RTX) to the treatment of rheumatic diseases is significant. However, there is great concern about the risk of infection. To determine the incidence of infection and subsequent outcome in patients treated with RTX. Methods: We retrospectively collected and analyzed information on rheumatic disease patients who received RTX at Shinonoi General Hospital or Kitasato University Medical Center from April 1, 2021, to September 30, 2024, using electronic medical records. Results: Sixty patients (15 males and 45 females) received RTX during the observation period, with a mean age of 72.0 years. The most common underlying disease was MPA (n=34), GCA (n=13), SSc (n=7), and others (n=6). During the period, 29 patients (38 cases) developed some kind of infection, of which 15 (18 cases) had COVID-19 and 7 had bacterial pneumonia. 3 of the COVID-19 cases were severe, 5 were moderate II, and 2 cases died. There were no significant differences in age between patients with and without infection, or between mild/moderate I and moderate II/severe cases among COVID-19 patients. Conclusion: COVID-19 was the most common infectious disease that affected patients after RTX administration, and more than 40% of these patients had moderate II or more severe disease.

P1-227

Mycotic Abdominal Aortic Aneurysm due to Non-typhoidal Salmonella in a patient with rheumatoid arthritis

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Conflict of interest: None

Background: Non-typhoidal Salmonella (NTS) usually causes gastroenteritis, with over 95% of cases foodborne. About 5% may progress to bacteremia, potentially leading to vascular complications. We report a case of mycotic abdominal aortic aneurysm (MAAA) caused by NTS in a patient receiving rheumatoid arthritis (RA) treatment. **Case:** The patient, a 79-year-old male, was diagnosed with RA at age 67 and treated with infliximab (IFX) 200 mg/8 weeks, methotrexate (MTX) 8 mg/week, and prednisolone (PSL) 5 mg/day. On X-Y-12, he developed diarrhea, fever, and back pain. He presented in shock at a local clinic on X-Y and was transferred to our hospital. Examinations revealed COVID-19, severe neutropenia, sepsis (Gram-negative rods in blood), and MAAA. After consultation, antibiotics were started with planned surgery, but worsening symptoms led to emergency aortic graft surgery for impending rupture. **Discussion:** This case highlights how immunosuppressive therapy and COVID-19 led to neutropenia and sepsis, resulting in MAAA after NTS infection. MAAA has a high mortality rate, requiring early intervention. Vascular complications should be considered in immunocompromised patients with NTS infections. Relevant literature is briefly reviewed.

P1-228

Sixteen cases of Clostridioides difficile infection in immunosuppressed patients

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Conflict of interest: None

[Objectives] *Clostridioides difficile* infections (CDI) are overgrowths in the intestines, often after antibiotic use, causing colitis and diarrhea. CDI is common in patients who are hospitalized, on long-term antibiotics, or immunosuppressed (for whom it can be life-threatening). [Methods] This report describes 16 immunosuppressed patients treated for CDI between 2015 and 2024. [Results] Their average age was 76 years (6 males, 10 females). Underlying conditions included rheumatoid arthritis (n=7 cases), systemic lupus erythematosus (n=3), mixed connective tissue disease (n=1), ANCA -associated vasculitis (n=2), relapsing polychondritis (n=1), interstitial pneumonia with autoimmune features (n=1), and asthma-COPD overlap (n=1). Corticosteroids were used in 12 patients; all had prior exposure to antibiotics and proton pump inhibitors or H2 blockers. CDI was diagnosed in 8 patients within one month of remission treatment for their primary disease. Treatment involved metronidazole (n=10) and oral vancomycin (n=6). Four patients experienced recurrence; all improved. [Conclusion] Our analysis shows that frequently using corticosteroids, PPIs, and broad-spectrum antibiotics in autoimmune diseases increases the risk of CDI. Prompt stool testing is crucial when gastrointestinal symptoms arise.

P1-229

25-hydroxy Vitamin D level in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Calcidiol: 25 (OH)D that is the precursor of calcitriol: 1,25 (OH)D has been reported to have various functions in recent years. Its importance in infection defense and immunomodulation has been reported in many cases, especially in relation to respiratory tract infections. We measured and examined 25 (OH)D levels in patients with rheumatoid arthritis (RA). [Methods] Between June-September 2024, 39 patients had investigated 25 (OH)D blood samples at follow-up for RA patients. Mean age 72.1 years (54-86), 7 males and 32 females, including. 3 patients used Vit. D supplements at the time of investigation. 30 ng/ml or less was considered insufficiency, and 20 ng/ml or less was considered deficient. [Results] Overall, the mean 25 (OH)D level was 19.0±8.2 ng/dl. The number of fulfillment cases was 8.3% and deficient cases was 63.9%, The number of patients who did not use supplements was 18.3±7.7 ng/dl. Supplement users had 27.8±20.5 ng/dl. There was no significant difference between gender and calcitriol medicin use. [Conclusion] In combination with previous studies, the Japanese population today is vitamin D deficient. Vit. D supplementation should be considered as part of measures against surgical site infections and respiratory tract infections.

P1-230

The causative bacteria and drug susceptibility in case of fever of non-perioperative patients withrheumatoid arthritis

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Conflict of interest: None

[Objectives] In RA patients, fever can arise from non-perioperative infections. We investigated causative bacteria and antibiotic susceptibility in blood culture cases to determine effective treatments. [Methods] We analyzed 115 positive blood culture cases from 2019 to 2023, including 55 RA and autoimmune disease patients. Suspected diagnoses included UTI (38 cases), pneumonia (19 cases, 4 with both), unknown infection source (39 cases), and others (23 cases). Comprehensive and statistical analyses were conducted on UTI, pneumonia, and unknown infection source cases, and on RA and autoimmune disease groups. [Results] E. coli was the most common in UTI cases (25/42). Meropenem (MEPM), amikacin (AMK), and fosfomycin (FOM) showed significant susceptibility in comprehensive analysis. In RA and autoimmune disease groups (23 cases), MEPM and AMK were significantly effective. E. coli was also common in pneumonia (5/23) and unknown source cases (15/39). No antibiotics showed significant susceptibility in pneumonia cases. In unknown infection source cases, MEPM, AMK, and minocycline (MINO) were effective, while ampicillin, cefazolin, and cefmetazole were not. [Conclusion] For fever in RA patients, when causative bacteria are unidentified, AMK and MINO can be considered based on suspected diagnosis.

P1-231

A case of SLE with marked leukopenia leading to hand osteomyelitis due to Capnocytophaga infection triggered by cat bite

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Conflict of interest: None

60 years old woman. 2 months ago, she developed oral ulcer. 1 month ago, a cat bit her right thumb and her thumb swelled up. She presented with fever and butterfly rash and was referred to our clinic. The diagnosis of SLE was made based on marked leukopenia with WBC 870 /mm3, ANA 640 fold and hypocomplementemia. Considering the hemophagocytic syndrome-like condition, steroid pulse therapy was started, followed by glucocorticoids and tacrolimus. Her thumb lesion was diagnosed as pyogenic arthritis and antimicrobials were started. As white blood cells recovered, her thumb swelling worsened and a subcutaneous abscess appeared and grew. Capnocytophaga spp. were detected in the culture. MRI showed osteomyelitis, which improved with antimicrobials, drainage, and joint fixation surgery. Because of marked neutropenia due to SLE, the symptoms of suppurative arthritis due to cat bite appeared minor, and inflammation became clearer with neutrophil recovery. In rheumatic disease, leukopenia and immunosuppressive drugs mask infections, potentially putting patients at risk for progressive infections. Capnocytophaga is transmitted by dog and cat bites and rapidly leads to sepsis in some cases, with a high fatality rate. We should be aware of zoonosis in pet-owning rheumatic disease patients.

P1-232

Gram stain of the joint aspiration for the diagnosis of pyogenic arhtitis

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Conflict of interest: None

[Objectives] Gram staining for pyogenic arthritis is a commonly used diagnostic method. We investigated the sensitivity and specificity of Gram staining of joint fluid in order to examine the usefulness of Gram staining of joint fluid in pyogenic arthritis. [Methods] We examined the sensitivity of Gram staining of joint fluid by extracting samples that were culture-positive in bacterial tests of joint fluid punctured with suspected pyogenic arthritis at our hospital from 2012 to 2023, and calculated the specificity of Gram staining of joint fluid by extracting samples that were culture-negative. [Results] In 26 cases of pyogenic arthritis (13 knees, 6 hips, 4 shoulders, 2 ankles, and 1 wrist) in which puncture joint fluid culture was positive, Gram stain was positive in 15 of 16 cases within 7 days of the onset of infection. (Sensitivity: 93.8%) In contrast, 7 of 10 cases were Gram stain-positive when signs of infection had been present for more than 8 days (sensitivity: 70%). All cases with negative joint fluid culture results were Gram-stain negative. (specificity 100%) [Conclusion] Gram staining of joint fluid for pyogenic arthritis at our hospital showed high sensitivity and specifity.

P1-233

Adjustment of immunosuppressive therapy at serious infection in patients with autoimmune and rheumatic diseases and clinical outcomes

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Conflict of interest: None

[Objective] To describe the adjustment of immunosuppressive therapy at serious infection in patients with autoimmune and rheumatic diseases (AIRDs) in our practice and explore its association with clinical outcomes. [Methods] We retrospectively identified 169 cases with AIRDs who were admitted to our hospital for the treatment of infection. Information on age, sex, AIRD, comorbidity, treatment, infection, length of hospitalization, and prognosis was collected. [Results] Median age was 74 years and 107 cases were women (63.3%). The most common AIRDs were rheumatoid arthritis, Sjogren's syndrome, and microscopic polyangiitis, whereas the most common site of infection was the respiratory system. In 158 cases receiving glucocorticoids (GCs), the GC dose was increased in 122 (77.2 %). On the other hand, in 77 and 43 cases receiving immunosuppressants (ISs) and biologics, the dose of IS/biologics was decreased in 60 (77.9%) and 39 (90.7%), respectively. In total, 26 cases (15.4%) died. The presence of lung disease at baseline was significantly associated with death, while the increase of GCs and the decrease of ISs/biologics were not. [Conclusion] In our practice, the dose of GC was frequently increased, while that of IS/biologics was decreased at serious infection in patients with AIRDs.

P1-234

A case of VEXAS syndrome with mixed blood stream infection due to Kodamaea Ohmeri and Carbapenem resistant Enterobacter (CRE)

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Conflict of interest: None

[Case] 72-year-old male [Disease Course] X-3 year, he was diagnosed with VEXAS syndrome based on UBA-1 mutation, neutrophilic skin rash, interstitial pneumoniae and macrocytic anemia. High-dose glucocorticoid therapy was initiated. Although his condition was stabilized with upadacitinib and tacrolimus, he suffered from recurrent UTIs due to a urinary catheter. X-2, he admitted with fever and pyuria and was treated with cefmetazole. X+7, he developed erythematous rash on his lower limbs, which progressed to mucosal erosions across his body. Toxic epidermal necrolysis (TEN) induced by cefmetazole was suspected. Although fever subsided with high dose GC, TPN via a PICC was necessary alongside GC tapering. X+42, CRE was detected in blood cultures, we initiated treatment with cefiderocol. Further blood cultures identified *Kodamaea ohmeri*, which was treated with micafungin but failed to resolve the infection, leading to respiratory failure due to acute respiratory distress syndrome. [Conclusion] In this case, immunosuppression, skin and mucosal breakdown predisposed the patient to complicated bloodstream infections with unusual pathogens. While the outcome was poor, we aim to disseminate knowledge on managing these rare pathogens for improved future outcomes.

P1-235

A case of pyogenic arthritis due to M. intracellulare

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Conflict of interest: None

(Objective) We report a case of left knee arthritis caused by non-tuberculous mycobacteria (NTM) that was successfully treated with lesion curettage and pharmacotherapy. (Methods) The patient was a 67-year-old female who presented with left knee pain. PCR testing for Mycobacterium tuberculosis and non-tuberculous mycobacteria in the joint fluid was conducted, which returned positive for M. intracellulare. Consequently, treatment with CAM/EB/RFP was initiated. One week later, arthroscopic lesion curettage and lavage were performed. After six weeks of anti-tuberculosis medication, the clinical symptoms improved, and CRP levels normalized, allowing for the cessation of medication. The patient maintained a state of remission for two months, and a total knee arthroplasty was performed three months post-surgery. The postoperative course was favorable, with no recurrence of infection. (Results) (Conclusion) We experienced a case of purulent arthritis caused by M. intracellulare. **Clinical Significance:** In cases of unexplained joint effusion and elevated inflammatory responses, the possibility of non-tuberculous mycobacterial infection should be considered.

P1-236

A case of tuberculous arthritis evaluated with musculoskeletal ultrasonography

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Conflict of interest: None

In early 2023, a 73-year-old woman with overlap syndrome (SSc, SLE, and RA) presented with left elbow swelling and a subcutaneous mass in her left upper arm. MRI indicated bursitis and synovitis in the left shoulder and elbow, implying aggravation of RA. The left upper arm mass was considered to be a fluid collection along the LHB. A subcutaneous mass in the upper arm was punctured in November, revealing Mycobacterium tuberculosis in culture. The patient was diagnosed with tuberculous arthritis and muscle abscess, and she began four-drug anti-tuberculosis therapy. Musculoskeletal ultrasonography revealed thickened subacromial and subdeltoid bursae with fluid and rice body accumulation, abscesses in the infraspinatus and biceps muscles, and significant synovial hyperplasia in the left elbow. After 9 months of treatment, the ultrasound findings and symptoms improved. Tuberculous arthritis is rare, and its chronic nature complicates its differentiation from exacerbation in RA patients. Ultrasound, ideal for examining shallow areas like subcutaneous tissue and muscle, enables continuous evaluation of lesion distribution and detailed observation of synovitis and abscesses. This case highlights the value of sequential ultrasonographic monitoring of tuberculous arthritis.

P1-237

A Case of Mycobacterium chelonae Infection Diagnosed by Prolonged Culture Period

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Conflict of interest: None

[Case] A 96-year-old man with a history of rheumatoid arthritis developed right knee pain and elevated inflammatory markers. Synovial fluid was inflammatory, and culture was negative. An exacerbation of rheumatoid arthritis was suspected. Gram-positive rods (GPR) were detected in 1 out of 2 blood cultures after 143-hour incubation but were considered contamination. One month later, the right knee pain worsened with marked redness extending to the proximal lower leg. Ultrasound showed inflammation around the right patellar tendon and a small fluid accumulation. Though the fluid culture was negative after 48 hours, a prolonged incubation revealed the presence of GPR, later identified as Mycobacterium chelonae. Re-examination of the previous blood culture also identified the same bacterium. The patient was diagnosed with disseminated M. chelonae infection and was treated with combination antibiotic therapy, resulting in symptom improvement. [Discussion] In cases of suspected infection with negative initial cultures, consideration of atypical pathogens and extended incubation times may be crucial. Additionally, when GPR is detected, considering mycobacteria and discussing additional tests with the laboratory can be useful.

P1-238

Survey of RA patients regarding our clinic US-guided intra-articular triamcinolone acetonide injection (IATAI)

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Conflict of interest: None

[Objective] There are still few medical institutions that perform IATAI, which is considered a basic technique for the treatment of RA, and it is not sufficiently performed, especially in the clinical practice of rheumatologists in the Internal Medicine Department. [Method] We asked RA patients who visited our clinic from June to September 2023 to answer anonymously on a 5 points scale for 10 questions, including satisfaction with IATAI, degree of improvement in QOL, recommendation level, selectivity of IATAI at the time of local recurrence, and satisfaction with combination therapy with Bio, and analyzed them by age, duration of disease, and treatment. [Results] We received responses from 111 people. Although there were no significant differences in age, duration of disease, or treatment the results were high, with a satisfaction rate of approximately 90%, and a recommendation rate of approximately 90%. IATAI selection rate was significantly higher ($P<0.008$) and the recommendation rate was also significantly higher ($P<0.002$) in the JAK/Bio group than in the DMARDs group. [Conclusion] The evaluation of IATAI is high, and the selection rate in cases of local recurrence was also high, suggesting its usefulness, and it is expected that joint injections will become more widespread.

P1-239

A case of acute myocardial infarction suspected to be caused by myocardial bridge in a patient with rheumatoid arthritis

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Conflict of interest: None

A patient with elderly-onset rheumatoid arthritis was started on golimumab about one year ago. Consequently her disease activity had been completely remission gradually. The day before admission, she experienced chest pain while playing tennis and visited her local doctor the next day. She was referred to our hospital because of ECG changes. Although her chest pain was relieved, we diagnosed acute anterior myocardial infarction and performed an emergency coronary angiography. There was no significant stenosis, but squeezing of the left anterior descending branch #7 was observed. Myocardial deviation enzymes were mildly elevated at the time of presentation, and we diagnosed the patient with MINOCA (Myocardial Infarction with Non-Obstructive Coronary Artery disease) due to myocardial bridge (Myocardial bridge; MB). After adding a beta1-blocker and a coronary dilator, her chest pain did not recur. She has been in remission for rheumatoid arthritis with continued golimumab. [Discussion] We have recently experienced a case of myocardial ischemia caused by MB, which was thought to have developed due to increased activity after rheumatoid arthritis achieved remission. We report this case with some discussion of the literature.

P1-240

A case of rheumatoid arthritis suspected of being an autoimmune inflammatory syndrome induced by adjuvants

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Conflict of interest: None

Case: Female, 53 years old. She developed polyarticular arthritis in June X. She was diagnosed with RA after being referred to our department in July of the same year, and was found to be RF-positive and ACPA-positive. Although treatment was started, the patient continued to have high disease activity. During the medical interview, it was discovered that she had undergone bilateral breast augmentation in the past and had neglected to have the implant back removed, even though it had broken. We explained that this may have been related to the onset of RA, and we tried to persuade her to have the implant removed, but she did not agree. We then strengthened the treatment for RA, and her condition improved. [Discussion] In this case, RA may have developed as a result of the damage to the silicone implant following breast augmentation surgery. It was thought to be Group I, which presents with typical symptoms of collagen disease in human adjuvant disease. There are reports that it is difficult to see improvements in ASIA due to removal if the period from insertion to removal of the silicone is long. In this case, strengthening immunosuppressive therapy was effective in treating RA even without removing the silicone.

P1-241

A Case of Seronegative Rheumatoid Arthritis After Omalizumab Administration

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Conflict of interest: None

[Case] 66-year-old female [Chief Complaint] Polyarthralgia [Present History] She developed poorly controlled bronchial asthma. In July of Year X, omalizumab was administered, after which polyarthralgia appeared one week later. On examination, she exhibited swelling and tenderness in both wrist and finger joints, with no additional findings suggestive of other collagen vascular diseases. Blood tests revealed negative rheumatoid factor and anti-CCP antibody, an antinuclear antibody titer of 1:40, negative results for other autoantibodies, CRP of 2.54 mg/dl, ESR of 79 mm/h, and MMP-3 of 320.9 ng/ml. Joint ultrasound indicated active proliferative synovitis in the wrists, finger, and toe joints, while no apparent bone erosion was observed on X-rays. In September of Year X, a hip replacement was performed for left hip osteoarthritis, with intraoperative findings suggestive of synovitis. After surgery, a diagnosis of seronegative rheumatoid arthritis was made, and treatment with methotrexate 6 mg/week and prednisolone 5 mg/day was initiated. [Clinical Significance] Cases of chronic arthritis have been reported following the administration of biologics targeting type 2 inflammation, including omalizumab. This report provides a detailed case and includes a brief literature review.

P1-242

a case of polyarthritis caused by Nontuberculous mycobacterial infection

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Conflict of interest: None

Case: A patient was 75 years old female who had aplastic anemia and diabetes mellitus as a comorbidity. She presented with pain and swelling of the bilateral wrist joints, and was diagnosed as seronegative rheumatoid arthritis originally. Tacrolimus and prednisolone were applied for her treatment, but her joint symptoms worsened. She was admitted to our hospital. At the time of her initial examination, she complained of pain, swelling and stiffness in the bilateral wrist joints. Fluorescent staining of joint puncture fluids of bilateral wrists revealed positive, which were later identified as Mycobacterium kansasii. Adoministration of isoniazid, rifampicin and ethambutol and surgical intervention of bilateral wrist joints resulted in clinical improvement. Conclusion: We report a case of polyarthritis caused by Nontuberculous mycobacterial infection, which causes usually monoarthritis. Our case highlights the need to consider this rare infection in the differential diagnosis of polyarthritis especially in immunosuppressed patients.

P1-243

A Case of Open Wedge High Tibial Osteotomy in a Rheumatoid Arthritis Patient with Stable Disease Activity

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Conflict of interest: None

[Introduction] With advancements in pharmacotherapy, more RA patients are experiencing knee pain primarily due to OA. We report a case of an RA patient with stable disease activity who underwent OWHTO with favorable outcomes. [Case] The patient, a 62-year-old woman diagnosed with RA at age 35, was treated with MTX (8 mg/week), showing no swollen or tender joints, CRP 0.1 mg/dl, MMP-3 31.6 ng/ml, and SDAI 8.1. Knee ROM was limited to 0-125°, and X-ray showed KL grade 2 and 19.2% varus in %MA. MRI indicated a degenerative tear in the medial meniscus with no synovitis. Based on these findings, OA was deemed the primary pathology, warranting OWHTO. Preoperative scores were JOA 70, KS 58, and FS 60. Arthroscopy confirmed cartilage degeneration and a meniscal tear in the medial compartment, with no synovitis. After partial medial meniscectomy, OWHTO with a 9 mm opening was performed, followed by internal fixation removal at 1.5 years. At 2.5 years post-surgery, ROM improved to 0-150°, with SDAI 2.1, JOA 100, KS 97, and FS 100, indicating a favorable outcome. [Clinical Significance] OWHTO may be a valuable option for RA patients with stable disease activity and OA-dominant knee pain.

P1-244

Factors that contribute to the improvement of locomotion by artificial knee replacement surgery

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Conflict of interest: None

[Objective] Knee osteoarthritis (knee OA) contributes to locomotive syndrome (LS), and total knee arthroplasty (TKA) can improve LS. This study examines factors associated with LS improvement after TKA. [Methods] We studied patients who underwent TKA for knee OA between July 2020 and June 2022 with 2-year follow-up. LS was evaluated using stand-up test, 2-step test, and LOCOMO25 before surgery and at 2 years. KSS, quadriceps strength, knee ROM, walking speed, and physical activity were analyzed for their relationship with LS improvement. [Results] Of 141 patients (117 females, mean age 75±7 years), preoperative LS grades were: grade 3: 121, grade 2: 14, grade 1: 4. At 2 years, they improved to: grade 3: 68, grade 2: 46, grade 1: 18. All LS measures improved, with LOCOMO25 showing strongest correlation. Multivariate analysis revealed only KSS and walking speed significantly influenced LS improvement. [Conclusion] TKA can improve LS grade, particularly LOCOMO25 scores. As in previous studies, LS improvement correlated with walking speed. The association with KSS suggests psychological aspects, not just physical improvement, may influence post-TKA LS outcomes.

P1-245

Comparison of Locomo 25 improvement levels between unilateral versus simultaneous bilateral total knee arthroplasty at 2 years after surgery

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Conflict of interest: None

[Objectives] To compare the percentage of improvement in locomotion25 at 1 year postoperatively in patients who underwent unilateral TKA with those who underwent unilateral bilateral total knee arthroplasty (TKA) in a single term. [Methods] Patients who underwent TKA at our hospital from July 2020 to June 2022 were included in the study. The overall level of locomotion at preoperative and 2 years postoperatively, including each of the items of the rise test, 2-step test, and locomotion 25, was evaluated and compared between the two groups (bilateral and unilateral). [Results] There were 113 subjects (82 in the unilateral group and 31 in the bilateral group). The percentage of patients with improved LoComo 25 tended to be higher in the bilateral group, but the difference was not significant (48 patients in the unilateral group: 58.5% / 24 patients in the bilateral group: 77.4%, p=0.08). There were no significant differences in the percentages of improvement in other parameters between groups. [Conclusion] It is still possible that bilateral one-phase TKA improves complaints in both lower extremities at the same time, resulting in a significant improvement in locomotion compared to the unilateral group, but no significant difference was found due to the small number of cases.

P1-246

Evaluation of the Safe Zone for Acetabular Cup Screws Using 3DCT Imaging

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Conflict of interest: None

[Objectives] To investigate the angles at which screws can be safely inserted into the acetabulum without penetrating the inner cortical bone. [Methods] Hip CT data from five female patients who underwent total hip arthroplasty (THA) for left idiopathic femoral head necrosis, without acetabular dysplasia, were used. The cup was assumed to be positioned in the native acetabulum of the left hip with a 40° abduction angle and 15° anteversion angle, and aligned to the horizontal plane. Using 3DCT, the length and angle of the longest screw in the sagittal plane were measured at 15° intervals based on a reference line from the cup center to the ASIS. Additionally, the angles for screws longer than 25 mm were also measured in the same plane. [Results] The average length of the longest screw was 125.2 mm, all inserted within a range of 45-60° laterally from the reference line and 50-56° in the sagittal plane from the cup edge. The angles for inserting screws longer than 25 mm were 0-75° and 150-180° laterally from the reference line, with an average sagittal plane angle of 30.8-56.6° and 17.2-38.9°, from the cup edge. [Conclusion] This study identified the safe zone for screw insertion in THA, ensuring safe placement without penetrating the inner acetabular table.

P1-247

A Case of TKA Infection Treated with Implant Retention by CLAP (ContinuousLocal Antibiotics Perfusion)

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Conflict of interest: None

[Objectives] We report a case of Periprosthetic Joint Infection (PJI) after Total Knee Arthroplasty (TKA) in which Continuous Local Antibiotics Perfusion (CLAP) was successfully used to preserve the implant. [Methods] A double-lumen tube was placed in the knee joint during surgery for PJI. Gentamicin was injected from the tube. [Results] The patient is a 64-year-old woman with diabetes and rheumatoid arthritis. she underwent a cleaning and debridement for a TKA-PJI caused by E. coli (AmpC) and was started on CLAP. On day 19 after surgery, her blood test results were comparable to those before the onset of the disease, and she was switched from intravenous to oral antibiotics. At 6 weeks after surgery, she was discharged to home. At 9 weeks after surgery, there was no recurrence of infection, and she was able to do her usual activities. [Conclusion] In PJI, biofilm formation around the implant makes it difficult for antibiotics to work. In this case, the infection was caused by drug-resistant bacteria, but the infection was successfully subsided with implant retention. CLAP, which can deliver high concentrations of antibiotics locally, helped the treatment succeed.

P1-248

Two Cases of Non-surgically Treated Proximal Humerus Fractures in Patients with Collagen Disease

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Conflict of interest: Yes

Case 1: 61-year-old woman The patient fell and was diagnosed with bilateral proximal humerus fractures (right: 2-part, left: 3-part). She has a history of neuro-sarcoidosis, Sjögren's syndrome, diabetes, osteoporosis, and hyperlipidemia. She opted for conservative treatment and started the Ishiguro method after a week. Eight months later, she experienced a cerebral infarction, leading to mild left hemiplegia at the one-year follow-up. JOA score was 75.5, and Shoulder-36 scores showed satisfactory results, with imaging showing bilateral malunion. **Case 2: 63-year-old man** The patient fell at home and was diagnosed with a left proximal humerus 4-part fracture. His medical history includes SLE, osteoporosis, situs inversus, and myocardial infarction. He chose conservative treatment and began the Ishiguro method after a week. At the six-month follow-up, his JOA score was 74.5, with Shoulder-36 scores showed satisfactory results, and imaging showed malunion. **Conclusion:** Patients with collagen diseases often decline surgery due to multiple health issues. The Ishiguro method yields satisfactory outcomes but can result in malunion.

P1-249

Factors affecting the postoperative course of patients with proximal femoral fractures who were living at home before injury

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Conflict of interest: None

[Objectives] Proximal femoral fractures (fractures) are a common injury in elderly patients. Fractures may have significant impacts on activity of daily living (ADL). At our hospital, fracture patients begin rehabilitation the day after surgery, and are transferred to the rehabilitation hospital to regain ADL. This study aimed to clarify factors related to the postoperative course by comparing fracture patients who returned home and admitted facility [Methods] The subjects were older than 60 years 114 patients underwent surgery for fractures at our hospital and lived at home before injury. The subjects were classified into the home group and the facility group and two groups were compared. The factors examined were age, sex, presence of members living together, period from injury to surgery, type of surgery, gait ability before injury, and presence of complications. Complications were examined collagen disease, Parkinson's disease, dementia, and cerebral infarction. [Results] There were significant differences in the gait ability before injury, the presence of Parkinson's disease, and dementia. [Conclusion] Factors related to the postoperative course of fracture patients included the gait ability before injury, and the presence of Parkinson's disease and dementia.

P1-250

Necrosis of the extremities associated with septic shock in a patient with malignant rheumatoid arthritis, which may have been exacerbated by the administration of noradrenaline

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Conflict of interest: None

A 66-year-old woman with MRA. TKA on both knees and TEA on right elbow were performed. SASP, ABT and PSL were used. She was transported to our hospital due to the appearance of fever, weakness, abdominal pain, diarrhea, and shortness of breath. During the examination, her blood pressure dropped although a fluid was administered, there was little reaction, so NA was administered. She was diagnosed with septic shock associated with pyelonephritis. On the same day as the NA was administered, cyanosis gradually appeared in the extremities, and within 7 weeks, necrosis progressed. Eventually, Necrosis spread over a wide area of the limbs. After her general condition stabilized, the necrotic area dried out, but signs of infection were observed in the necrotic area and ulcer area. Due to the implants she had in her limbs, it was decided that amputation would be preferable, and he was transferred to our department for surgery. The right upper arm amputation and the left femoral amputation were performed. The preserved limb maintained dry necrosis. After the surgery, the wound and general condition were both favorable. When catecholamines are administered to treat shock patients, peripheral blood flow becomes poor, and in rare cases, amputation may be required due to extensive necrosis.

P1-251

Clinical Experience with Total Knee Arthroplasty Using the Under-Vastus Approach

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Conflict of interest: None

[Objectives] The vastus medialis-preserving approach in total knee arthroplasty (TKA) is beneficial for maintaining the extensor mechanism. The 2022 Japanese Orthopaedic Association TKA registry shows that the sub-vastus approach was used in only 5.60% of primary TKAs, suggesting its potential for wider adoption. This study reports our experience using the under-vastus approach. [Methods] We reviewed 342 knees treated with primary TKA using the under-vastus approach between October 2017 and December 2023. [Results] The study included 51 males and 291 females, with an average age of 74 years. OA was the cause in 322 cases, RA in 15, and other conditions in 5. The average operation time was 115 minutes, with 35 ml of intraoperative blood loss. No transfusions were needed, and three postoperative hematomas resolved with conservative treatment. One case involved a partial tear of the vastus medialis, which required suturing. [Conclusion] The under-vastus approach is associated with early functional recovery, preserves the vastus medialis, reduces patellar trauma and blood loss, and enables minimally invasive surgery. Our experience shows it is a safe and effective method for TKA.

P1-252

Survey on Ozoralizumab Autoinjector Subcutaneous Injection

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Conflict of interest: None

[Objectives] Ozoralizumab is the sixth TNF inhibitor with Ozoralizumab syringe subcutaneous injection formulation (“Ozoralizumab SC”), and it was released in January 2023. As switching from SC to Auto Injector (“Ozoralizumab AI”) at our hospital, we conducted a questionnaire survey on patients’ pain and impressions of AI, and examined the usefulness of AI from the nurse’s perspective. [Methods] We researched the relation between the pain when the patients inject Ozoralizumab, and the disease activity status, patient’s background, disease diagnosis, and treatment intervention status, using our original questionnaire. [Results] Although 62.9% (17/27) of the patients indicated that they would be able to self-inject, 40.7% (11/27) of the patients requested a monthly visit. We thought it was one of the factors that prevented them change to self-injection. The patients think that AI is convenient and easy. The older they get, the less they feel pain with the AI injection (P=0.018). [Conclusion] Many patients don’t have a negative image of the injection with Ozoralizumab. And they feel it is convenient and easy. We nurses think that Ozoralizumab AI is one of the most useful devices for introducing self-injection.

P1-253

A Study on the “Nursing Practice Ability Scale for RA Nurses” as an Objective Measure: Verification in a General Hospital with Acute Care Wards

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Conflict of interest: None

[Objectives] To compare practical abilities of nurses engaged in rheumatoid arthritis (RA) care (RA group) and those not engaged (non-RA group) using the “Nursing Practice Scale for Rheumatology Nurses” and to evaluate its effectiveness as an objective tool. [Methods] Questionnaires were distributed to 121 nurses in wards/clinics with rheumatology departments and 109 in wards without such departments, yielding 98 valid responses. Reliability was confirmed with Cronbach’s alpha, and group differences were analyzed with the Mann-Whitney U test. [Results] The RA group scored 75.25, and the non-RA group scored 77.61, with no significant difference (p=0.067). Chi-square testing confirmed model fit for the RA group. Regular RA nursing experience was suggested to support maintenance and enhancement of Factor 1 (RA knowledge/skills), Factor 2 (listening skills), and Factor 3 (facilitating RA care). [Conclusion] Regular RA care experience may improve Factors 1, 2, and 3. The “Nursing Practice Scale for Rheumatology Nurses” may effectively evaluate nurses with RA experience and could serve as a general nursing skills scale when applied to diseases routinely encountered by non-RA nurses.

P1-254

Characteristics of home medical care for patients with rheumatic diseases and the care required for them

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Conflict of interest: None

[Objective] In a super-aging society, the demand for home medical care for rheumatic disease patients is rising. This study aims to identify the characteristics of home care for these patients and required skills. [Method] We analyzed 22 home-based rheumatic disease patients receiving care at our clinic. [Results] The average age was 81.0 years, with a disease duration of 27.3 years. Two patients needed assistance level 2, 19 needed care levels 1 to 5, and one refused certification. Four had ADL decline, four had malignant tumors, one had a neurological disease, four had fractures, four had respiratory diseases, and two had dementia. Thirteen patients were cared for by spouses, five by children, three lived alone, and one lived in senior housing. All but one received home nursing care with interprofessional collaboration. Three developed mild pressure ulcers. Six patients died at home, nine died after hospitalization. Causes of death were malignant tumors (4), respiratory diseases (7), and old age (4). Five respiratory deaths were from pneumonia, two from worsening rheumatic lung disease. [Conclusion] Pain management and joint protection are critical in home care for rheumatic patients. Interprofessional collaboration is essential, with special attention to respiratory diseases.

P1-255

The Utility of Self-Foot Care

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Conflict of interest: None

Objective: Foot-related issues such as calluses and footwear concerns are common among patients with rheumatoid arthritis This study assessed the effectiveness of self-foot care in preventing declines in activities of daily living (ADL), **Methods:** Patients were instructed on affordable and simple foot care methods and monitored over time to ensure they could continue independently. The care methods emphasized long-term sustainability and adaptability to each patient's needs. **Results:** Within a month, calluses improved, and walking-related pain decreased. Patients also addresses skin dryness through proper skincare. By the second visit, they could trim calluses confidently, determining the right depth and frequency, saying, "This feels just right". **Conclusion:** Through proper instruction, patients understood their individual foot care needs, avoiding infection and pain from over-trimming. For patients who visit the clinic less frequently, self-foot care is crucial. Regular self-care reduced pain, expanded movement, and improved quality of life (QOL). Many patients expressed regret for not starting earlier. Going forward, earlier foot care guidance during routine visits is planned.

P1-256

Report on a Survey of Treatment Preferences in Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

[Objective] We report survey results on treatment preferences among rheumatoid arthritis (RA) patients. [Methods] We surveyed 55 RA patients at our hospital's rheumatology clinic, dividing them into two groups: those using biologic DMARDs (bDMARDs) or JAK inhibitors (JAKi) and those not using these medications. We examined treatment preferences between the groups. [Results] Among 55 patients (8 men, 47 women; average age 68.9±11.5 years), no significant differences were observed in SDAI, CDAI, or DAS28-CRP scores between the bDMARDs/JAKi user group (N=16) and non-user group (N=39). More non-users expressed a desire to reduce medication costs, especially those under 75. In the non-user group, significantly more patients wanted to reduce the number of medications, with about 80% aged 60 or older. Additionally, 16 patients (29%) indicated "no specific preferences" regarding treatment. [Conclusion] This survey suggests that high medication costs hinder bDMARDs and JAKi use, especially for patients under 75. Many RA patients wish to reduce their medication load, highlighting polypharmacy issues. Pharmacists should alleviate financial burdens and improve treatment safety. Coordinated care with physicians and nurses is essential to optimize treatment based on patient needs.

P1-257

Analysis of pregnancy outcomes complicated by systemic lupus erythematosus (SLE) in a single center

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Conflict of interest: None

[Objective] To identify maternal and fetal outcomes, as well as risk factors, in pregnancies complicated by SLE. [Methods] Women under 45 years of age who attended both the Rheumatology and Obstetrics at the institution in past 10 years were included in the study. Their medical records were retrospectively reviewed to gather backgrounds, characteristics, disease status, treatments, and adverse pregnant outcomes. [Results] Among 445 subjects, 27 pregnancies were complicated by SLE, with 3 resulting in miscarriages, and 20 deliveries occurring at our hospital. The mean maternal age was 32.6 years (±SD4.2), Four pregnancies (20%) resulted in preterm delivery, and the mean birth weight was 2699 g (±SD465.5), with 25% classified as low birth weight. Fetal growth restriction (FGR) occurred in 6 cases (30%), and premature rupture of membranes (PROM) in 7 cases (35%). The median SLEDAI score at the time of conception was 4 (2-16), and the average prednisolone (PSL) dose was 4.65 mg (±SD3.52). Disease requiring additional PSL during pregnancy occurred 4 patients (20%). Analysis of factors related to PROM showed a significant association with an increase in PSL dose during pregnancy (p=0.011). [Conclusions] An increase in PSL dose during pregnancy with SLE may contribute to the risk of PROM.

P1-258

Compliance with pregnancy and childbirth-related SLE QIs in our maternal outpatients

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Conflict of interest: None

[Objectives] In 2023, we developed Japan's first quality indicator (QI) for pregnancy and childbirth in SLE as a tool to improve the quality of care. The aim of the present study was to assess compliance with the QI in our maternal outpatients. [Methods] Of the 33 SLE patients in our maternal outpatient from October 2014 to October 2024, 31 pregnancies and 35 pregnancies were managed in our obstetrics and gynecology department. Compliance with 21 QIs assessable using electronic medical information, as well as pregnancy outcomes, complications and disease activity were investigated retrospectively. [Results] Of the 33 patients with SLE, 31 (94%) had 35 successful pregnancies, of which 5 are currently pregnant. Median age at conception was 34 (IQR 25-42), median PSL dose at conception was 5 mg/day (0-10) and median SLEDAI at conception was 4 (3-6). In 24 pregnancies that resulted in live births, there were 4 (17%) fetal growth retardation, 5 (20%) gestational hypertension and 6 (25%) preterm births. Compliance with 21 QI items was 100% for one pregnancy planning-related item, 100% for three of the six laboratory-related items and 100% for 14 drug-related items. [Conclusion] Compliance with pregnancy and childbirth-related SLE QIs tended to be high at our hospital.

P1-259

Analysis of Bone Mineral Density Using AI-Assisted Osteoporosis Diagnostic System before and after Pregnancy in Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), may be at high risk of pregnancy-related osteoporosis. We herein assessed bone mineral density (BMD) in patients with SLE or RA before and after pregnancy using an AI-assisted osteoporosis diagnostic system that estimates BMD with high accuracy solely from frontal chest X-rays (CXR). [Methods] Patients with SLE or RA who delivered at our hospital from 2010 to 2023 and who had a CXR within 3 years before delivery and 3 years after delivery were included. BMD of the proximal femur was estimated by the AI system. [Results] 17 patients with SLE (mean age 34.0±4.6 years old, mean disease duration 10.6±6.1 years) and 7 patients with RA (mean age 39.3±3.7 years old, mean disease duration 8.0±4.8 years) were included. 3/17 (17.6%) of the patients with SLE and 3/7 (42.8%) of the patients with RA had osteopenia before pregnancy with a Young Adult Mean (YAM) value less than 80%. 9/17 (52.9%) of the patients with SLE and 1/7 (14.3%) patient with RA showed a decrease in BMD during pregnancy. [Conclusion] A substantial number of patients with SLE and RA have low BMD before pregnancy and experience BMD

loss during pregnancy. Clinicians need to be careful regarding BMD when caring for those patients.

P1-260

Importance of infertility treatment in pregnancy for RA who wish to have a child

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Conflict of interest: None

[Objectives] We analyze clinical indicators related to the period of natural pregnancy (NP) and infertility treatment (IT), and examine treatment strategies when trying to conceive. [Methods] We used the data of RA patients who have been treated at the planning for pregnancy, and compared the time to pregnancy (TTP) between the NP group and the IT group. We retrospectively analyzed the relationship between TTP and patient background, disease activity, and treatment agents. [Results] 51 pregnancy cases were included in our study. IT was performed in 16 cases (31.4%), and TTP was significantly longer in the IT group than in the NP group ($P<0.01$). There were no significant differences in pregnancy outcomes between two groups. In the NP group, 14 cases (40%) had more than 6 months of TTP, and the age at the start of trying to conceive was lower ($P=0.03$), the rate of biologics use tended to be lower ($P=0.07$), and GC dosage tended to be higher ($P=0.08$). 7 cases (46.7%) had undergone IT for more than 6 months, and the age at the time of conception tended to be older ($P=0.08$). [Conclusion] It was suggested that pregnancy can be prolonged even if the age at the start of trying to conceive is young. RA patients who hope to have children should promptly select biologics and consider IT.

P1-261

Prospects and challenges for the establishment of transitional outpatient clinics for congenital immunodeficiency and autoinflammatory syndromes

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Conflict of interest: None

[Objectives] In recent years, one of the challenges for treating patients with childhood-onset congenital immunodeficiency and autoinflammatory syndromes is the transition to adult medicine after adulthood. Since 2016, we have been accepting adult patients who have been treated in pediatric departments of other hospitals. In May 2024, a team consisting of physicians from the departments of infectious diseases, pediatrics, clinical genetics, hematology, and respiratory medicine was formed to share cases and provide consultation. [Results] As of the end of October 2024, 12 cases are currently shared within the team. 8 have chronic granulomatous disease, and 2 have common variable immunodeficiency. Two patients with chronic granulomatous disease have died since the team was formed. [Conclusion] The team regularly discusses cases and regularly shares information with specialists outside the hospital. On the other hand, many issues remain, such as the lack of experience of internal medicine physicians in treating various diseases, the lack of information on treatment and prognosis in adulthood, problems with the social security system, and patients' own confusion about changing to an adult attending physician. We will continue to seek solutions to these issues.

P2-001

***N*-acetylgalactosaminyl transferase 12 (GalNAc-T12) suppresses the cartilage destruction in OA and RA**

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Conflict of interest: None

[Objectives] We previously showed that the SNP rs2295926 belonging to *GALNT12* gene (*N*-acetylgalactosaminyl transferase 12; GalNAc-T12) is strongly associated with rapid joint destruction in the patients with RA. We also found that GalNAc-T12 contributes to the survival and proliferation of chondrocytes. Here we examined the effect of GalNAc-T12 on the cartilage destruction in OA and RA by using mouse model. [Methods] C57BL/6 mice were induced OA by subjecting to the destabilization of the medial meniscus (DMM mice). Further, DBA1/J mice were induced RA by injecting with anti-type II collagen antibody cocktail and LPS (CAIA mice). Both model mice were treated with GalNAc-T12 in the joint and assessed for cartilage degeneration by using OARSI scoring system. [Results] Eight weeks after the subjection of DMM, OARSI score was significantly increased in mice. However, GalNAc-T12 prevented the cartilage degradation and significantly reduced the OARSI score in DMM mice. Similarly in CAIA mice, cartilage destruction was improved, and OARSI score was significantly decreased 4 weeks after the injection with GalNAc-T12. [Conclusion] GalNAc-T12 suppresses the cartilage destruction in OA and RA by contributing to the characteristics of chondrocytes including the survival and proliferation.

P2-002

IL-6 Prevents Intrinsic Apoptosis in RA-FLS via Bik

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Conflict of interest: None

[Objectives] IL-6 is highly presents in sera and joint fluid of patients with RA. We have previously reported that IL-6 cooperates with TNF-α to regulate the cell cycle of RA-FLS, while its effects on synovial cell death remain unclear. In this study, we examined the effect of IL-6 trans-signaling on RA-FLS cell death. [Methods] RA-FLS were treated with IL-6/soluble IL-6receotor (sIL-6R), Dexamethasone (DEX). We examined cell viabilities by WST8 assay, expression of intrinsic apoptosis-related proteins including Bcl2 family by western blotting and fluorescent immunostaining, and Bcl-2-interacting killer (Bik) expression in RA-FLS by qPCR. Finally, expression vector of Bik was introduced into RA-FLS to measure the resistance against DEX-induced apoptosis by WST8 assay. [Results] DEX decreased cell viabilities in a concentration-dependent manner. IL-6/sIL6R prevented DEX-induced apoptosis. DEX induced cell death accompanied by Bik/Cytochrome c expression in RA-FLS, while trans-signaling suppressed it. The trans-signaling was appeared to repress Bik mRNA expression by DEX. Upon overexpressing Bik, IL-6 trans-signaling appeared to decrease its resistance to DEX-induced apoptosis. [Conclusion] IL-6 trans-signaling suppresses intrinsic apoptosis on RA-FLS, presumably due to Bik.

P2-003

Evaluation of bone microstructure using clinical 3T-MRI in RA

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Conflict of interest: None

[Objectives] To evaluate bone microstructure in patients with rheumatoid arthritis (RA) using a clinical 3T-MRI [Methods] Patient backgrounds, such as duration, bone mineral density (DXA), bone metabolism markers, and steroid therapy were investigated in 20 RA patients. The bone structure MRI imaging site was the tibial subchondral bone of the knee joint, using an Achieva 3.0T TX with TR/TE: 10/4 ms, slice thickness: 0.3 mm, FOV 120X120X22 mm, voxel size 0.3X0.3X0.3 mm. VGSTUDIO MAX was used for image analysis to determine bone volume/total volume (BV/TV), trabecular number (Tb. N), trabecular thickness (Tb. Th), and trabecular separation (Tb. Sp) were measured. In addition, five patients with osteoarthritis (OA) were included in the study to compare the results with those of RA patients. [Results] BV/TV showed a strong positive correlation with Tb. Th and a strong negative correlation with Tb. N and Tb. Sp, respectively. Bone structural parameters were not significantly correlated with BMD, bone metabolism markers, inflammation markers, etc. In comparison between RA and OA, there was no significant difference. [Conclusion] We evaluated bone microstructure in RA patients using clinical 3T-MRI.

P2-004

Examination of ultrasonographic findings and serological factors, including the flexor side, in cases with hand and finger symptoms without joint synovitis

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Conflict of interest: None

[Objectives] In cases of pain and stiffness in the hand and fingers without arthritis, tendonitis is often found on US. Therefore, we examined the extensor and flexor tendons in 156 cases without arthritis using US. [Methods] Positive US findings were tendon swelling, synovial fluid accumulation, and PD signal positivity (PD (+)). [Results] In all cases, Tendonitis were significantly more common on the flexor side than on the extensor side at the wrist, MCP, and PIP joints (all $p < 0.0001$). Three groups were compared: 103 cases of RF (-) ACPA (-) (SN group), 28 cases of RF (+) ACPA (-) (RF+ group), and 25 cases of ACPA (+) (ACPA+ group). On the extensor side, there were no differences among the three groups in tendonitis above the wrist. There were no differences in tendonitis above the MCP joint, and PD (+) was the least common in the SN group ($p = 0.019$). On the PIP joint, tendonitis ($p=0.021$) and PD (+) ($p=0.008$) were most common in the RF+ group. On the flexor side, there were no differences between the wrist and MCP joint, and tendonitis above the PIP joint were the least common in the SN group ($p=0.030$). [Conclusion] Tendonitis were more common on the flexor side than on the extensor side, and were less common in the SN group.

P2-005

Significance of Disproportionate Articular Pain (DP) in Predicting the Treatment Response to b/tsDMARDs in Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

[Objectives] In RA patients, a discrepancy of 7 or more between the tender joint count (TJC) and the swollen joint count (SJC), referred to as Disproportionate Articular Pain (DP), is associated with a lower treatment response. This study retrospectively examined the impact of DP on treatment outcomes in RA patients newly initiated on b/tsDMARDs. [Methods] We enrolled RA patients who were initiated on b/tsDMARDs, and continued treatment for at least 8 weeks at our hospital. Clinical data, including TJC, SJC, and DAS28-CRP, were collected at 0, 4, 8, 12, and 24 weeks after treatment initiation. Treatment response was evaluated using the EULAR response criteria (Good). Patients were stratified by DP status (DP [+] or DP [-]), and propensity score matching (PSM) was applied to adjust for potential confounders. The treatment response at each week was compared between the groups. [Results] From 243 RA patients, 27 patients were selected for each group after PSM adjustment. DAS28-CRP at week 0 was significantly higher in the DP (+) group (5.3 vs. 4.2, $p=0.002$). The treatment response was significantly lower in the DP (+) group at 4 weeks (26% vs. 52%, $p=0.049$) and 8 weeks (26% vs. 66%, $p=0.002$). [Conclusion] DP may significantly impact the early (4-8 weeks) treatment response in RA patients.

P2-006

Clinical factors associated with radiographic remission at 1 year after the initiation of rheumatoid arthritis treatment

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Conflict of interest: None

[Objectives] It is essential to achieve not only clinical remission but also radiographic remission in the early stage of RA. In this study, we investigated the clinical factors associated with the maintenance of radiographic remission at 1 year after the start of RA treatment. [Methods] We consecutively selected patients who were first diagnosed with RA and started treatment at our hospital between January 2018 and April 2023. Disease activity indexes, musculoskeletal ultrasound (MS-US) and radiographic findings at wrist and finger joints, and treatment details were analyzed retrospectively. [Results] 276 subjects were included (mean age 60.5 years, rheumatoid factor positive 212 (77%), anti-CCP antibody positive 208 (75%)). The disease activity indexes at the start of treatment were 21.6 for SDAI and 19.8 for CDAI. ΔmTSS after 1 year was 0.47±1.21. Multivariable analysis revealed the presence of intra-erosive power Doppler signal on MS-US or "active erosion" at the initial visit as a factor associated with radiographic remission ($\Delta mTSS \leqq 0.5$) at 1 year (OR 0.131, 95% CI 0.059-0.294, $p<0.001$). [Conclusion] The presence of "active erosion" at the time of RA diagnosis is an important risk factor for future joint destruction.

P2-007

Investigation of the usefulness of evaluating RA disease activity using RAPID3 in actual clinical practice

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Conflict of interest: None

[Objectives] To study the usefulness of RAPID3 in assessing disease activity in RA treatment. [Methods] We used RAPID3 to evaluate the disease activity of RA in 622 RA patients attending Nagoya University Hospital. We also investigated the correlation with other disease activity assessments and the factors associated with achieving low disease activity (LDA). [Results] Patient profile: mean age 66.4±14.4 years, male 24.6%, disease duration 14.8±10.9 years, MTX use 59.8%, b/tsDMARDs use 40.4%, Rheumatic Disease Comorbidity Index (RDCI) 0.9±1.1. The mean RAPID3 score was 6.6±6.0, 37.3% were in remission, and 55.2% had low disease activity. The correlation coefficient with CDAI was high at 0.725 ($p<0.001$), and the number of swollen and tender joints and CRP were low (0.285, 0.236, 0.145, all $p<0.001$). Patient background factors associated with achieving LDA were age (OR: 0.98, 95% CI: 0.96-0.98, $p<0.001$), disease duration (0.97 [0.95-1], $p<0.001$), MTX use (1.46 [1.05-2.02], $p=0.02$), glucocorticoid (GC) use (0.62 [0.42-0.92], $p=0.02$), and RDCI

(0.82 [0.70-0.96], p=0.01). [Conclusion] RAPID3 correlated with existing disease activity evaluation, and older age, longer disease duration, more comorbidities, no MTX use, and GC use were factors that inhibited obtaining low disease activity.

P2-008

Current status of late-onset rheumatoid arthritis treatment at our hospital - Comparison with the revised 2024 Rheumatoid Arthritis Treatment Guidelines

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Conflict of interest: None

[Objective] To verify the status of treatment of late-onset rheumatoid arthritis (LORA) at our hospital with the LORA consensus statement in the revised 2024 Guidelines for the Treatment of RA. [Method] Among RA patients who visited our hospital from June to August 2024, we investigated the presence or absence and dosage of MTX, biological agents (bio), JAK inhibitors (JAKi), csDMARDs, and PSL, and compared the two groups and the presence or absence of MTX to verify the differences from the guidelines. [Results] There were no significant differences between the LORA and YORA groups in the rates of using MTX, bio/JAKi, or PSL. The doses of MTX were 7.4±2.6 mg/w in the LORA group and 6.7±2.8 mg/w in the YORA group, with no significant differences. The most common reasons for not concomitant use of MTX in both groups were remission with csDMARDs alone, followed by interstitial pneumonia, cognitive impairment, and discontinuation of MTX using bio or JAKi. The rate of JAKi use was significantly higher in LORA patients without MTX than those with MTX. [Conclusion] LORA treatment at our hospital generally complied with the guidelines. Further studies are awaited to determine the efficacy and safety of reducing MTX after induction of remission in LORA, as well as JAKi treatment without MTX.

P2-009

Exploratory study of patients optimal for golimumab treatment in rheumatoid arthritis cohort FIT-RA

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Conflict of interest: None

[Objectives] This study aimed to clarify the therapeutic effectiveness of golimumab (GLM) in rheumatoid arthritis (RA) and the factors related to its effectiveness. [Methods] In the FIT-RA (Fukui Ishikawa Toyama Database of Rheumatoid Arthritis), 132 patients treated with GLM were analyzed. Age-, sex-, and disease duration-adjusted logistic regression analyses were performed to explore factors related to achieving low disease activity (LDA) and remission (R) at 12 months. [Results] Twelve months after GLM initiation, LDA and R was achieved in 67% and 20% of the patients, respectively. The number of past molecular target drug use (OR 0.26), high SDAI value (OR 0.94), glucocorticoid use (OR 0.31), MTX use (OR 3.00), switch from other TNF inhibitor (vs. non-TNF inhibitor, OR 3.56), RF >150 IU/mL (vs. RF <150, OR 0.14) were related to achievement of LDA. [Conclusions] The profile of suitable cases was generally similar to that of other drugs. It was suggested that administering a sufficient dose of GLM and/or combination with MTX were necessary for patients with markedly high RF levels.

P2-010

Relapse and rheumatoid factor trends after TNF inhibitor withdrawal in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To clarify whether rheumatoid factor (RF) is associated with whether rheumatoid arthritis (RA) patients treated with TNF inhibitors and who have achieved remission and withdrawal from therapy have been able to do so without relapse. [Subjects] We studied RA patients who had TNF inhibitors at our hospital by March 2022, who had achieved DAS28 remission and were off the drug. We investigated whether they were seropositive or negative, whether RF had normalised at the time of withdrawal, whether RF had subsequently increased. [Results] The withdrawal rate was 5.2% (50/968). At the last observation, 36 patients (72%) were in remission or LDA, 73% (21/37) with seropositive RA and 69% (9/13) with seronegative RA. For 35 of the 37 seropositive RA patients whose RF was measured at withdrawal, 16 of 19 (84%) had normalised RF at withdrawal and 10 of 16 (63%) with elevated RF were able to maintain withdrawal. Of the 8 patients with elevated RF after withdrawal, 1 relapsed and 2 of the 11 patients without elevated RF relapsed. [Conclusion] There was no difference in maintenance of withdrawal after remission depending on whether the patient was seronegative or positive at diagnosis. There was no association between increased RF after withdrawal and relapse.

P2-011

Comparison of the clinical efficacy of abatacept and sarilumab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To compare the clinical efficacy at 52 weeks after treatment of abatacept (ABT) or sarilumab (SAR) for rheumatoid arthritis (RA). [Methods] A total 275 patients with RA who began therapy with ABT (n=160) or SAR (n=115) between January 2019 and September 2023 were enrolled. Clinical data were reviewed retrospectively from their medical records. Clinical outcomes were assessed. [Results] Baseline characteristics for the ABT and SAR groups were as follows: mean age 71.3 vs. 66.0 (p=0.014); disease duration 12.0 vs. 11.8 years (p=0.966); prior biologics/JAK inhibitor use 47.3 vs. 71.4% (p=0.001); methotrexate use 29.5 vs. 30.7% (p=0.378); glucocorticoid use 40.0 vs 38.6% (p=0.188); and CDAI 20.98 vs. 18.20 (p=0.071). The 52-week continuation rates were 55.2 vs. 68.3% (p=0.130). CDAI at 12, 24, and 52 weeks were 9.43 vs. 7.39 (p=0.036), 8.21 vs. 7.35 (p=0.259), and 8.12 vs. 7.09 (p=0.353), respectively. The remission rates at 52 weeks were 30.6 vs. 31.1% (p=0.933). Both groups demonstrated significant reductions in disease activity from 12 weeks onward, with no significant differences between groups except at week 12. [Conclusion] After 52 weeks of treatment with ABT or SAR for RA, both groups demonstrated comparable continuation rates, CDAI reductions, and remission rates.

P2-012

Evaluation of the Clinical Effectiveness of Ozoralizumab for Rheumatoid Arthritis

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Conflict of interest: None

[Objective] This study aimed to investigate the status and effectiveness of ozoralizumab (OZO) treatment in patients with rheumatoid arthritis (RA). [Methods] A total of 44 RA patients who received OZO treatment for over 12 weeks were included. Patient demographics, CDAI changes, and OZO continuation were examined. [Results] The average age was 69.9±16.0 years, with 85.4% female. Mean disease duration was 12.9±10.6 years, and 36.3% had an eGFR below 60 mL/min/1.73 m^2. Rheumatoid factor and anti-CCP positivity were 85.4% and 87.8%. Concomitant methotrexate (MTX) was used in 63.4%, glucocorticoids in 36.6%, and prior b/tsDMARDs in 61%. CDAI improved significantly from baseline (16.8±9.8) to 11.5±8.2 at 4 weeks and to 8.1±4.7 at 12 weeks. At 12 weeks, remission was achieved by 20.2% and low disease activity by 65.6%. During a mean observation of 33.4±22.1 weeks, nine patients discontinued OZO (two due to adverse events, seven due to insufficient efficacy). [Conclusion] RA patients treated with OZO at TBCR were older with a high rate of prior b/tsDMARDs use. Early improvements in CDAI were noted, with 20.2% achieving remission and 65.6% reaching low disease activity by 12 weeks.

P2-013

Treatment and Prognosis of Life-threatening Organ Involvement in Patients with Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: None

[Objectives] Eosinophilic granulomatosis with polyangiitis (EGPA) is a necrotizing granulomatous vasculitis with hypereosinophilia. As prognostic factors (Five-Factor Score: Medicine. 90. 2011), independent factors predictive of poor prognosis for EPGA were age>65 years, cardiac involvement. CNS involvement is rare and not included in this analysis. In recent years, treatment has become established. We investigated the efficacy of treatment and outcome of organ involvement. [Methods] We retrospectively studied 51 patients attended our hospital between 2000 and 2024. The age of onset was 60±12 years, and the response to treatment and prognosis were investigated. [Results] All patients were treated with GC, 11 with CY, 16 with IVIG, 29 with MEP, 17 with AZA, 4 with MMF and 2 with RTX. MEP was effective in reducing PSL. 8 patients had cardiac involvement, and did not recur after treatment. 11 patients had CNS involvement. Four patients died (age of death: 78±4 years). The cause of death was two with pneumonia, CNS disease in one refractory case, and cancer in one case. [Conclusion] Many patients with life-threatening lesions can maintain long-term remission if they are treated appropriately. On the other hand, elderly patients should be treated considering opportunistic infections.

P2-014

Differences macrophage activation between anti-MDA5 antibody-positive interstitial pneumonitis and systemic lupus erythematosus: analysis of cytokine profile

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Conflict of interest: None

[Objectives] To elucidate the differences in macrophage activation between anti-MDA5 antibody positive interstitial pneumonitis (MDA5) and systemic lupus erythematosus (SLE) by comparing their cytokine profiles. [Methods] The study included 39 patients with MDA5 and 31 with SLE, 9 of whom had macrophage activation syndrome (MAS). Serum cytokine levels were measured before treatment initiation, and their associations with ferritin and IP-10 levels were analyzed. [Results] IL-6, IL-8, IL-10, IL-15, IL-18, and TNF-α were elevated in patients with MDA5 and SLE compared to controls. IP-10 was elevated in MDA5 patients compared to both SLE patients and controls, while IFN-λ was elevated in MDA5 patients compared to SLE patients. In the high ferritin group (>500 ng/mL), IFN-λ was elevated in MDA5, whereas IFN-α was elevated in SLE. In MDA5, ferritin levels correlated with IP-10, IFN-α, and IFN-λ, whereas in SLE, they correlated with IP-10 and IFN-α. Additionally, IP-10 correlated with TNF-α and IL-6 in MDA5 patients and with IFN-α, TNF-α, and IL-15 in SLE patients. [Conclusion] The cytokine profiles of MDA5 and SLE showed some similarities; however, the cytokines involved in macrophage activation differed between the two diseases.

P2-015

Adverse effects and continuation rates of nintedanib for progressive fibrosing interstitial lung diseases

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Conflict of interest: None

[Background] Nintedanib is an important agent for progressive fibrosis, including collagen diseases. While liver dysfunction and diarrhea are known side effects, recent reports indicate proteinuria, though its frequency, clinical features, and continuation rates remain unclear. [Objective] To examine the types of side effects, reasons for dose reduction or discontinuation, and continuation rates of nintedanib. [Methods] We retrospectively analyzed cases of nintedanib initiated in our Center of Rheumatology from September 2018 to September 2023. [Results] Nineteen cases were identified. The median age was 72 years; 12 were female. Continuation rates were 84.2% at 1 month and 78.9% at 1 year. Three cases discontinued within 1 month due to diarrhea, liver dysfunction, and rash. One case discontinued within a year due to proteinuria, and two after 1 year due to diarrhea and proteinuria. [Discussion] In 2022, nephrotic syndrome was added as a caution in the package insert. Reports suggest drug-induced nephropathy with proteinuria and hematuria with renal biopsies showing microvascular damage. Although no cases showed renal function decline in our study, some cases developed proteinuria. Conclusion: Monitoring for proteinuria is advised in nintedanib treatment.

P2-016

Survey on Support for Rheumatoid Arthritis Patients Targeting Care and Welfare Workers

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Conflict of interest: Yes

[Objectives] To investigate knowledge of rheumatoid arthritis (RA) and related challenges in supporting RA patients among care and welfare workers. [Methods] A survey was conducted as part of the Ministry of Health, Labour, and Welfare's research grant. It targeted 1,000 members each of the Japan Care Manager Association (JCMA) and the Japan Association of Certified Social Workers (JACSW). [Results] Responses were received from 390 JCMA and 330 JACSW members. The average age was 53.6/52.6 years (JCMA/JACSW), with 78.1%/64.5% female and 11.6/11.3 years of experience. Among JCMA, 89.8% were care managers, and 34.6% of JACSW were social workers. RA knowledge awareness was 66.7%/53.6% for symptoms, 42.5%/27.0% for complications, 20.2%/10.6% for surgery, and 34.9%/20.4% for rehabilitation. Awareness regarding important considerations for medications was 58.0%/42.1% for glucocorticoids, 17.3%/5.7% for methotrexate, 12.4%/4.1% for biologics, and 5.2/5.4% for JAK inhibitors. Support provided included information on medical systems (43.6%/46.6%) and assistive devices (42.3%/39.9%). Differences from other patients included joint deformities (80.8%/77.9%) and frequent pain (63.2%/57.1%). [Conclusion] The need for more RA education for care and welfare workers was suggested.

P2-017

Correlation between leukocyte counts in synovial fluid, cytokine expression in synovial fluid, and blood examinations in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To evaluate the correlation between leukocyte counts in synovial fluid (SF), cytokines expression in SF, and blood examinations in patients with rheumatoid arthritis (RA). [Methods] We investigated SF-WBC and fractions, Blood-WBC and fractions, CRP, and MMP-3 in 30 RA patients who underwent SF examination from 2020 to 2022. The SF concentrations of cytokines (IL6, IL8, MCP1, MMP3, VEGF, GM-CSF) that have been reported to be expressed in synovial fibroblasts were evaluated using ELISA. [Results] A strong positive correlation was observed between SF-WBC and SF-Neu%. Serum CRP was positively correlated with SF-Neu%, and serum MMP-3 was also positively correlated with SF-WBC and SF-Neu%. The same tendency was observed when examining only the seropositive group (n=20) and the onset group (n=22). Serum CRP was positively correlated with SF-Mono% only in the onset group. SF-Neu% was positively correlated with SF-IL6, SF-VEGF and SF-RANKL. Serum CRP was positively correlated with SF-IL6, SF-VEGF and SF-MMP3. Serum MMP3 was positively correlated with SF-IL6. [Conclusion] An increase in WBC, mainly neutrophils, was observed in RA-SF, and this increase in neutrophils reflected an increase in IL-6, VEGF, and RANKL in SF, which was reflected in serum CRP and MMP-3.

P2-018

Serum D-dimer levels as a biomarker of RA disease activity

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Conflict of interest: None

[Objective] To investigate whether D-dimer (DD) could be used as serological biomarker of RA disease activity. [Methods] 72 RA patients who underwent total joint arthroplasty at our hospital were included in the study. Patients who had DVT, hematologic disease, malignancies, infections were excluded. 72 patients were classified into two groups: low activity group (10≧CDAI) and high activity group (CDAI>10). The association between DD and CRP, ESR, MMP-3, DAS28ESR, CDAI, and SDAI was evaluated by spearman correlation. Analyses of the receiver operating characteristic (ROC) curves and under the ROC curve (AUC) of DD, CRP, ESR, and MMP-3 levels were performed. Logistical regression analysis was used to identify the independent variables association with RA disease activity. [Results] DD levels were significantly higher in the high activity groups compared to the low activity groups. DD levels were positively correlated with CRP, ESR, MMP-3, DAS28ESR, CDAI, and SDAI. The AUC was 0.705 for DD, 0.587 for CRP, 0.602 for ESR, and 0.682 for MMP-3. Logistical regression analysis showed that DD was an independent variable associated with RA disease activity. [Conclusions] DD can be used as supplementary serological biomarker to assess RA disease activity, in addition to CRP, ESR, MMP-3.

P2-019

ACPA shows seasonal change

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Conflict of interest: None

[Objectives] To analyze seasonal changes in laboratory data related to rheumatoid arthritis. [Methods] We found that the median value of ACPA was high in September and low in April, while the median frequency of ACPA measurement was high in September and low in April. On the other hand, the median frequency of measurement was highest in September and lowest in April. The other test items are currently under investigation and will be presented at the conference. [Results] The absolute value of ACPA showed seasonal variation, which is a completely different pattern from the seasonal variation in disease activity published so far. [Conclusion] In the analysis of real-world data in Japan, ACPA showed a high median value in the fall and a low median value in the spring, unlike disease activity in RA.

P2-020

Discovery of autoantibody biomarkers for Rheumatoid Arthritis using citrullinated HuPEX, a human comprehensive protein array

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Conflict of interest: Yes

[Objectives] Rheumatoid factor and anti-citrullinated protein antibodies (anti-CCP antibodies) are important biomarkers used for the diagnosis of Rheumatoid Arthritis (RA). However, due to the presence of seronegative RA patients, there is a need for new autoantibody markers with higher sensitivity and specificity. We utilized human comprehensive protein arrays, HuPEX, which contain approximately 13,500 human proteins under non-dry conditions, to isolate new autoantibody biomarkers for RA using citrullinated protein arrays. [Methods] Citrullinated comprehensive protein arrays, referred to as citrullinated HuPEX, were created by citrullinat-

ing proteins with human peptidyl arginine deiminase 2 for screening RA autoantibodies. [Results] In the initial screening, more than 40 proteins were recognized by RA serum. These proteins were included in a secondary screening, which led to the identification of a candidate protein not previously reported as an RA biomarker. Results from further studies using 29 RA serum samples and 20 osteoarthritis serum samples showed that the ROC-AUC value for antibodies to the candidate protein was statistically significantly higher than that for anti-CCP antibodies. [Conclusion] Using Citrullinated HuPEX, we were able to isolate a novel autoantibody for RA.

P2-021

AI-Based Detection of NPSLE-Specific Brain Atrophy Using SynthSR-Enhanced MRI and BAAD Analysis

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Conflict of interest: None

[Objectives] Head MRI is commonly used to assess NPSLE, yet specific imaging markers remain undefined. Brain atrophy is frequent in NPSLE, though its relationship with symptoms is unclear. This study aimed to convert routine MRI scans to high-resolution 3D-T1-weighted images using the AI technology "SynthSR" and identify NPSLE-specific atrophy patterns via Brain Atrophy Analysis Diagnostic (BAAD). [Methods] Head MRI scans from Shimane University Hospital (January 2005 - December 2023) were analyzed. Subjects were divided into non-NPSLE/SLE (n=67, male=11:56, age=50.9±20.4) and NPSLE groups (n=16, male=2:14, age=47.3±15.1). FLAIR images were converted to 3D-T1-weighted images using SynthSR, and BAAD calculated cranial content, total brain, and local gray matter volumes. Brain atrophy patterns were analyzed via Mann-Whitney U tests. [Results] The NPSLE group exhibited significant atrophy in cranial content, white matter, occipital lobe, and cerebellum, while the SLE group showed significant temporal pole atrophy. [Conclusion] SynthSR allows for the detection of NPSLE-specific brain atrophy patterns via BAAD, even with routine MRI scans. This approach may enhance diagnostic capabilities for NPSLE, a challenging condition. Larger cohort studies are warranted.

P2-022

The Diagnostic Value of Vascular Ultrasound in Giant Cell Arteritis in daily clinical practice: A Single-Center Retrospective Study

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Conflict of interest: None

Objective: To evaluate the diagnostic performance of color Doppler ultrasonography (CDUS) for detecting giant cell arteritis (GCA) in daily clinical practice. **Methods:** This retrospective study included patients suspected of GCA who underwent CDUS from April 1, 2020, to June 30, 2024. Clinical data were collected from electronic medical records. Two certified sonographers (Y.M., E.T.) evaluated the superficial temporal artery, axillary artery, brachial artery, facial artery, common carotid artery, and vertebral artery. Aplio i700 (Canon) with an 18 MHz linear probe was used. The diagnosis of GCA was confirmed by a rheumatologist's clinical judgment after more than six months of follow-up. CDUS results were based on halo sign. **Results:** A total of 108 patients were included. GCA was diagnosed in 37 (34.3%) cases. Temporal artery biopsy was performed in 44 patients (40.7%), with 25 (56.8%) being positive. CDUS detected abnormalities in 41 patients (37.9%). The sensitivity, specificity, positive predictive value, and negative predictive value of CDUS for diagnosing GCA were 91.9% (95% confidence interval, 78.1-98.3), 90.1% (80.8-95.9), 82.9% (67.9-92.8), and 95.5% (87.5-99.1), respectively. **Conclusion:** CDUS provided high diagnostic accuracy for diagnosing GCA in daily clinical practice.

P2-023

A Study of the Rate of Achievement of Steroid-Free Patients with Giant Cell Arteritis (GCA) in Our Hospital

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Conflict of interest: None

[Objectives] to clarify the rate of achievement of steroid-free status and characteristics in gca patients. [Methods] we retrospectively examined the clinical characteristics of patients with gca diagnosed and treated at our hospital from april 2016 to october 2024. [Results] of 40 patients with gca, 32 patients (12 males and 20 females) met the above criteria. the median age at onset was 75.3 years, and crp 11.2 mg/dL. all patients were treated with steroids, 6 (18.8%) with steroid pulse, 18 with tocilizumab (tcz) and 3 with methotrexate. the steroid-free status was 23 patients (71.8%), and the mean time to steroid-free was 503.9 days, compared to 715 days in the steroid group (p=0.136) and 445 days in the tcz group (p=0.136). two deaths were unrelated to the primary disease, and infections were observed in two patients in the tcz group (urinary tract infection and herpes zoster). [Conclusion] the steroid-free status of gca in our hospital was higher in the tcz group, suggesting that the time to completion of steroid treatment can be shortened in this group, although there was no significant difference. there was no significant difference in the risk of complications such as infection.

P2-024

Prognostic Factors Related to Long-Term Outcomes in Giant Cell Arteritis: A Single-Center Retrospective Observational Study

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Conflict of interest: None

[Objectives] To evaluate poor prognostic factors related to the long-term outcomes of giant cell arteritis (GCA). [Methods] Retrospective data extraction was conducted for GCA cases evaluated by Color Doppler Ultrasound (CDUS), contrast-enhanced CT, or PET-CT from April 1, 2012, to June 30, 2024. The association between clinical findings, imaging findings, the onset of cerebral infarction, and prognosis was analyzed. [Results] There were 75 GCA cases included, with a median age of 76 years (70-81), and the follow-up period was 1051 days (560-2406). Cerebral infarction occurred in 5 cases (6.7%) and mortality in 10 cases (13.3%). In imaging findings of large vessels, vertebral artery lesions were significantly associated with the occurrence of cerebral infarction (18.8% vs. 3.6%, P = 0.038). There was no correlation between treatment content and prognosis. The coexistence of myelodysplastic syndromes (MDS) diagnosed after the onset of GCA was reported in five cases (6.7%) and was a significant risk factor for mortality [HR: 0.13 (95% CI: 0.028, 0.63) P = 0.011]. [Conclusion] Vertebral artery lesions identified on imaging in GCA were risk factors for the onset of cerebral infarction. Additionally, GCA cases complicated by MDS during the course were found to have a poor prognosis.

P2-025

Evaluation of the Diagnostic Utility of the Outcome Measures in Rheumatology (OMERACT) Ultrasonography Score for Cranial Giant Cell Arteritis

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Conflict of interest: None

[Objectives] To evaluate the efficacy of the Outcome Measures in Rheumatology (OMERACT) ultrasonography score for giant cell arteritis (GCA) in diagnosing cranial GCA. [Methods] We retrospectively analyzed 55 patients with suspected cranial GCA who underwent temporal artery biopsy (TAB) between April 2010 and August 2024. The OMERACT GCA ultrasonography score (OGUS) was calculated using six cranial sites. We compared OGUS values between GCA and non-GCA groups and performed ROC analysis. [Results] The study included 40 GCA and 15 non-GCA patients. The non-GCA group had a higher proportion of males; however, there were no significant differences between the groups regarding sex, atherosclerosis risk factors, or clinical symptoms such as headache and fever, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or hemoglobin (Hb) levels. Platelet counts were significantly higher in the GCA group (p=0.0036). The OGUS score was significantly elevated in the GCA group (1.52±0.55 vs. 1.20±0.20, p=0.027). ROC curve analysis revealed an AUC of 0.70, with an optimal OGUS cutoff value of 1.35 (sensitivity: 60%, specificity: 87%). [Conclusion] OGUS demonstrated effectiveness in diagnosing cranial GCA and is considered to be a useful non-invasive diagnostic tool.

P2-026

Consideration of optimal treatment for elderly patients with rheumatoid arthritis (RA) based on age-specific analysis of methotrexate (MTX) treatment

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Conflict of interest: None

[Objectives] With the aging population, elderly-onset RA is increasing. MTX is a key drug for RA treatment, but its safety and efficacy in elderly patients are uncertain. This study aims to analyze MTX use in RA patients based on age of onset to determine optimal treatment strategies for elderly patients. [Methods] This retrospective cohort study included 479 RA patients from our database, with 363 (76%) being women. The average patient age was 68.3 ± 16.1 years, disease duration 11.3 ± 10.4 years, and onset age 57.5 ± 17.4 years. Patients were divided into four groups based on age of onset: under 60 years, 60s, 70s, and 80+ years. [Results] The MTX initiation rate was highest in the <60 year old group and decreased significantly with age. There were no significant differences in continuation rates or maintenance doses between age groups. The incidence of MTX-associated lymphoproliferative disorder (MTX-LPD) increased with age, and the proportion of patients requiring chemotherapy for MTX-LPD also increased with age. [Conclusion] While MTX initiation rates decreased with age, continuation rates and doses remained stable across groups. However, the increasing incidence of MTX-LPD in older patients underscores the need for careful monitoring during treatment.

P2-027

Comparison of efficacy and safety of JAK inhibitor baricitinib and IL-6 inhibitor sarilumab using propensity score matching in each phase of the RA treatment algorithm

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Conflict of interest: None

[Objectives] We compared the efficacy and safety of JAK inhibitors and IL-6 inhibitors using propensity scores in the treatment RA. [Methods] We studied two groups (461 cases in total) of patients who met the ACR/EULAR RA classification criteria: 191 cases treated with JAK inhibitor baricitinib and 270 cases treated with IL-6 inhibitor sarilumab. In raw data and propensity score matching data, treatment continuation rates and treatment responses were compared using CDAI. [Results] In a comparison of 168 patients after propensity score matching, the treatment continuation rate at 48 weeks was 75.9% for baricitinib and 77.7% for sarilumab, which was not significantly different (Log-rank, p=0.1765). The CDAI LDA/REM achievement rate at 12 weeks was 82.4% for the baricitinib group and 83.0% for the sarilumab group. The CDAI improvement rate at 4 weeks after the start of treatment contributed to the LDA/REM achievement rate in both groups (p<0.0001, p=0.0178). Herpes zoster was observed in 16 patients only in the baricitinib group (p<0.0001), and malignant tumors was observed in baricitinib group (6 patients) and the sarilumab group (4 patients) (p=0.3312). [Conclusion] These results suggested that treatment selection should take into account risk factors for adverse events.

P2-028

Clinical outcomes of toe arthroplasty for forefoot deformities due to rheumatoid arthritis

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Conflict of interest: None

[Objectives] To investigate the clinical outcomes of toe plasty for forefoot deformity in patients with rheumatoid arthritis (RA). [Methods] Twenty-three patients who underwent surgical treatment between December 2005 and May 2023 and whose radiological evaluation was traceable to the Japanese Society for Surgery of the Foot RA foot and ankle scale (JSSF scale) were included in this study. The mean age at surgery was 59±12 years, and the mean disease duration was 20.6±7.9 years. The Larsen classification of the MTP joint of the big toe was grade 1 in 2 foot, grade 2 in 11 foot, grade 3 in 16 foot, and grade 4 in 1 foot. All patients underwent Mitchell's procedure on the MTP joint of the big toe and shortened oblique osteotomy on the second to fifth toes. [Results] The mean postoperative follow-up was 10.7±5.2 years, and the JSSF scale improved significantly from 57.6 points preoperatively to 72.1 points at the last follow-up. The M1-M2 angle improved from 11.6° preoperatively to 10.8° at the last observation, the M1-M5 angle improved significantly from 29.8° preoperatively to 20.4° at the last observation. [Conclusion] Foot and toe arthroplasty for forefoot deformity in RA patients significantly improved functional prognosis and pain, and the long-term results were favorable.

P2-029

Outcome of joint-preserving surgery for rheumatoid forefoot deformity complicated by severe hallux valgus

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Conflict of interest: None

[Objectives] 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] 28 patients who underwent surgery between 2018 and 2024 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 63.4, which significantly improved to 88.0 points at final follow-up. The preoperative HV angle improved significantly from 54.4degrees to 10.6 degrees, the preoperative M1M2, M1M5 angle improved significantly from 18.2, 35.1degrees to 6.9, 14.7degrees. Hardy classification 5 to 7 was 28 preoperatively and 2 at the time of the study. The recurrence of hallux valgus was 10.7%. [Conclusion] The modified Scarf and offset-osteotomy are useful in RA forefoot deformity associated with severe hallux valgus.

P2-030

A case of pulmonary hypertension with systemic lupus erythematosus improved by belimumab

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Conflict of interest: None

[Case] 51-year-old female [Chief complaint] Dyspnea on exertion [History of current illness] In November of X-1, the patient was diagnosed with SLE. At this time, UCG showed no findings suggestive of PAH. In July of X, the patient presented with dyspnea on exertion, and UCG showed TRPG of 60 mmHg. In November of X, right heart catheterization (RHC) showed high values of mean pulmonary artery pressure (mPAP) of 37 mmHg and pulmonary vascular resistance (PVR) of 5.31 Wood units, and the patient was diagnosed with SLE-PAH. Macitentan was added, but in March of X+1, dyspnea on exertion worsened, and in April of X+1, UCG showed a persistently high TRPG of 52.2 mmHg. In June of X+1, belimumab was introduced to improve SLE disease activity, and dyspnea on exertion gradually improved, and in November of X+1, RHC showed mPAP of 17 mmHg and PVR of 2.3 Wood units. Thereafter, SLE and SLE-PAH activity stabilized, and in May of X+4, RHC showed stable mPAP of 13 mmHg and PVR of 1.26 Wood units. [Discussion/Clinical Significance] SLE-PAH is a disease in which PAH can be expected to improve by suppressing disease activity of SLE. As far as we have searched, there have been no reports of SLE-PAH improving with the administration of belimumab, so we report this case together with a literature review.

P2-031

The potential of early combination of hydroxychloroquine, immunosuppressants, and belimumab for SLE to shorten the duration of glucocorticoid administration and to reduce or discontinue dose: A single-center retrospective study of 169 patients

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Conflict of interest: Yes

[Objectives] The therapeutic goal of SLE is to achieve social remission with GC and concomitant drugs. This requires reduction of GC ≧5 mg/day or even discontinuation, if possible. [Methods] SLE patients who had been treated at our department for at least 1 year as of July 2024 were statistically examined by collecting their status at 5 mg PSL and at the investigation. [Results] 169 cases were included. 90.5% female with a mean age at onset of 37 years, and a mean SLEDAI of 14. The mean disease duration at the study was 14 years. 90% were treated with GC, 89% with HCQ, 70% with IS, and 54% with belimumab, and the duration from GC initiation to each drug initiation strongly correlated with the total GC duration. The daily PSL dose was reduced to 0.9 mg, and 90 were discontinued. The patients receiving IS or BEL was significantly higher than those who discontinued, and the GC dose was reduced to 2.5 mg. HCQ or BEL initiation before PSL5 mg significantly shortened the time to GC discontinuation. After an average of 2 years follow-up, minor flare was observed in 3 cases. [Conclusion] Early concomitant drugs introduction allows shortening the duration of GC administration and reducing the dose to near discontinuation, but follow-up after discontinuation is also important.

P2-032

The association between sleep health status and neuropsychiatric symptoms in systemic lupus erythematosus: From the PLEASURE-J study

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Conflict of interest: None

[Objective] We examined whether sleep health status at diagnosis in systemic lupus erythematosus (SLE) patients affects the development of neuropsychiatric symptoms (NPSLE). [Methods] SLE patients aged 6-40 years, diagnosed within one year of disease onset, were studied from the PLEASURE-J cohort. Patients were divided into sleep disorder and control groups based on Pittsburgh Sleep Quality Index (PSQI) cutoff score (5.5). The primary endpoint was a comparison of the prevalence of NPSLE at the onset of SLE between the two groups. [Results] A total of 167 cases with PSQI scores were analyzed (mean age 27.0±5.8 years, 150 females). The median PSQI score was 8, indicating high sleep disorder prevalence. Components such as "habitual sleep latency" and "sleep efficiency" had high scores. The prevalence of NPSLE at the onset of SLE was not different between the two groups (14 cases in the sleep disorder group (12%) vs 4 cases in the control group (10%), P=0.71). Post-hoc analysis showed PSQI scores significantly associated with NPSLE within one-year post-diagnosis (P=0.01, OR: 1.37 [95% CI 1.07-1.76]). Patients with NPSLE tended to have higher "sleep efficiency" scores. [Conclusion] PSQI score in SLE patients might be a predictive factor for developing NPSLE up to 1 year thereafter.

P2-033

Disease Characteristics and Influencing Factors in Patients with Juvenile-onset and Adult-onset Systemic Lupus Erythematosus; The ANSWER-SLE Cohort Study

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Conflict of interest: Yes

[Objectives] To clarify differences in SLE disease activity and organ damage based on age at diagnosis. [Methods] We assessed organ damages using the Systemic Lupus International Collaborating Clinics Damage Index (SDI) and influencing factors in the ANSWER cohort (n=701). Juvenile-onset SLE (J-SLE) was defined as age <18 years (n=95), and adult-onset SLE (A-SLE) as age ≧18 years (n=606). We applied multivariate linear regression analysis to assess factors influencing SDI and performed 1:2 matching by sex and current age (n=83, n=166, respectively). [Results]

Compared to A-SLE, no difference in SLEDAI was observed, but J-SLE had a higher median SDI (2.2±2.4 vs. 1.2±1.6, p=0.0023), with retinal changes, optic atrophy, neuropathy, angina, avascular necrosis, and reduced GFR being more frequent. Multivariate analysis revealed HCQ had a protective effect on SDI (Est. -0.68, p=0.003), while immunosuppressants (Est. 0.6, p<0.001), cyclophosphamide (CY, Est. 3.0, p=0.008), anti-Sm, dsDNA antibodies (Est. 0.83, p<0.001), and glucocorticoids (GC, Est. 0.05, p=0.001) had detrimental effects. [Conclusion] Although several biases cannot be excluded, J-SLE presented with multiple organ damages. HCQ had a protective association, while CY and GC had worsening associations with SDI.

P2-034

Temporal Changes in Health-Related Quality of Life in Patients with Systemic Lupus Erythematosus: A Five-year Prospective Study

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Conflict of interest: None

[Objectives] The relationship between HRQoL and disease activity and organ damage in patients with SLE is controversial. We investigated the temporal relationship between SF-36 and SDI or dose of glucocorticoids (GCs). [Methods] From a prospective cohort of Japanese patients with SLE, we extracted cases that completed the SF-36 at a certain point (baseline) and 5 years later. The temporal relationship between SF-36 and SDI or GC dose was analyzed longitudinally using univariate analysis. [Results] 70 patients with SLE were analyzed. At baseline, 66 patients were women, the average age was 43 years, the average disease duration was 13 years, and the average prednisolone-equivalent GC dosage was 10 mg/day. No statistically significant relationship was observed between the increase in SDI and the decrease in the SF-36 physical component summary (PCS) or mental component summary (MCS) scores. The PCS scores tended to increase more in patients with decreased GC dose than in those with non-decreased GC dose (3.7 vs. -1.6 $p = 0.095$). The increase in PCS scores was correlated with a decrease in GC dosage ($r = 0.58$). [Conclusion] This study suggested that a quiescent disease course indicated by a reduction in GC dosage was associated with improvement in PCS scores among patients with SLE.

P2-035

Association of SLE disease activity index (SLEDAI-2K/ SLE-DAS), Physician General Assessment (PGA) and glucocorticoids use in daily practice: The ANSWER-SLE cohort study

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Conflict of interest: None

[Objective] Simple measures of SLE disease activity in routine practice include the SLEDAI-2K, SLE-DAS and PGA (0-3 scale), and to determine how relevant these activity measures are to adjusting glucocorticoid use (PSL equivalent) at each visit. [Methods] Patients enrolled in the ANSWER-SLE cohort, with SLEDAI-2K, SLE-DAS, PGA and PSL doses all assessable on at least two visits back to the last observation date, were included and the correlation between each disease activity index and PSL dose was The correlation between each disease activity index and PSL dose was evaluated. The predictive accuracy of PSL dose for each indicator was compared using a generalised linear mixed model. The prediction accuracy was assessed by calculating the root mean square error (RMSE). [Results] Mean SLEDAI-2K, SLEDAS, PGA and PSL doses were 3.7, 3.2, 0.4 cm3 and 5.5 mg/mL, respectively. PSL dose did not correlate with SLEDAI-2K, SLE-DAS or PGA. The predictive accuracy (RMSE) of each measure for PSL dose was 0.89, for SLEDAI-2K and 0.89 for PGA, and none of the individual measures per examination differed in relation to PSL dose. [Conclusion] It has been shown that individual indices of disease activity are not directly related to the adjustment of the dose of GC per visit in routine SLE practice.

P2-036

Analysis of Decision Regret Scale (DRS) in SLE Patients Attending Our Facility

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Conflict of interest: None

[Objectives] While remission maintenance and reduction of steroids are validated for improving SLE prognosis, these do not always align with patients' subjective evaluations. The Decision Regret Scale (DRS), a Patient-Reported Outcome (PRO), evaluates treatment regret and is associated with Shared Decision Making (SDM). This study aimed to analyze SLE treatment evaluations using DRS. [Methods] From July to September 2024, we distributed DRS questionnaires to SLE patients undergoing 1) steroid reduction or 2) biological agent introduction. DRS scores (0-100, with higher scores indicating stronger regret) were analyzed in relation to age, disease duration, DORIS remission, steroid dose, and SDI. [Results] Among SLE patients, 132 had ongoing steroid use, and 35 had biological agents. DRS scores for criteria 1 and 2 were positive (0-25) in 61% and 57%, regretful (50-100) in 10% and 3%. Except for correlations between criterion 1's DRS with age or SDI, no significant associations were found. [Conclusion] Approximately 10-40% of patients may need QOL assessment and SDM reassessment. DRS is a practical measure for evaluating treatment interventions in SLE patients; its assessment and improvement over time may enhance care quality. Further analysis on the DRS-Lupus-PRO relationship is ongoing.

P2-037

Efficacy of plasma phosphoethanolamine as a novel biomarker for rheumatoid arthritis-associated depression

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Conflict of interest: Yes

[Objectives] Plasma PEA has been reported to be a useful diagnostic biomarker for depression. We examined the efficacy of PEA as a biomarker for RA-associated depression. [Methods] This study included 123 registered RA patients. The psychiatrist conducted a structured interview, and the psychiatrist's diagnosis was defined as the Gold Standard. These questionnaire items were converted into Scales A and B. [Results] This included 11 patients with depression. The patients were divided into two groups according to the presence or absence of depression. No significant difference was found between the groups regarding plasma PEA. The Scale A score and the ratio of Scale A score to PEA were significantly lower among patients with depression. The Scale B score was significantly high. The ROC curve produced the following cutoff values. A score of 1.36 or more on the PEA, 6.479 or more on the Scale A to PEA ratio, and 1 or more on Scale B was considered a cutoff. The serum PEA had a specificity of 81.8%, a sensitivity of 40.7%, and the AUC was 0.565. The Scale A had

81.8%, 85.2%, and 0.913. Scale B had 27.3%, 22.2%, and 0.801. [Conclusion] Plasma PEA alone presents a weak performance as a diagnostic biomarker for depression in patients with RA. However, a composite measure may be used as it.

P2-038

Efficacy of HIF-PH inhibitors for patients with renal anemia complicated by rheumatoid arthritis

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Conflict of interest: None

[Objectives] HIF-PH inhibitors have recently appeared as a treatment for renal anemia. Some anemias associated with rheumatoid arthritis have reduced iron availability due to chronic inflammation. [Methods] HIF-PH inhibitor daprodustat was started for 9 cases (1 male, 8 female, mean age 81.3±5.6 years, morbidity period 15.1±13.9 years) that could be diagnosed with chronic kidney disease and renal anemia among rheumatoid arthritis cases, and anemia and iron dynamics, mean blood cell volume (MCV), mean corpuscular hemoglobin amount (MCH), with an average observation period of 11.2±6.4 months, DAS CRP28 was examined retrospectively. [Results] In all cases, daprodustat was continued, and the dose at the end of the observation period was 4.7±1.4 mg. Hb before and after the start was significantly increased → 9.7±1.0 g/dL to 11.4±0.8 g/dL ($p<0.01$). An improvement in iron utilization were observed, but not significant. DAS CRP28 showed an improvement but not significant. [Conclusion] For renal anemia complicated by rheumatoid arthritis, daprodustat was shown to significantly improve anemia. It has been suggested that there is a possibility of improving iron utilization due to chronic inflammation, but more cases need to be examined.

P2-039

A retrospective study of 15 cases of hemophagocytic syndrome in a single center

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Conflict of interest: None

[Objectives] To investigate the clinical outcomes of autoimmune-associated hemophagocytic syndrome (AAHS). [Methods] We extracted data on hospitalized patients diagnosed with HPS from January 2015 to October 2024. [Results] Two patients were excluded (virus and malignancy-associated HPS) and 13 were analysed. The cohort included 2 men and 11 women, with a median age of 50 years (interquartile range [IQR] 31-74). The median duration of hospital stay was 22 days (IQR 10-33), and the median follow-up period from admission was 46.7 months (IQR 14.3-77.9). The underlying autoimmune diseases included adult-onset Still's disease in 7 patients, systemic lupus erythematosus in 4, Sjögren's syndrome in 1, and mixed connective tissue disease in 1. Ten patients experienced HPS at the initial onset of autoimmune disease. Treatments included glucocorticoids for 12 patients, calcineurin inhibitors for 6, tocilizumab for 5, etoposide for 4, methotrexate for 4, cyclophosphamide for 2, and ruxolitinib for 2. Three patients (23%) died during hospitalization, including 2 with celebral involvement (cerebral infarction) and 1 with cardiac involvement (arrhythmia). [Conclusion] Patients with AAHS who have celebral or cardiac involvement show a poor prognosis, and treatment strategies need to be improved.

P2-040

Association Between Cardiovascular Risk Assessment and 10-Year Cardiovascular Disease Incidence in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] This study aimed to assess the utility of cardiovascular risk assessment methods in Japanese rheumatoid arthritis (RA) patients, according to the 2015/2016 EULAR recommendations for cardiovascular disease (CVD) risk management. [Methods] Hisayama-cho score (HS) was used for calculating the 10-year atherosclerosis risk in RA patients at Saitama Medical University Hospital, who received carotid ultrasound (US) from 2006-2009 and a follow-up US three years later. We analyzed associations between CVD incidence over 10 years and carotid plaque score (CPS) or HS. [Results] Over 10 years, five CVD events were observed in 87 RA patients (average 59 yo and 72% female), with an incidence rate of 4.3 per 1,000 person-years. Compared to RA patients without CVD, those who developed CVD had higher initial (4.3±5.2 vs. 1.4±2.2, P=0.013) and follow-up (4.9±3.4 vs. 2.5±3.0, P=0.038) CPS and greater RA disease activity (DAS28-ESR: 6.1±1.2 vs. 4.2±1.4, P=0.005). Conversely, HS was lower in CVD cases (0±0 vs. 3±2, P=0.014). [Conclusion] In Japanese RA patients, CPS by US and RA disease activity were associated with CVD development over 10 years, suggesting their potential usefulness in assessing cardiovascular risk.

P2-041

A Retrospective Study on the Effectiveness of Baricitinib in Patients with Rheumatoid Arthritis Complicated by Interstitial Lung Disease

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Conflict of interest: None

[Objectives] Interstitial lung disease (ILD) is commonly associated with RA, and patients have a low survival rate similar to idiopathic pulmonary fibrosis. In this study, we retrospectively evaluated the efficacy of BAR, a promising medication for RA-ILD. [Methods] We enrolled 64 RA patients treated with BAR from Jan 2018 to May 2023. We focused on those with ILD confirmed by chest CT who continued BAR for 52 weeks, assessing DAS28-CRP, prednisolone (PSL) dosage, KL-6, and chest CT changes retrospectively over this period. [Results] Ten patients met the inclusion criteria, with a median age of 69.5 (59.8-76.3) years. All patients tested positive for RF and ACPA, with RF at 229.0 (73.3-343.3) IU/L and ACPA at 184.4 (38.8-504.7) U/mL. The baseline DAS28-CRP was 3.7 (2.9-4.6), PSL dosage was 2.0 (0.8-5.0) mg, and KL-6 was 456.0 (349.3-618.8) U/mL. At 52 weeks, DAS28-CRP significantly improved to 2.7 (2.5-3.1), $p < 0.05$. The PSL dosage was 0.5 (0.0-1.9) mg, $p = 0.058$. KL-6 was 487.5 (383.2-760.0) U/mL, $p = 0.296$. CT findings showed improvement in 2 patients, stability in 7, and gradual worsening in 1. [Conclusion] BAR administration in RA-ILD patients improved RA disease activity and reduced PSL dosage. This study suggests the potential effectiveness of BAR in managing RA-ILD.

P2-042

Effects of JAK inhibitors in acute exacerbation of interstitial lung disease associated with rheumatoid arthritis

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Conflict of interest: None

[Objective] Acute exacerbations of RA-ILD have a poor prognosis, with limited treatment evidence. This study compared acute exacervation in RA-ILD cases treated with and without JAK inhibitors (JAKi) to assess their efficacy. [Methods] Five RA-ILD cases treated with JAKi from Feb to July 2024 were enrolled. Six cases from Dec 2015 to Jan 2021 served as historical controls. [Results] JAKi-treated patients had a median age of 79 [72-85] years, with 4/5 male and disease duration of 21 [10-34] years. All were RF and anti-CCP. positive, RA-ILD with UIP pattern. Their P/F ratio

was 228 [80-319], and all required oxygen therapy. Three patients used upadacitinib (1 at 15 mg, 2 at 7.5 mg), and two used baricitinib (2 mg). Initial PSL dose and patient background were similar between groups, but the PSL dose after four weeks was lower in the JAKi group (12.5 mg vs. 27 mg). In the non-JAKi group, two deaths occurred due to RA-ILD-related respiratory failure. [Discussion] JAKi may reduce respiratory failure risk and allow early PSL reduction in RA-ILD acute exacerbations. Multicenter validation is needed.

P2-043

Evaluation of changes in spinal balance, bone mineral density, and bone metabolism markers over 3 years in 25 patients over 70 years old at the start of treatment among those who had received continuous treatment with upadacitinib for 3 years

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Conflict of interest: None

[Objective] We investigated the relationship between UPA and spinal balance and osteoporosis in 25 patients over 70 years of age at the start of treatment with upasitinib (UPA) over a 3-year period. [Methods] We investigated the relationship between UPA and spinal balance and osteoporosis based on changes in patient background, SVA, bone mineral density, and bone metabolism markers during the first 3 years after treatment in 25 RA patients over 70 years old who started UPA treatment. The mean age of patients at the start of treatment was 74.8 years, DAS28CRP: 3.8, CDAI: 5.3, SDAI: 7.2, SVA SVA: 49.3 mm, femoral neck YAM value: 81.1%, urinary NTX: 57.4nM BCE/mM/Cre. [Results] Disease activity after 3 years of treatment with UPA improved to remission to low disease activity with mean DAS28ESR: 2.4, CDAI: 3.1, SDAI: 3.2, mean SVA: 66.1 mm, YAM value: 77.3%, urinary NTX: 37.1 nM BCE/mM/Cre and the mean YAM and urinary NTX values improved in patients without osteoporosis drugs. [Conclusion] In patients whose disease activity was controlled by UPA, bone mineral density and bone metabolism markers improved on average, even in patients who were not treated with osteoporosis drugs, suggesting that UPA has an effect on osteoclasts in the bone marrow.

P2-044

Evaluating the Effectiveness of JAK Inhibitors in Late-Onset RA

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Conflict of interest: None

[Objective] With an aging society and increasing life expectancy, the number of late-onset rheumatoid arthritis (RA) patients is rising. This study aimed to evaluate the efficacy of JAK inhibitors (JAKi) in late-onset RA patients. [Methods] This study included 284 RA patients aged 65 or older who received JAKi treatment for over 24 weeks. late-onset RA (L group: 105 cases) was defined as RA onset at 65 or older. The two groups' backgrounds were adjusted using inverse probability of treatment weighting (IPTW) to assess late-onset RA characteristics. Disease activity (SDAI), continuation rates, and herpes zoster incidence were compared. [Results] The L group had a higher average age, shorter disease duration, lower RF positivity, lower prior b/tsDMARDs usage, and higher CRP than the Y group. After IPTW adjustment, significant differences disappeared except for disease duration and RF positivity. Mean SDAI improved from baseline (19.5±13.3 in L group / 18.5±12.4 in Y group) to 8.7±9.6 / 9.9±11.2 at 24 weeks. At 24 weeks, remission rates were 36.8% (L group) and 43.1% (Y group), and continuation rates were 75.4% (L group) and 82.9% (Y group, p=0.3). [Conclusion] After IPTW adjustment, the efficacy of JAK inhibitors showed no notable difference between late-onset and young-onset RA.

P2-045

Prednisolone tapering in patients with systemic lupus erythematosus: effects of metformin and SGLT2 inhibitors

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Conflict of interest: None

[Objectives] To compare the efficacy of the prednisone (PSL) sparing effect between metformin (Met) and SGLT2 inhibitors (SGLT2i) in patients with SLE treated with low-dose PSL. [Method] SLE patients with HbA1c<6.5% who were treated with hydroxychloroquine and had anti-dsDNA antibodies measured using the TriNetX Global Collaborative Network were selected. This study included patients prescribed MT or SGLT2i for the first time and taking 10 mg or less of PSL equivalent daily and compared the rate of discontinuation of PSL at 1 year and whether there was a difference in relapse (taking 20 mg or more of PSL equivalent) after 3 months of discontinuation of PSL. [Results] 835 in the MT group (89.3% female), with an average age of 57 years. 236 in the SGLT2i group (78.8% female), with an average age of 57 years. At after 1 year, significantly higher number of patients discontinuing in the SGLT2i group (236/835 vs. 172/236, p<0.005). The relapse rate was identical for both groups [risk difference 1.639% (95%CI-5.545-8.824)]. In the Kaplan-Meier analysis, there was also no significant difference in the rate of recurrence-free survival after discontinuation of PSL. [Conclusion] Initiation of SGLT2i may be useful to gradually reduce or discontinue PSL without increasing relapse rates.

P2-046

A Comparative Study of Bile Acid Loading Test and Protein Leakage Scintigraphy in Patients with Systemic Lupus Erythematosus with Hypoalbuminemia

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Conflict of interest: None

[Objective] Protein-losing gastroenteropathy and malabsorption syndrome are known to be gastrointestinal lesions that cause hypoalbuminemia in systemic lupus erythematosus (SLE). We investigated the incidence of protein-losing gastrointestinal disease and malabsorption syndrome in patients with active SLE. [Methods] Active SLE who were admitted to our department between May and October 2024 and had a serum albumin level of <3.5 g/dL were enrolled. We performed the bile acid loading test and protein leakage scintigraphy before starting remission induction therapy and compared the positive rates of these tests. [Results] Of 12 patients, 11 of whom were female (91.6%), with an average albumin level of 2.58 g/dL, an average SLEDAI of 18.25, and 8 cases (66.7%) with lupus nephritis. 10 patients (83.3%) were positive for bile acid loading test, and 11 cases (91.6%) were positive for protein leakage scintigraphy. 9 cases (75%) were positive for both tests. 3 cases (25%) who had enteritis symptoms were positive for both tests. Even though in the remaining 9 cases without enteritis symptoms, 8 cases (89%) were positive for either of the tests. [Conclusion] We demonstrated the positive rate of protein-leakage scintigraphy and bile acid load test in active SLE patients with hypoalbuminemia.

P2-047

Efficacy and safety of avacopan in antineutrophil cytoplasmic autoantibody-associated vasculitis: A retrospective cohort study in Japan

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Conflict of interest: None

Objectives: This study aimed to assess the real-world experiences and outcomes of avacopan treatment for antineutrophil cytoplasmic autoantibody-associated vasculitis in Japan. **Methods:** We performed a single-centre retrospective analysis of 21 patients with newly diagnosed or relapsed autoantibody-associated vasculitis who received avacopan. The co-primary outcome was clinical remission at 6 and 12 months. **Results:** Of 21 patients, 20 (95.2%) achieved clinical remission at 6 months, and 19 (90.4%) at 12 months. However, 10 (47.6%) patients had adverse events due to avacopan; the most common being elevated liver enzymes in 8 (38.1%) patients, and 9 (42.9%) stopped avacopan. Meanwhile, patients who discontinued avacopan still achieved similar rates of clinical remission at 6 months, maintained remission at 12 months, and had reduced glucocorticoid doses, compared to those who continued avacopan. **Conclusions:** A high frequency of adverse events associated with avacopan, especially liver enzyme elevation, and a high number of early discontinuations were observed. Meanwhile, regardless of the early discontinuation of avacopan, good outcomes and glucocorticoid dose reduction were observed.

P2-048

Continuation Rates of Avacopan for Microscopic Polyangiitis in Our Hospital

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Conflict of interest: None

Avacopan, a complement C5a receptor inhibitor, was launched in June 2022 in Japan to treat ANCA-related vasculitis. Only a few literature reports exist in Japan. We conducted the present study to identify the continuation rate of Avacopan. We conducted a retrospective observational study of microscopic polyangiitis using Avacopan at one institution, Showa University Northern Yokohama Hospital, from June 7, 2022, to September 30, 2024. The median age of the patients was 81 years, and 6 were women. Eleven patients received it for remission induction therapy and one for relapse. Twelve patients were MPO-ANCA positive, and one was ANCA negative. All patients received glucocorticoids, and the median prednisolone dose was 43 mg. Nine patients underwent steroid pulses, and seven were RTX. Six months after initiation, 38.5% (5 patients) continued Avacopan. The reasons for discontinuation in the seven patients included hepatic failure and thrombocytopenia in 4 patients each, with one overlapping reason. All patients who discontinued due to side effects improved to normal within a median time of 10 weeks. The continuation rate six months after initiation of Avacopan was 38.5%, but in all cases where side effects occurred, they were reversible and improved after discontinuation.

P2-049

Investigation of the effect of introducing abacopan on improving renal function in patients with persistently low disease activity AAV in the remission maintenance phase

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Conflict of interest: None

Objective: The ADVOCATE trial in AAV patients showed that the C5a receptor inhibitor abacopan was effective for sustained remission at 52 weeks with prednisone tapering and had positive effects on renal function. However, its efficacy alone in low disease activity during remission maintenance is unclear. This study evaluates abacopan's efficacy and safety in remission maintenance. **Methods:** Eight AAV patients in the remission phase on abacopan 60 mg/day at our hospital were observed for over 12 weeks. Changes in renal function (eGFR), proteinuria (UPCR), CRP, and prednisone dose were compared to baseline. **Results:** The group included one male and seven females, median age 82 years. One had PR3-MPA, seven had MPO-MPA; four used rituximab for induction. At 12 weeks, eGFR increased by 8.4% (39.2 to 42.5 mL/min/1.73 m^2), CRP improved by 30% (0.8 to 0.5 mg/dL), ANCA levels dropped from 17.4 to 8.5, and prednisone was reduced from 7 mg to 4 mg. Two cases showed liver dysfunction, improving with dose adjustment. **Conclusion:** Although limited by sample size, abacopan may be a viable treatment for elderly AAV patients with residual activity during remission maintenance.

P2-050

Three cases of hypophosphatasia

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Conflict of interest: None

[Case 1] 58-year-old female [Chief complaint] Joint pain in the fingers [History of current illness] Diagnosed with seronegative RA or PsA without rash. After the addition of denosumab, ALP (IFCC) was 20 U/L, and urinary PEA 115.7 nmol/ng, suggesting hypophosphatase, and the p. Phe327Leu variant was detected in the ALPL gene. [Case 2] 51-year-old female [Chief complaint] Joint pain in the fingers, hand, and elbow [History of current illness] Hypophosphatasia was suspected. ALP (IFCC) was 14 U/L, and urinary PEA was 90.5 nmol/ng, suggesting hypophosphatase, and the p. Leu520ArgfsTer86 variant was detected in the ALPL gene. [Case 3] 49-year-old female [Chief complaint] Headache, dizziness [History of current illness] She was referred due to suspected aftereffects of COVID-19. ALP (IFCC) was 14 U/L and urinary PEA of 112.1 nmol/ng, suggesting hypophosphatase, and hetero large deletion was observed in the ALPL gene. [Discussion] Hypophosphatasia is a hereditary metabolic disease caused by a mutation in the ALPL gene, which reduces the activity of tissue-nonspecific alkaline phosphatase. ALP (IFCC) value was below 20 U/L and her urinary PEA was high, suggesting hypophosphatasia, and genetic testing led to the diagnosis.

P2-051

Clinical characteristics and prognosis of elderly-onset rheumatoid arthritis

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Conflict of interest: None

Objective: To evaluate the clinical characteristics and prognosis of elderly-onset rheumatoid arthritis patients at our Rheumatology Center. Methods: We assined 141 patients who were diagnosed as rheumatoid arthritis by the 2010 ACR/EULAR classification criteria and divided into two groups: older than 65 years old (older group) and younger than 65 years old (younger group). Results: There were 74 patients in the older group and 67 patients in the younger group. The median age was 73.5 years in the elderly group and 55.0 years in the younger group. Compared to the younger group, the older group had a shorter time from onset to diagnosis, higher swelling and tender joints, higher CRP and erythrocyte sedimentation rate, more rheumatoid factor and anti-CCP antibody negative cases, higher DAS28CRP, DAS28ESR, SDAI and CDAI, HAQ. Disease activity after one year of treatment and bone destruction after one year were also comparable. Conclusion: Although most elderly-onset rheumatoid arthritis patients are seronegative, and high disease activity at the onset of disease with high-HAQ, appropriate treatment may be expected to control disease activity, improve ADL, and inhibit bone destruction.

P2-052

Trends in treatment for patients with late-onset rheumatoid arthritis in our department

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Conflict of interest: None

[Objective] Our objective was to investigate trends in the treatment of patients with late-onset rheumatoid arthritis (LORA) in our department. [Methods] Patients were divided into the disease onset: at <65 years (young-onset RA: YORA) and the disease onset: ≧75 years (LORA). Additionally, YORA was further subdivided into those currently <65 years (y-YORA) and ≧65 years (e-YORA). Chronological changes in treatment and disease activity were compared. [Results] A total of 348 patients were evaluated. There were significantly fewer females in the LORA group. The usage rate and dosage of methotrexate (MTX) were significantly lower in the LORA group. The usage rate of biologics (Bio) was significantly lower in the e-YORA and LORA groups, with tumor necrosis factor-α inhibitors being significantly less used. However, there was no significant difference in usage rate of Janus kinase inhibitor among the groups. The usage rate of glucocorticoids (GCs) was significantly higher in the e-YORA and LORA groups, although there was no significant difference in dosage among the groups. There was no significant difference in DAS28-ESR among the groups. [Conclusions] In treating LORA, it is necessary to consider the balance between treatment efficacy and risks.

P2-053

The Actual Condition of Elderly Rheumatoid Arthritis in a Very Elderly Community

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Conflict of interest: None

[Objectives] We would like to investigate future issues by looking at the characteristics of elderly rheumatoid arthritis (RA) patients who visit our hospital. [Results] If we define the elderly as those 65 years of age or older, 71.6% of all RA patients attending our hospital are elderly. The percentage of patients aged 75 years or older is as high as 41.6%, and this percentage is increasing. Those aged 85 and over are considered very elderly, accounting for 7.7% of the population, but this number has more than tripled over the past 10 years. The mortality rate within 5 years for very elderly patients is 55% and the most common causes of death are infections and cancer. With aging, renal function declines significantly, and the use of methotrexate and the percentage of patients who use it decrease. Inflammatory responses were not significantly different between the non-elderly and the late elderly. In recent years the number of very elderly people using biologics/JAK inhibitors has gradually increased and there is no significant difference between generations. [Conclusion] Though various complications emerge with aging, it is important to reduce disease activity and prevent deterioration of quality of life by effectively using easy-to-use drugs, even in very elderly patients.

P2-054

Association between rheumatoid arthritis and healthy life expectancy: An historical cohort study using KDB

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Conflict of interest: None

[Objectives] In an ageing society, extending healthy life expectancy (HALE) is crucial. While rheumatoid arthritis (RA) affects life expectancy and QOL, its impact on HALE remains unclear. This study aimed to investigate the effect of RA on HALE. [Methods] This study included individuals from Hakui City, using data from the National Health Insurance Database (KDB) between 2012 and 2022. RA and non-RA groups were compared using propensity score matching. The primary endpoint was the occurrence of an unhealthy state or death. The secondary endpoint was the annual medical cost. [Results] Propensity scores were calculated for 5,295 of which 56 were selected for the RA group and 224 for the non-RA group. The mean age was 70.1 years and the mean follow-up was 6.3 years. In the RA group, all patients received antirheumatics with 5.7% on biologics. The primary endpoint was reached by 10 patients (17.9%) in the RA group and 23 patients (10.3%) in the non-RA group ($p = 0.12$). The median annual medical costs were 482,000 yen in the RA group and 151,000 yen in the non-RA group ($p < 0.01$). [Conclusion] HALE was comparable between RA and non-RA groups, suggesting the effectiveness of RA treatments. However, the higher medical costs of RA patients highlight the need to address the economic burden.

P2-055

Examination of Risk Factors for Reduced Healthy Life Expectancy in RA Patients

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Conflict of interest: None

Objective: This study identifies risk factors for shortened healthy life expectancy in RA patients, comparing those initially “healthy” but “unhealthy” after one year (deterioration group) to those with maintained/improved health, focusing on pain. Methods: mHAQ, joint pain site, and foot health questionnaires were conducted on 131 RA outpatients and repeated after one year. Patients transitioning from “healthy” to “unhealthy” were the deterioration group; others were the maintained/improved group. Groups were compared, and health deterioration risk factors evaluated via multivariate analysis. Results: Mean age was 65.0 years, with 100 females (76.3%). Initially, 81 patients (61.8%) were healthy. The deterioration vs. maintained/improved groups had 22 patients (16.2%) vs. 109 patients (83.2%), mean ages of 69.5 vs. 64.1 years, 19 females (86.3%) vs. 81 females (74.3%). Univariate analysis showed significant factors: age (69.5 vs. 64.1), initial lower limb pain (22.7% vs. 49.5%), and lower limb pain onset after one year (27.3% vs. 7.34%). Multivariate analysis indicated older age and lower limb pain onset as significant risk factors. Conclusion: Lower limb pain onset significantly impacts health deterioration, requiring prompt diagnosis and treatment.

P2-056

Association between dietary tomato intake and blood eosinophil count in middle-aged and elderly Japanese

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Conflict of interest: None

[Objectives] We explored the association between dietary tomato intake and blood eosinophil counts in Japanese adults. [Methods] This population-based, cross-sectional study included 1,013 participants aged 40 years and older. The dietary tomato intake was assessed using a brief-type self-administered dietary history questionnaire. The peripheral blood eosinophil count was measured, and an elevated blood eosinophil count was defined as a value that exceeded the ≧75th percentile. [Results] The mean age of the participants was 62.5 ± 11.2 years, with 474 (46.8%) being male. 252 participants exhibited elevated blood eosinophil counts. In the multivariable logistic regression model with adjustment for potential confounding factors, a 10 g increase in tomato intake was inversely associated with an elevated blood eosinophil count (odds ratio, 0.895; 95% confidence interval, 0.834-0.961). Except for chronic kidney disease, the baseline participant characteristics did not influence this association. [Conclusion] Low dietary tomato intake was associated with an elevated blood eosinophil count in middle-aged and elderly Japanese. These results warrant further investigation through longitudinal studies.

P2-057

Ultrasound Findings in Polymyalgia Rheumatica Associated with Giant Cell Arteritis

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Conflict of interest: None

[Objectives] Giant cell arteritis (GCA) can complicate polymyalgia rheumatica (PMR). However, MSUS findings specific to PMR associated with GCA have not been reported. [Methods] We retrospectively reviewed 20 patients diagnosed with GCA who underwent MSUS between 2016 and 2024 (GCA-PMR group) and compared them with 20 age- and sex-matched patients with PMR without GCA (PMR-only group). Patient demographics and MSUS findings. MSUS findings were semi-quantitatively assessed on a scale of 0-3 using gray scale and power Doppler methods. [Results] The GCA-PMR group consisted of 4 males and 16 females, with a mean age of 77 years. The median CRP level before treatment was 8.5 mg/dL in the GCA-PMR group and 6.4 mg/dL in the PMR-only group. The median duration from symptom onset to diagnosis were 90 and 132 days in the GCA-PMR and PMR-only groups, respectively. MSUS analysis revealed that both the total GS and PD scores for the shoulder and knee joints were significantly higher in the PMR-only group than in the GCA-PMR group. Additionally, MSUS findings were detected in some patients with GCA who did not fulfill the 2012 PMR classification criteria. [Conclusion] The degree of arthritis in GCA-associated PMR appeared to be less pronounced than that in isolated PMR.

P2-058

Ultrasound Findings in Six Cases of Immune-Related Adverse Event-Associated Arthritis

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Conflict of interest: None

[Objectives] Immune checkpoint inhibitors (ICIs) have become a central treatment modality for malignancies; however, immune-related adverse events (irAEs) are also frequently observed. The clinical features of irAE-associated arthritis remain poorly understood; therefore, we investigated the findings of irAE-associated arthritis using musculoskeletal ultrasound (MSUS). [Methods] We retrospectively reviewed six cases of irAE-associated arthritis diagnosed in our department. Patient background and MSUS findings were analyzed in detail. [Results] Three patients were male and three were female, with a mean age of 72 years. Malignancies include lung cancer, hepatocellular carcinoma, malignant melanoma, and breast cancer. The ICIs administered were pembrolizumab, nivolumab, and atezolizumab. Additionally, three patients received ipilimumab and one received bevacizumab in combination. The median duration from the onset of arthritis to irAE diagnosis was 39 days. MSUS did not reveal synovitis typical of rheumatoid arthritis (RA). Instead, the findings predominantly included tenosynovitis, ligamentitis, and enthesitis of large joints. [Conclusion] MSUS has proven useful for understanding the pathophysiology of irAE-associated arthritis.

P2-059

Do Bone Erosions Occur in Polymyalgia Rheumatica? Investigation Using Hand CT

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Conflict of interest: None

[Objectives] While it is commonly stated that bone erosions are rarely observed in polymyalgia rheumatica (PMR) outside the sternoclavicular junction, there are no reports assessing bone lesions using CT imaging. This study aimed to evaluate the frequency of bone erosions in rheumatoid arthritis (RA) and PMR through hand CT and assess its utility in distinguishing these conditions. [Methods] This retrospective cohort study included 44 RA patients and 29 PMR patients who underwent hand CT at our hospital from January 2018 to September 2024. The presence of bone erosions was the dependent variable, while sex, age, disease duration, and CRP levels were independent variables in logistic regression analysis. [Results] Bone erosions were identified in 33 (75%) RA cases and 13 (45%) PMR cases. A significant association was found between PMR and the presence of bone erosions (odds ratio 0.28, 95% CI 0.088-0.82, p= 0.013), with sex and age not being significant factors. After adjusting for CRP and disease duration, PMR remained significantly associated with bone erosions (odds ratio 0.17, 95% CI 0.049-0.61, p=0.0062). [Conclusion] Although the frequency of bone erosions in PMR is lower than in RA, their presence can occur. Hand CT is a valuable diagnostic tool for assessing bone erosions in PMR.

P2-060

Evaluation of the utility of CT in diagnosing Axial Spondyloarthritis

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Conflict of interest: None

ESSR recommends MRI for imaging assessment of axial spondyloarthritis (Axial SpA). However, repeated MRI sessions can be a burden in clinical practice, highlighting the need for a diagnostic imaging method feasible in a single session. [Objectives] To evaluate the utility of CT in diagnosing Axial SpA. [Methods] We examined cases diagnosed with Axial SpA at our hospital from April 2018 to October 2024, comparing clinical features and positive rates of imaging findings. Positive findings on CT and X-ray included anterior longitudinal ligament ossification, sacroiliac joint (SI) erosion, and joint space narrowing. MRI findings were evaluated using ESSR criteria. [Results] The study included 41 cases, with 5 HLA-B27-positive cases (12.8%) and 20 male patients (48.7%). Median age at diagnosis was 59 years (interquartile range: 49-71), and median time to diagnosis was 16.5 years (2.0-29.2). Positive rates were as follows: SI: X-ray 55.6%, CT 85%, MRI 63.4%; cervical spine: X-ray 28%, CT 62.5%, MRI 46.7%; thoracic spine: X-ray 38.9%, CT 94.6%, MRI 40%; lumbar spine: X-ray 36.4%, CT 73.7%, MRI 42.3%. [Conclusion] In diagnosing Axial SpA, CT showed high sensitivity in both the sacroiliac joint and spine and was particularly useful for screening cases with a longer disease duration.

P2-061

A case report: severe nuchial tenderness of Sternoclavicular arthritis in patient with PAO

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Conflict of interest: None

46 years old, male [chief complaint] nuchialgia, left shoulder arthralgia [present medical history] He came to appeal to the left neck, glenohumeral joint for pain for the left sternoclavicular joint swelling pain though he was followed up by NSAIDs prescription. The improvement of the symptom is not seen; is swelling, pain to our hospital introduction consultation. [test result] The swelling and tenderness was observed left sternoclavicular joint in X+4 month. There is the bone thickening of the left sternoclavicular joint in X-P. There is T2-empasised MRI high intensity area spilling over into sternocleidomastoid muscle. [Progression] Three steroid injections were performed under ultrasound guidance, resulting in relief. During follow-up, the swelling gradually decreased but did not disappear. Treatment was completed with the goal of releasing the restriction of neck movement. [Discussion] It is very rare to complain of non-continuous neck pain accompanied by restricted rotation. After detailed examination, it was presumed that inflammation in the sternoclavicular joint had spread to the sternocleidomastoid muscle, causing the symptoms. Ini-

tially, crystal-induced arthritis was suspected, but no obvious crystals were found in the aspirated sample.

P2-062

Overestimation and underestimation of renal function in outpatient of our department

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Conflict of interest: None

[Objectives] We evaluated the renal function of outpatients at our department. [Methods] Among patients who were visiting the hospital every 3 months, 100 consecutive patients were included from Sep 11, 2024. We evaluated the magnitude of discrepancy, CKD determination, and the effect of drugs for eGFRcre using creatinine and eGFRcys using cystatin. [Results] Among the 100 patients, 54 whose eGFRcre exceeded the CKD determination G3a (60), of whom 22 (40.7%) had eGFRcys below 60. Among RA patients, 17 had eGFRcre above 60, but 3 of these (17.6%) showed a worsening in CKD determination by eGFRcys. Conversely, 19 patients had eGFRcre below 60, among whom 14 (73.7%) had eGFRcys greater than eGFRcre, and 6 (31.5%) improved in CKD determination by eGFRcys. A patients had an eGFRcre of 37.6 and an eGFRcys of 51.2, and MTX was avoided based on the eGFRcre result (All eGFR values are in mL/min/1.73 m^2). [Discussion] Regardless of the disease, patients were identified whose CKD determination worsened or improved when assessed by eGFRcys, and renal function was either overestimated or underestimated by eGFRcre. [Conclusion] It was concluded that measuring eGFRcys as needed would allow for a more accurate assessment of kidney function and better determination of appropriate medication dosages.

P2-063

A case of rheumatoid meningitis with meningeal biopsy

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Conflict of interest: None

[Case] A 74-year-old woman. She was diagnosed with RA at another hospital when she was 50, and has been treated with PSL 3 mg/day, MTX 6 mg/week, ETN 50 mg/week, Stage IV, Class IV, and has been in a wheelchair since X-7. On September 26, X, a patient with right upper limb weakness suddenly appeared and was admitted to our Neurology Department. Contrast-enhanced MRI showed high DWI and FLAIR signal in the left parietal sulcus and contrast effect in the same area, suggesting rheumatic meningitis. CSF revealed clear and colorless, protein 25.4 mg/dL, alb 125.2 mg/L, glucose 58 mg/dL, cell count 1 /μL, IgG 2.4 mg/dL, RF <5 IU/mL, ACPA 0.6 U/mL, IL-6 3.2 pg/mL, culture were negative (serum IgG 1124 mg/dL, RF 165 IU/mL, ACPA 108 U/mL). A subxiphoid meningeal and soft membrane biopsy was performed on November 1, and the patient is scheduled to receive an increased dose of steroid as rheumatoid meningitis. [Clinical Significance] Rheumatoid meningitis is a rare complication of RA in the central nervous system and is often difficult to diagnose because there are no specific markers in blood or spinal fluid and biopsy is difficult. In this report, we describe a case of rheumatoid meningitis in which a meningeal biopsy was performed, with discussion of the literature.

P2-064

A case of refractory leg ulcers treated by immunosuppressive therapy and skin grafting

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Conflict of interest: None

[Case] A 61-year-old man. He has treated diabetes mellitus for 8 years and rheumatoid arthritis (RA) for 6 years at other hospital. Leg ulcers were caused 6 months ago and didn't heal. He was suspected of having collagen disease and visited our department. Blood test showed high titers of RF, anti-CCP antibody, antinuclear antibody and anti-dsDNA antibody, while HbA1c were normal. Nerve conduction test showed mononeuritis multiplex. Leukocytoclatic vasculitis was seen in ulcer biopsy. He was diagnosed with leg ulcers of rheumatoid vasculitis and systemic lupus erythematosus (SLE). The administration of corticosteroids, hydroxychloroquine, intravenous cyclophosphamide and belimumab improved his laboratory data and ulcers. He received skin grafting because ulcers were wide range, and ulcers were not relapsed. [Clinical Significance] It is said that the causes of lower leg ulcers in rheumatoid vasculitis are often arteriovenous insufficiency and trauma, while those in SLE are often venous, multifactorial, and vasculitis. Survival rate of skin grafting will improve by wound bed preparation and immunosuppressive therapy before and after surgery. We report a case that refractory ulcers were treated by the combination of immunosuppressive therapy and skin grafting.

P2-065

A case of tentative diagnosis as rheumatoid arthritis with lymphoproliferative disorder, presumed to be associated with methotrexate

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Conflict of interest: None

[Objectives] We present a case in whom lymphoproliferative disorder during RA therapy questioned the RA diagnosis. [Case] A 63-year-old male experienced bilateral shoulder pain in 1996 and recurrent polyarthritis in 2015. Lab findings indicated TJC 2, SJC 4, RF 128 IU/ml, ACPA 754 U/ml, and CRP 4.28 mg/dl, leading to an RA diagnosis and MTX initiation. He developed pulmonary and liver complications, and despite various DMARDs, inflammatory markers remained unresponsive except for a brief efficacy with IL-6 inhibitors. After restarting MTX in 2022, no improvement occurred. An increase in sIL-2 R prompted a referral to a hematologist, who diagnosed low-grade B-cell lymphoma. Rituximab (RTX) treatment led to remission. [Results] (i) Inflammatory markers worsend with all DMARDs except sarilumab and RTX. (ii) Bone marrow biopsy and flow cytometry confirmed B-cell lymphoma. (iii) Cytogenetic analysis showed a germline mutation as 46, XY, inv (3) (p13q25). [Discussion] This case suggests that chromosomal defect may lead to B-cell lymphoma with RA-like symptoms, exacerbated by MTX. It raises the possibility of B-cell hyperactivation being central to RA pathology or MTX-induced lymphoma, highlighting the complex relationship between RA and lymphoma and questioning the RA diagnosis by itself.

P2-066

A patient with rheumatoid arthritis with fasciitis and myositis

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Conflict of interest: None

Background: Necrotizing vasculitis is one of the common complications in patients with rheumatoid arthritis (RA). However, it is unusual to have fasciitis and myositis as a clinical presentation of necrotizing vasculitis in RA. Case: A 55-year-old man presented to our hospital with fever, bilateral thigh pain, morning stiffness, and joint pain. Physical examination revealed symmetric polyarthritis involving the fingers, shoulders, and ankles. Laboratory tests showed an elevated rheumatoid factor (497 IU/mL), though anti-CCP was negative. He did not have myositis-specific antibodies, nor ANCA. MRI of the thigh exhibited bilateral high signal intensity in the fascia on STIR sequences. A CT angiogram of the limbs showed no vascular stenosis. Muscle and fascia biopsy revealed lymphocytic and plasmacytic infiltration in the vessel walls and perivascular ar-

eas, as well as fibrinoid necrosis. He was diagnosed with RA with fasciitis and myositis. He was treated with prednisolone and intravenous rituximab. After the treatment, the arthritis and the thigh pain resolved and a follow-up MRI resulted in a resolution of the affected area. Conclusion: Fasciitis and myositis due to necrotizing vasculitis could be accompanied by RA and should be considered among the differential diagnosis of RA.

P2-067

Incidence and characteristics of rheumatoid arthritis-associated lymphoproliferative disorder in the AORA registry

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Conflict of interest: None

[Background] Rheumatoid arthritis-associated lymphoproliferative disease (RA-LPD) occurs during rheumatoid arthritis (RA) treatment and is one of the important complications, with symptoms such as fever, weight loss, and lymphadenopathy. [Objectives and subjects] We investigated the incidence, patient background, methotrexate (MTX) dosage and administration period, and outcome of RA-LPD in cases of RA-LPD in the Akita Orthopedic Rheumatology Group (AORA registry). [Results] Nine cases were diagnosed with RA-LPD between 2011 and 2023. The age at onset was 70.4±8.0 years, and the duration of RA was 14±10.2 years. The incidence rate was 0.08/100 PY. MTX was used in all cases, with the dose of MTX being 8.5±2.6 mg/week and the duration of MTX administration until onset being 7.5±7.1 years. In five cases (56%), LPD improved with MTX discontinuation alone. [Discussion] The incidence rate in the AORA registry was comparable to previous reports. Risk factors for RA-LPD have been reported to be older age, MTX treatment, and long-term RA. Similar results were obtained in the AORA registry. [Conclusion] The incidence of RA-LPD and patient background were similar to previous reports. As the AORA registry contains many elderly patients, it is useful to continuously monitor the RA-LPD status.

P2-068

Clinical Characteristics of Patients Requiring Chemotherapy in Methotrexate-Related Lymphoproliferative Disease

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Conflict of interest: None

[Objectives] To clarify the differences between patients with methotrexate-related lymphoproliferative disease (MTX-LPD) who regress after MTX discontinuation alone and those requiring chemotherapy. [Methods] A retrospective review of 16 MTX-LPD patients (7 discontinuation-only group, 9 chemotherapy group) between 2011 and 2024, comparing patient backgrounds and outcomes. [Results] 71% of discontinuation-only group were women, whereas all patients in the chemotherapy group were men (p=0.005). There were no significant differences between the discontinuation-only and chemotherapy groups in age at disease onset, MTX use, or time to lymphoma onset. The most common lymphoma histology was diffuse large B-cell lymphoma, accounting for 71% of patients in the discontinuation-only group and 55.6% in the chemotherapy group; no patients in the discontinuation-only group had Ann Arbor Classification Stage III or IV advanced disease, compared with 77.8% in the chemotherapy group (p=0.0032). Mortality due to LPD was not observed in the discontinuation-only group and was 75% (p=0.14) in the chemotherapy group. [Conclusion] Our results suggest that chemotherapy is more likely to be required in patients in advanced stages at the time of MTX-LPD diagnosis.

P2-069

A case of multiple pulmonary masses in a patient with rheumatoid arthritis that disappeared with immunosuppressive therapy

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Conflict of interest: None

[Case] A 69-year-old woman had been treated with methotrexate (MTX) for rheumatoid arthritis (RA) and in remission. She visited her family doctor for shortness of breath, and a chest X-ray revealed multiple pulmonary mass shadows. She was referred to our hospital for suspected lung cancer. A bronchoscopy biopsies revealed only nonspecific inflammatory findings, with no malignancy. PET-CT showed FDG accumulation in all masses. She was hospitalized due to fever and hemoptysis. The titer of CRP was high, and the masses were enlarging. The possibility of primary lung cancer, MTX-associated lymphoproliferative disorder (MTX-LPD), and rheumatoid nodules was ruled out, and treatment was performed in accordance with rheumatoid vasculitis (RV). Steroid and cyclophosphamide were administered. The titer of CRP normalized. As the PSL dose was tapered, the mass shadow gradually disappeared. [Clinical Significance] When induction therapy was administered in accordance with RV, the titer of CRP normalized and the mass shadow disappeared after a delay. There have been no reports of multiple lung masses in RV, and there is no histological evidence, so the diagnosis remains unclear. The possibility that the lesion was not detected by biopsy and that it was actually MTX-LPD remains a limitation.

P2-070

Case Report: Elderly patient with dementia complicated with organizing pneumonia and rheumatoid arthritis

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Conflict of interest: None

[Case] 84-year-old female. She is a patient of our hospital with Alzheimer's disease and osteoporosis. She had difficulty in communicating due to dementia. On day X, she came to our hospital for fever and lack of appetite that had developed a week ago. She was admitted to our hospital on day X+7 for further examination and treatment as her inflammatory response did not improve, and CT scan showed pneumonia in the right upper and lower lobes. Gastric fluid culture was negative, and there was no improvement in the image of pneumonia after changing antibiotics. The knee joint fluid culture was negative. She was diagnosed with organizing pneumonia associated with rheumatoid arthritis due to positive RF and anti-CCP antibodies. PSL 30 mg (0.5 mg/kg) was started on day X+17 and significant symptomatic improvement was obtained. CT taken on day X+35 showed marked improvement of pneumonia. The patient was discharged on day X+53 after gradual reduction of PSL. [Clinical Significance] Elderly patients with dementia often have difficulty in expressing their symptoms. Although there are some reports of organic pneumonia and rheumatoid arthritis occurring simultaneously, they are relatively rare. We will report our case, including a literature review.

P2-071

A case of membranous nephropathy developed during the course of treatment for 16 years of rheumatoid arthritis

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Conflict of interest: None

[Case] A 75-year-old woman developed rheumatoid arthritis (RA) in X-16 and was treated with methotrexate (MTX) and tacrolimus (TAC). The disease activity of RA stabilized, but in year X-1, serum albumin levels began to decline and reached 3.5 g/dl. Despite stable renal function, proteinuria (3+, 5.9 g/g·Cre) and hematuria (2+, 5-9/HPF) were observed. A renal biopsy was performed in March of year X. Pathological findings showed mild thickening of the basement membrane by PAS staining, formation of minute spikes in the basement membrane by PAM staining, and deposition of IgG, IgM, and C3 along the glomerular basement membrane by fluorescent antibody method. Electron microscopy showed that deposits were distributed widely under the basement membrane epithelium, and the patient was diagnosed with stage II membranous nephropathy. After renal biopsy, prednisolone 25 mg and cyclosporine 150 mg were started, and MTX and TAC were discontinued. Serum albumin increased to 3.8 g/dl, and both proteinuria and hematuria became negative. [Clinical Significance] When nephrotic syndrome appears during the course of treatment for RA, it is often due to amyloidosis or treatment drugs. However, it may be associated with the underlying disease, and a renal biopsy should be considered.

P2-072

A Case of Nontuberculous Mycobacterial Cutaneous Ulcers in a Patient with Rheumatoid Vasculitis

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Conflict of interest: None

[Case] An 88-year-old man with rheumatoid arthritis diagnosed in 2001 had been treated with salazosulfapyridine. In 2017, he was referred to our department for worsening arthritis. Based on polyarthritis, a rheumatoid nodule on the left elbow, mononeuritis multiplex in the left common peroneal nerve area, interstitial pneumonia, complement depletion, and anti-CCP antibody positivity, Rheumatoid Vasculitis was diagnosed. His disease was controlled with prednisolone and tocilizumab. In December 2023, multiple small ulcers appeared on the tips of his left toes, and he was hospitalized for evaluation. Differential diagnoses included rheumatoid vasculitis, peripheral arterial disease, and stasis ulcers due to leg edema. On hospital day 4, a pustular lesion appeared on the dorsum of his left foot with a Gaafky grade 4 smear. PCR for Mycobacterium tuberculosis and MAC were negative, suggesting nontuberculous mycobacterial infection excluding MAC. His ulcers improved with three-drug chemotherapy. Bacterial species identification was not achieved after 13 weeks of culture. [Discussion] Toe ulcers in rheumatoid vasculitis can manifest as extra-articular symptoms, requiring broad differential diagnoses. Considering infections, including nontuberculous mycobacteria, is essential.

P2-073

Long-term efficacy, safety, and withdrawal of Abatacept for early rheumatoid arthritis under the evaluation of ultrasonography: A single-center prospective analysis (SOROBAN Study)

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Conflict of interest: None

Objective: To evaluate the long-term efficacy, safety, and withdrawal of Abatacept (ABT) in early Rheumatoid Arthritis (RA) patients, showing the residual power Doppler (PD) signals of ultrasound examination under the therapy of csDMARDs. Method: ABT was initiated in RA patients with positive PD signal under treatment of csDMARDs. ABT was withdrawn at the time of disappearance of PD signal. RA disease activity (DAS28-CRP, SDAI, CDAI, mHAQ) and ultrasound exam (Gray-scale (GS) and PD score in 40 joints) every 24 weeks and modified Total Sharp Score (mTSS) every 48 weeks were evaluated until 240 weeks after the administrations of ABT. Result: Five (50%) out of 10 RA patients were able to withdraw ABT, and restarting ABT was needed in only one patient (10%). In ABT withdrawal patients, ΔmTSS was -2.08 (vs all patients -0.75) and GS was 1.00 (vs all patients 2.75) at week 240. One Gastrointestinal Stromal Tumor (GIST) and one Pneumocystis jirovecii pneumonia (PCP) were seen in this study. Conclusion: It is suggested that ABT have the effect of suppression of bone destruction progression for a long time even after withdrawal. On the other hand, extra attention should be paid to the onset of malignancy and infectious disease even under the adequate screening prior to ABT initiation.

P2-074

Ozoralizumab improves patient pain VAS early after treatment initiation

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Conflict of interest: None

[Objectives] Ozoralizumab (OZR) is the first nanobody biologic agent approved in 2022 for the treatment of rheumatoid arthritis (RA). It is the newest anti-TNF inhibitor, therefore, there are still few reports on its clinical outcomes in real-world settings. In this study, we investigated the short-term outcomes of OZR. [Methods] Ten patients with RA (7 females, 3 males) who received OZR and were followed up for more than 3 months were included. CRP, DAS28, MMP-3, and patient pain visual analog scale (ptVAS) scores were assessed at 0, 4, 8, 12, 16, and 24 weeks after initiation of OZR. [Results] The mean age was 68.4 years old, and the concomitant use of MTX was 50% (mean 8.0 mg/week). Three patients were naïve. Three patients discontinued OZR due to inefficacy at 12, 16, and 16 weeks, and one patient discontinued at 12 weeks due to drug eruption. CRP, DAS28-ESR, and MMP-3 showed no significant improvement at any point compared to baseline. On the other hand, the ptVAS improved significantly from 49.0 at baseline to 31.5 at 4 weeks ($p<0.05$), and continued to improve up to 24 weeks ($p<0.05$). [Conclusion] Animal experiment demonstrated rapid migration to the site of inflammation as a characteristic of nanobody. Pain relief shortly after the start of OZR was observed in this study.

P2-075

The efficacy of ozoralizumab in rheumatoid arthritis: Retrospective analysis of real-world data

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Conflict of interest: None

[Objectives] Ozoralizumab (OZR) is an anti-TNFα nanobody developed in Japan, approved for RA in 2022. However, there is still little evidence. [Methods] The efficacy of OZR was retrospectively evaluated in 38 patients received OZR. Seven patients with DAS28CRP < 2.3 at the time of administration were excluded. [Results] Patient background was follows: age 71 [59-78.5] years, disease duration 13 [2.9-23.3] years, concomitant MTX use in 46.9%, 71.8% switched from bDMARDs/JAK, 46.9% had a history of TNFi, and 50% had difficult-to-treat RA (D2TRA). After 12 weeks of OZR administration, DAS28CRP significantly decreased from 4.04 [3.08-5.04] to 3.23 [2.22-4.27]. In addition, 35.5% achieved DAS28 remission at 12 weeks, and low pain VAS and HAQ-DI were associated with DAS28 remission. Furthermore, DAS28 significantly decreased from 4.13 [3.33-5.46] to 3.13 [1.8-4.75] at 12 weeks in patients without a history of TNFi, whereas in patients with a history of TNFi, DAS28 did not decrease, from 3.68 [2.62-4.62] to 3.49 [2.57-4.19] at 12 weeks. In D2TRA patients, DAS28 significantly decreased from 4.02 [3.22-5.24] to 3.18 [2.06-4.78] at 12 weeks. [Conclusion] OZR is effective even in D2TRA patients with a long disease duration, but the effect may be weaker in patients with a history of TNFi.

P2-076

Comparative Study on the Treatment Efficacy of Golimumab and Ozoralizumab for Rheumatoid Arthritis at Our Hospital

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Conflict of interest: None

[Objectives] Golimumab and ozoralizumab, both subcutaneously administered TNF inhibitors every four weeks, were compared in this study for their treatment outcomes at our hospital, with a particular focus on cases transitioning from golimumab to ozoralizumab. [Methods] We included 105 golimumab patients (35 males, 70 females, ages 42-93, dosages 50 mg in 47 cases and 100 mg in 58 cases) and 35 ozoralizumab patients (10 males, 25 females, ages 50-86). The analysis covered 14 cases that switched treatments. Measurements of CRP, DAS28 (CRP), CDAI, and NRS were taken at 4, 8, 12, and 24 weeks, alongside continuation rates. [Results] At 24 weeks, the golimumab group showed improvements from CRP 0.85 to 0.41, DAS28 (CRP) from 2.89 to 2.44, CDAI from 10 to 8, and NRS from 4 to 3. The ozoralizumab group improved from CRP 0.99 to 0.08, DAS28 (CRP) from 2.77 to 2.06, CDAI from 12.5 to 8.1, and NRS from 3.4 to 2.1. The switch group exhibited notable improvements: CRP from 1.48 to 0.10, DAS28 (CRP) from 2.98 to 1.80, CDAI from 13.3 to 6.5, NRS from 2.8 to 1, with a 75% continuation rate. [Conclusion] Both TNF inhibitors are effective, with particularly notable results in patients switching to ozoralizumab. Continuous clinical studies are recommended.

P2-077

Comparison of Efficacy Between Ozoralizumab and Golimumab in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Ozoralizumab is an anti-human TNFα variable domain of heavy chain antibody, approved for difficult-to-treat rheumatoid arthritis (RA) patients. This study aims to investigate the advantages of ozoralizumab over the conventional TNF inhibitor golimumab. [Methods] We conducted a retrospective analysis of 23 patients treated with ozoralizumab and 20 with golimumab. [Results] Both medications were primarily initiated in older patients with a disease duration of over 10 years. A higher proportion of patients in the ozoralizumab group had prior biological treatments, especially those with difficult-to-treat cases. Most discontinuations of ozoralizumab occurred in patients not receiving methotrexate (MTX). In contrast, about one-third of golimumab patients were maintained on a regimen of 100 mg every four weeks. The incidence of MTX non-use was greater in the ozoralizumab cohort (70% vs. 60%). [Conclusion] Ozoralizumab appears to be more frequently initiated in difficult-to-treat RA cases compared to golimumab, with comparable therapeutic outcomes. Both treatments were effective even without MTX; however, ozoralizumab may demonstrate superior efficacy, as indicated by its use in a higher proportion of complex cases and the dosing patterns observed in golimumab-treated patients.

P2-078

Sarilumab continuation rates and methotrexate dose trends in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Methotrexate (MTX) is an anchor drug in the treatment of rheumatoid arthritis, but has many side effects of concern. In the present study, we investigated the retention rate of patients treated with sarilumab (SAR) and dose trends in MTX concomitant use. [Methods] This study included patients who received SAR at Showa University Hospital between February 2018 and September 2023 and excluded those who had discontinued MTX within one year of SAR introduction or are currently receiving MTX for < 1 year. Descriptive statistics were used to compare both groups. [Results] The analysis included 26 patients (mean age; 58.5 [50-71] years, 14 [53.8%] women, and mean duration of disease; 7 [1-15.3] years). Eighteen (69.2%) patients remained on SAR for one year and 15 (83.3%) were on MTX at SAR induction. Of the 15 patients, 11 (73.3%) had their MTX dose reduced by one year, and 6 (40.0%) could discontinue treatment. In the MTX discontinuation group, more patients tended to have a naive history of bDMARDs before SAR induction than in the continuous MTX group (n=9). The MTX dose at induction decreased from 10 (9-13) mg/week to 8 (5-12) mg/week at one year. [Conclusion] MTX may be discontinued or its dose reduced if SAR can be administered continuously.

P2-079

Analysis of the effectiveness of electric device of etanercept (SmartClic/ClicWise: ClicWise) in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] Analysis of the effectiveness of Clicwise [Methods] 1. We followed up ten patients whom we have reported a). One patient has already discontinued Clicwise due to its heaviness and restarted syringe (Sy) Ref). 2. Two patients switched. Clicwise from Sy (by their families). 3. One patient (87YO female) started self-injection of Clicwise from Sy by her son, 4. Five newly introduced patients (one by her son, one after adalimumab by nurses). [Results] 1. One patient went back to Sy due to the injection trouble. One patient successfully renewed the device by the announcement. 2. A daughter of the patient suffered tremor when she used Sy, but the problem was resolved by Clicwise. 3. She has no problem. 4. One patient had an injection trouble at the first use, so we have changed the device. One patient discontinued etanercept due to the elevation of anti-DNA antibody. [Conclusion] Clicwise might be useful for elderly patients, injection by the families, and newly introduction. However, improvement of the wight or mechanical reliability should be ameliorated. Ref) Ito S, et al. Self-reports concerning an autoinjector device for etanercept (SmartClic/Clicwise) from eleven Japanese patients with rheumatoid arthritis. Clinical Rheumatol Rel Res (in press)

P2-080

Efficacy and Safety of Ozoralizumab in Patients with Rheumatoid Arthritis: A Retrospective Study

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Conflict of interest: None

Objective: This study evaluated the efficacy and safety of ozoralizumab (OZR) in rheumatoid arthritis (RA) patients. **Methods:** A retrospective analysis was conducted on RA patients treated with OZR at our hospital until April 2024. **Results:** Eleven patients (10 females, 1 male) were included, with a mean age of 68.4 years and average disease duration of 11.7 years. Baseline DAS28-ESR and simplified and clinical disease activity indices (SDAI/CDAI) scores were 4.01 and 24.3/22.4, respectively. None were bio-naïve, and 90.9% had difficult-to-treat RA following the failure of ≧2 biological or targeted synthetic DMARDs. Prior treatments included TNF inhibitors (2 patients), IL-6 inhibitors (4), abatacept (1), and JAK inhibitors (4). Within six months, three patients (27.3%) achieved remission or low disease activity per SDAI criteria and continued OZR. Seven patients (63.6%) showed no response and switched therapies. Two of four patients who transitioned from JAK inhibitors to OZR experienced

rapid arthritis worsening. One patient stopped treatment due to a generalized skin rash. **Conclusion:** OZR had limited effectiveness in patients with difficult-to-treat RA. Some experienced rapid RA symptom worsening after switching from JAK inhibitors to OZR.

P2-081

A case report of parathoracic abscess developed in a RA patient using golimumab

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Conflict of interest: None

[Case] A 77-year-old woman with a history of RA for 28 years. She had received golimumab for 8 years, and the drug dose doubled to 100 mg every 4 weeks because of aggravation of scleritis 3 years ago. MTX and tacrolimus were also used, and the patient was in remission. She developed back pain and fever without any causes. Blood test showed high WBC count of 11800 and CRP 16.0 mg/dl. MRI showed a high-signal area on STIR from the 5th to the 12th thoracic vertebra anteriorly. Blood culture was negative. The origin of the inflammatory organism is unknown, but parathoracic abscess was strongly suspected. The patient was hospitalized and placed on bed rest, and antibiotic therapy was started. Pain and fever improved promptly and the patient is currently doing well with no recurrence. [Clinical Significance] Respiratory infections such as bacterial pneumonia have been reported as side effects of golimumab, a TNF inhibitor, but spinal infections are rare. Spinal infections such as parathoracic abscess should also be considered when back pain and fever occur in RA patients using TNF inhibitor.

P2-082

The efficacy of Ozoralizumab therapy in D2T rheumatoid arthritis

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Conflict of interest: None

[Objectives] To evaluate the efficacy in Ozoralizumab therapy with rheumatoid arthritis (RA) and tapering of methotrexate. [Methods] This study comprised 8 patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received Ozoralizumab therapy with methotrexate for 6 months. The outcomes were assessed with the disease activity during 6 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 2.9 to 2.8) and CDAI (from 2.7 to 2.0) decreased significantly from baseline to Week 24. DAS28ESR Remission achieved in 8 cases at Week 24. Ozoralizumab was also effective with RA patients of in adequate response to antiIL6 inhibitor therapy. The average dose of methotrexate was 7.3 mg. The average dose of glucocorticoid was 3 mg. No adverse event was observed. [Conclusion] These results suggested that Ozoralizumab therapy is effective in patients with RA of an inadequate response to other biologic DMARDs.

P2-083

Real-world clinical experience with ozoralizumab in rheumatoido arhritis

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Conflict of interest: None

(Objective) This study aimed to assess the clinical effects and adverse events of otilimab (OZR) at our hospital. (Methods) Patients with rheumatoid arthritis who received OZR between September 2022 and April 2024 and were followed for over six months were included. Data were retrospectively collected from medical records, focusing on disease activity, adverse events, and treatment continuation. (Results) Fourteen patients (5 males, 9 females), average age 66.6 years, were treated with OZR. Eleven (78.6%) were autoantibody-positive, with an average disease duration of 5.4 years. Twelve (85.7%) had no prior biologics use. Disease activity significantly decreased post-treatment. Two patients stopped after one dose, and three discontinued within six months due to inefficacy. No adverse events were observed. Dose reduction of other medications was noted. (Discussion) OZR is expected to be as effective as TNF inhibitors, particularly in autoantibody-positive patients, with quick effects in some cases. Despite our small sample size, OZR also showed efficacy in autoantibody-negative patients. (Conclusion) OZR had a 60% continuation rate at six months, with significant improvement in disease activity and no adverse events during follow-up.

P2-084

Safety and Efficacy of Biologics, JAK Inhibitors Monotherapy in Elderly Rheumatoid Arthritis (RA) Patients

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Conflict of interest: None

[Objectives] Elderly patients with rheumatoid arthritis (RA) often have other complications and are often taking multiple drugs. Therefore, by administering Biologics (Bio) or JAK inhibitors (JAKi), it is expected that treatment effects can be achieved while reducing the dosage. [Methods] 57 patients aged 75 years or older with RA (6 Etanercept, 14 Tocilizumab, 1 Golimumab, 8 Abatacept, 5 Sarilumab, 5 Ozoralizumab, 1 Tofacitinib, 5 Baricitinib, 1 Peficitinib, and 4 Upadacitinib, 7 Filgotinib). We evaluated CRP, DAS28ESR, and patient global VAS up to 52 weeks after receiving Bio or JAKi. [Results] The mean age was 80.5 years, CRP at start was 2.48 mg/mL, DAS28ESR was 4.63, global VAS was 51.2 mm, CRP 0.51 mg/mL after 4 weeks, DAS28ESR 3.43, global VAS 33.9 mm, CRP 0.36 mg/mL, DAS28ESR 3.07, global VAS 29.1after 8 weeks. After 52 weeks, the effect was maintained. As for adverse events, the onset of herpes zoster was observed in 3 patients treated with Bio and 3 cases with JAKi administration, but no infections requiring hospitalization or adverse cardiovascular events were observed. [Conclusion] In elderly RA patients who are inadequately effective with csDMARD, Bio or JAKi monotherapy can be expected to have a sufficient therapeutic effect and drug reduction.

P2-085

Analysis of Factors Associated with Decreased Bone Mineral Density Using the Second Metacarpal DIP Method in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objective] We have previously reported the utility of the second metacarpal DIP method, which can be performed without a DXA device, in diagnosing osteoporosis in rheumatoid arthritis (RA) patients. This study aimed to identify factors linked to decreased BMD in RA patients to enhance osteoporosis diagnosis efficiency. [Methods] We measured BMD using the DIP method in RA patients suspected of osteoporosis. We investigated the influence of factors on YAM values and analyzed risk factors for YAM values below 70%. [Results] We measured YAM in 123 RA patients (99 females, 24 males, mean age 74.5 years), with an average of 71.7%. Sixty patients (48.8%) had YAM below 70%. YAM was significantly lower in patients aged 75+ than those under 75 (66.9% vs. 76.9%, p=0.0002). Non-remission patients by HAQ had lower YAM than those in remission (66.4% vs. 74.4%, p=0.006), and those with a fracture history had lower values than those without (67.0% vs. 73.5%, p=0.027). Multivariate analysis showed age (OR 1.06, p=0.018) and female sex (OR 3.17, p=0.030) were significant risk factors for YAM below 70%. [Conclusions] Prioritizing the examination of RA patients aged 75 or older and females when using the second metacarpal DIP method may improve osteoporosis diagnosis efficiency.

P2-086

Changes in bone metabolism markers in secondary osteoporosis associated with rheumatoid arthritis

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Conflict of interest: None

[Objectives] RA patients are considered to have a high incidence of secondary osteoporosis with a history of PSL use and decreased activity. In this study, we investigated changes in bone metabolic markers in RA patients. [Case] A total of 194 patients aged 36 to 96 years, with disease duration ranging from 2 months to 54 years, were studied at our hospital and affiliated facilities. We compared values of ACPA, RF, lumbar spine and femur BMD, Ca, P, 25 (OH)VitD, PINP, BAP, TRACP-5 b were compared and examined. [Results] Mean age: 72 years, Mean disease duration: 13.7 years, Mean ACPA: 321 U/ml, Mean RF: 123 IU/ml, MTX use: 124 patients, PSL use: 46 patients, Biologic use: 116 patients, Mean BMD: lumbar spine 0.86 g/cm2, femur 0.59 g/cm2, Mean Ca: 9.16 mg/dl, Mean PINP: 49.2 μg/ml, Mean BAP, and mean TRACP-5b: 410 mU/dl. Eight patients used teriparatide, 20 used denosumab, 7 used romosozumab, 38 used bisphosphonates, 38 used activated vitamin D3, and 7 used selective estrogen receptor modulators. [Conclusion] Negative correlation was observed between MTX dosage and TRACP-5b positive correlation between PSL dosage and PINP, and negative correlation between PSL dosage and BAP. There was a correlation between rheumatoid arthritis drugs and bone metabolism markers.

P2-087

One-question screening method for vertebral compression fractures in elderly patients with acute low back pain

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Conflict of interest: None

Objective Vertebral compression fractures (VCFs) are a red flag in elderly patients with low back pain (LBP). In this study, we report a one-question screening method for VCF limited to elderly patients aged 75 years and older. Methods We included elderly patients aged 75 years and older with acute LBP. The questionnaire item was subjective pain intensity (NRS), with 0 for no pain and 10 for the worst imaginable pain, and pain intensity: 0-10 was used as a variable, excluding those who could not answer NRS. MRI made VCF diagnosis in all cases, and cases of pyogenic spondylitis and spinal malignancies were excluded. Diagnostic accuracy was examined by multivariate analysis using NRS, age, and sex as variables. Results Of the 113 subjects (female: 58.4%), 71 (62.3%) had VCF. In the logistic model, NRS and age were significantly related variables, and the diagnostic accuracy was AUC value: 0.79 and accuracy rate: 66.4%. Moreover, 26 of 28 patients (92.9%) aged 84 years or older and with NRS 8 or higher had a high probability of VCF. Conclusion The results suggest that more than half of the elderly patients with acute LBP have VCF. It was also shown that severe pain (NRS 8 or higher) in the very elderly is very likely to be VCF.

P2-088

Evaluating Vertebral Fractures in Patients with Rheumatoid Arthritis by Using AI Software

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Conflict of interest: None

[Objective] Patients with rheumatoid arthritis (RA) are at risk of insufficiency fractures, but there are not enough studies about the prevalence and levels of vertebral fractures. This study aims to investigate the prevalence of vertebral fractures in RA patients using AI software. [Methods] This study included 33 RA patients (mean age 68.7 years) and 98 non-RA patients (mean age 64.1 years). Thoracolumbar X-rays and AI (Smart QM) co-developed with SHIMADZU assessed deformities, finally doctors diagnosed fractures. The Smart QM Vertebral Body Measurement Software measures vertebral bodies using a quantitative measurement method. [Results] RA Patients had a high incidence of vertebral fractures than non-RA patients (RA 24.2%, non-RA 14.2%). The incidence of vertebral fractures in RA patients was significantly higher in the thoracic region (RA 24.2%, non-RA 8.2%) than the lumbar region (RA 12.1%, non-RA 10.2%). Using AI, it took 47.3 seconds to measure the thoracic and 58.6 seconds for the lumbar region per patient. [Conclusions] Taking X-rays of thoracic vertebrae in RA patients is important as they develop fractures significantly more frequently than non-RA patients. Evaluating thoracic vertebrae fractures is complicated, but using AI software makes it faster and highly accurate.

P2-089

To reduce the incidence of fragility fractures, improving the diagnosis rate of severe osteoporosis is crucial, and spinal imaging plays a key role in this process

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Conflict of interest: Yes

Objective: Anabolic agents are used for patients at high risk of fractures, typically those with severe osteoporosis, diagnosed by (a) bone density, (b) fragility fracture history, and (c) spinal imaging. In practice, however, all three criteria are often unavailable. This study examines diagnostic rate differences for severe osteoporosis based on combinations of these criteria and suggests ways to improve accuracy. **Method:** The study included 104 patients treated for proximal femoral fractures at our hospital from March 2022 to June 2024. Diagnostic rates were assessed with four combinations: 1. (a) alone, 2. (a) + (b), 3. (a) + (c), and 4. (a) + (b) + (c). **Results:** Patients averaged 84 years, with 85% being female. Fracture types included 52% intertrochanteric, 52% femoral neck, and 2% subtrochanteric. Excluding the current fracture from fragility history, severe osteoporosis diagnostic rates were 50%, 55%, 71%, and 73% across combinations 1-4. Adding fragility history raised the rate by 5%, and spinal imaging increased it by 21%. **Conclusion:** Spinal imaging can improve the severe osteoporosis diagnostic rate by 1.5 times compared to bone density testing alone, aiding in better treatment decisions and potentially improving patient outcomes.

P2-090

Association with toe grip strength, muscle strength and bone density -research at healthy medical college students-

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Conflict of interest: None

[Objectives] Lower limb muscle strength are important for the diagnosis of sarcopenia. Therefore, we focused on toe grasp strength, which is a lower limb muscle strength. [Method] 150 consenting adolescent medical students (118 males and 32 females) with no comorbidities were included in the study. Toe grasp strength was measured, skeletal muscle index (SMI) was measured using the InBody570, and bone mineral density was measured by quantitative ultrasound (QUS) to determine the speed of ultrasound transmission (SOS). [Results] The average toe grasp strength for males was 23 kg and 15 kg for females. The mean SMI and SOS were 7.5 and 7.9, and 1562 and 1577, respectively, for males (53 and 65) and females (15 and 1577). There were no significant differences for females. In multivariate analysis, the factor associated with increased bone mineral density and SMI in men was toe grasp strength. SMI is associated with total body muscle mass, and toe-grasp strength affects standing, walking, and jumping movements, and is related to body weight and level of daily living. [Conclusion] We investigated the association between toe grasp strength, skeletal muscle index, and bone mineral density in adolescent medical students.

P2-091

Investigation of the usefulness of comprehensive geriatric assessment in reducing ADL in patients with osteoporotic vertebral fracture

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Conflict of interest: None

[Objectives] The number of osteoporotic vertebral fractures (OVF) is increasing with the aging of the population, and the decline in ADL due to pain and neurological disorders has become a problem. We examined whether the G8 Screening tool, one of the comprehensive geriatric assessments for the elderly, can predict ADL decline in OVF patients. [Methods] Patients with OVF who were admitted to our hospital from April 2020 to March 2023 and treated conservatively were included in the study. [Results] Subjects were 152 cases (male: female 46: 105), mean age 83.6 years (64-97), hospitalization 53.2 days (2-249), fractured vertebra (T7: T8: T9: T10: T11: T12: L1: L2: L3: L4: L5 = 5: 1: 4: 2: 12: 24: 42: 28: 15: 11: 6), G8 mean score was 10.9 (4-16); G8 cutoff value was set at 10, 81 patients (53.2%) were in the high value group and 71 patients (46.7%) were in the low value group. Femoral YAM values averaged 67.1% in the high G8 group and 57.8% in the low G8 group (p=0.02). The percentage of patients who were able to maintain independent walking before and after injury was 55% in the high G8 group and 11% in the low G8 group (p=0.008). [Conclusion] ADL decline is expected in patients with low G8, early surgical pain relief may be a treatment option.

P2-092

Experience of using belimumab for patients with systemic lupus erythematosus at our hospital

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Conflict of interest: None

[Objective] To determine the clinical characteristics, efficacy, and safety of belimumab (BEL) in cases of systemic lupus erythematosus (SLE) in our center. [Methods] Sixty-eight patients (61 women, 7 men) with SLE who had received BEL between 2017 and 2023 were included. We retrospectively examined age, sex, clinical background, complications, reason for induction of BEL, changes in SLEDAI and prednisone (PSL) dosage, and adverse events. [Results] The time from diagnosis of SLE to BEL introduction was 132 ± 112.9 months. At the last observation, BEL was discontinued in 40 patients. The time from introduction to discontinuation of BEL was 18.8 ± 17.5 months. Reasons for discontinuation were ineffectiveness in 16 cases, adverse events in 13 cases (death 2, pain on injection 5, infection 3, skin rash, urticaria 2, headache 1) and others in 11 cases (hospital transfer 5, remission 3, pregnancy 3). The dose of PSL reduced from 12.1 ± 12.5 to 5.3 ± 4.9 mg/day, and SLEDAI decreased from 2.72 ± 0.33 to 1.72 ± 1.91. [Conclusion] After commencement of BEL, disease activity improved and dose reduction of PSL could be achieved. No remarkable adverse events occurred except for two deaths of unknown causality.

P2-093

Effectiveness of Belimumab in SLE Patients with Clinically Active Serologically Quiescent Status

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Conflict of interest: None

[Objectives] To reduce dose of glucocorticoid (GC) in SLE patients who are clinically active with serologically quiescent (CASQ) is often difficult. We evaluated the effect of belimumab (BEL) on GC reduction and disease activity in SLE patients with CASQ status. [Methods] 48 SLE patients who received BEL were collected. CASQ was defined as the exacerbation clinically activivity after GC reduction, or those currently exhibiting clinically activity with C3, C4, and anti-DNA antibody (anti-DNAab) abnormality at BEL initiation. We analyzed C3, C4, anti-DNAab, PSL dosage, and SLEDAI-2K over 72 weeks. [Results] Nine patients met the criteria for CASQ status. Their median age was 47 years (IQR, 38-50). At the time of BEL initiation, 12 clinical symptoms were recorded: skin rash in 6, hematological symptoms in 4, articular symptoms in 1, and vascular symptoms in 1. The SLEDAI-2K score was 1.0 (0-2.0), and the GC dosage was 5.0 (4.5-6.0) mg. At the 72-week, 8 clinical symptoms improved. C3, C4, and anti-DNAab levels remained normal ranges. SLEDAI-2K was 0 (0-2.0) showing no worsening. The PSL dosage decreased to 5.0 (2.0-5.0) mg. [Conclusion] BEL may improve disease activity and decrease GC doseage in SLE patients with CASQ status.

P2-094

Factors for remission by belimumab in patients with SLE

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Conflict of interest: None

[Objectives] We have explored the factors for belimumab (BE)-induced clinical remission in cross sectional study. [Methods] Forty five patients with SLE were divided into three groups such as Doris remission (R), low disease activity (L) and no response (N) decided at September 2024. Before treatment with BE, factors of sex, age duration of disease, SLEDAI, immunological activity and glucocorticoid (GC) dose were examined in each group. Differences between group R+L and group N were also examined in above mentioned factors. [Results] Each R, L and N was 22, 17 and 5 cases, respectively. Sex, age duration of disease, SLEDAI and BE treatment period were not significant different between each group and group R+L compared with group N. Each lupus nephritis, APS, arthritis and MCTD in R+L group was 91, 83, 90 and 100%, respectively. On the other hand, anti-dsDNA antibody (AU/ml) in group R (462±410) was significantly ($P<0.05$) higher than group N (68±94), and C3 (U/ml) in group (R+L) (72±27) were significantly lower than group N (95±13). [Conclusion] We indicated that factors for BE-induced DORIS remission might be higher immunological activities such as anti-dsDNA antibody and C3 level and disease type in patients with SLE by cross sectional analysis.

P2-095

Belimumab is Useful for Maintaining Remission in Lupus Nephritis -Treatment Experience in Our Institution-

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Conflict of interest: None

Objective: To examine the efficacy of BLM as a maintenance therapy for remission in patients with lupus nephritis. Methods: We targeted 25 patients diagnosed with lupus nephritis at our institution between 2017 and 2024, who were induced into remission with GC and IMs. The patients were stratified into two groups: those who received BLM as part of their maintenance therapy and those who did not. A retrospective comparison of renal outcomes was conducted between the two groups. Results: The BLM combination group consisted of 11 patients (2 males and 9 females, mean age 41.5±11 years), while the non-BLM group included 15 patients (2 males and 13 females, mean age 36.6 ±14 years). The pre-remission serum creatinine levels were 1.06 ±0.57 mg/dl and 1.22 ±0.58 mg/dl, respectively (not significant), and the final serum creatinine levels after treatment were 1.04 ±0.50 mg/dl and 1.76±2.03 mg/dl (not significant). In the combination group, renal remission was achieved in 9 patients (81%), with no cases of dialysis transition or death. In contrast, the non-combination group had renal remission in 5 patients (41%), with 5 patients transitioning

to dialysis and 1 death. Conclusion: The BLM combination group exhibited a high remission rate, suggesting its usefulness.

P2-096

Efficacy of Belimumab for the treatment of Systemic Lupus Erythematosus

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Conflict of interest: None

[Objectives] We retrospectively surveyed the clinical course in patients treated by Belimumab (BLM) in our hospital, and further investigated the benefit of BLM in patients had been already achieving Lupus low disease activity state (LLDAS) at the initiation of BLM. [Methods] Patients treated by BLM in our hospital from Feb. 2018 to Apr. 2023 were included. We analyzed characteristics and clinical course. We further analyzed the dose of Glucocorticoid (GC) at the baseline and at 48 weeks in patients with LLDAS. [Results] 48 patients were included in the study. At the baseline, the median age, duration of disease, and prednisolone (PSL) dose were 43 years old (IQR 33.8-54.3), 12.5 years (5.9-17.8), and 8.0 mg (5.0-10.5), respectively. The continuation rate of BLM over 72 weeks was 74.8%. At 72 weeks, PSL dose (9.0 vs 5.0 mg) was significantly reduced, and SLEDAI-2K (6.0 vs 2.0), C3 (90.0 vs 102.0 mg/dL), C4 (16.1 vs 22.2 mg/dL) and anti-ds-DNA antibody titer (7.68 vs 7.0 IU/mL) were significantly improved. By the subgroup analysis, PSL dose (7.0 vs. 4.0 mg) was significantly reduced in 7 patients with LLDAS at the baseline. [Conclusion] BLM was effective for improving disease activity and reducing GC dose in practice setting, and it could reduce GC dose in patients with LLDAS.

P2-097

A case of lupus nephritis in which remission maintenance therapy with belimumab was effective

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Conflict of interest: None

The patient was a woman in her 70s. In X-11, she developed systemic lupus erythematosus (SLE) due to thrombocytopenia, arthritis, and nephritis. Treatment was started at 60 mg/day of PSL, and CyA and MZB were used in combination because the blood concentration of TAC was abnormally high. PSL was gradually tapered to 5 mg/day, but there was no relapse for about 10 years. Overt proteinuria persisted, and HCQ 200 mg/day was added in X-1, but there was little improvement, so a kidney biopsy was performed in X, and relapse of lupus nephritis was confirmed. Remission induction therapy was performed by increasing the dose of PSL to 30 mg/day and combining it with MMF 1000 mg/day. Due to leukopenia, the dose of MMF was reduced to 500 mg/day, but when the dose of PSL was reduced to 10 mg/day, Pneumocystis pneumonia occurred. Three months later, she developed herpes zoster. It was determined that it was difficult to continue MMF, so it was changed to belimumab. Thereafter, there were no adverse events such as infections, and the patient has progressed without relapse despite gradually tapering PSL to 5 mg/day. We have observed a case in which remission maintenance therapy with belimumab was effective for lupus nephritis in which it was difficult to continue immunosuppressants.

P2-098

Three Cases of Pediatric-Onset Systemic Lupus Erythematosus Achieving Glucocorticoid-Free Status with Belimumab Combination Therapy

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Conflict of interest: None

Introduction: The advent of belimumab (BLM) has shifted the management goals of systemic lupus erythematosus (SLE) toward achieving glucocorticoid (GC)-free treatment. However, reports of GC-free achievement in child-onset SLE (cSLE) with BLM are still limited. **Case 1:** A 16-year-old boy, diagnosed with SLE and lupus nephritis (LN). Induction therapy with methylprednisolone pulse therapy (MPT) was administered, followed by maintenance therapy with prednisolone (PSL), hydroxychloroquine (HCQ), and mycophenolate mofetil (MMF), and the addition of BLM. PSL was discontinued at 24 months. **Case 2:** A 13-year-old girl, diagnosed with SLE and LN, and secondary Sjögren's syndrome. Induction therapy included MPT, followed by maintenance therapy with PSL, HCQ, and MMF, and the addition of BLM at 7 months. Both MMF and PSL were discontinued at 24 and 32 months, respecteively. **Case 3:** A 15-year-old girl diagnosed with SLE and LN. Induction therapy with MPT was followed by maintenance therapy with PSL, HCQ, MMF, and the addition of BLM. Both MMF and PSL were discontinued at 22 months post-treatment initiation. **Discussion:** All 3 cases achieved safe PSL discontinuation within approximately 2 years. This report compares the outcomes of cSLE cases treated with BLM leading to GC discontinuation.

P2-099

A Case of myelitis in a patient with systemic lupus erythematosus without positive MRI findings successfully treated with anifrolumab

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Conflict of interest: None

[Case] 41 y.o. male [CC] bilateral lower limb weakness, bladder-bowel disfunction (BBD) [HPI] 6yrs prior to admission (PTA), he developed systemic lupus erythematosus (SLE). 3wks PTA, fever, bilateral lower limb weakness, hypersensitivity below the navel level appered, followed by BBD. On physical exams, muscle weakness, proprioception abnormality on lower limb, bilateral hyperreflexia in PTR, ATR, decrease in anal tonus were found. LP showed elevated cell count with marked IL-6 elevation. Repeated spinal and brain MRI showed no HIA. He was diagnosed as SLE and myelitis (NPSLE) and treated with pulse-steroid, cyclophosphamide iv, and HCQ. His neuropathy had improved in 2 month. We introduced MMF and belimumab consecutively, but each was discontinued because his neurologic symptoms got worse. Finally, anifrolumab was successfully introduced with steroid tapering. [Discussion] MRI-negative myelitis can cause diagnostic delay, leading to poor prognosis. Anifrolumab in the treatment of SLE-related myelitis is rarely reported but can be a promising choice.

P2-100

A case of bullous lupus erythematosus treated with aniflorumab

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Conflict of interest: None

[Background] Anifrolumab (ANI), a human monoclonal antibody to type I interferon (IFN) receptor 1, is effective against systemic lupus erythematosus (SLE). We herein describe a case of bullous lupus erythematosus (BSLE) which improved with anifrolumab therapy. [Case] A 23-year-old, female patient noticed bullae on her palms three weeks before presentation. Two weeks earlier, she noticed bullae on her cheeks, arthralgia, and severe fatigue, which prompted her to visit our hospital. The bullae had grown to 5 cm in diameter and spontaneously resolved before her visit. Test results for antinuclear and anti-smith antibodies were positive while those for anti-desmoglein I/III and anti-BP180 antibodies were negative. SLE was diagnosed and treated with low-dose glucocorticoid (GC) and hydroxychloroquine. ANI was started for persistent fatigue. There was no relapse of BSLE or polyarthritis, and the severe fatigue improved markedly after the second infusion of ANI, allowing the patient to return to

work. [Clinical Significance] BSLE is caused by autoantibodies against type VII collagen. Dapsone is more effective than GCs or HCQ for BSLE. In this case, the patient responded well to anifrolumab, suggesting that the pathophysiology may be related to type I IFN rather than immune complexes.

P2-101

A case of Systemic lupus erythematosus patient developed facial paralysis after pregnancy and delivery was treated with Anifrolumab

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Conflict of interest: None

[Case] A 28-year-old woman with left facial nerve palsy in X-6 years was referred to our hospital because she tested positive for antinuclear antibodies and was diagnosed with SLE due to positive anti-ds-DNA antibodies and hypocomplementemia. She was started on prednisolone and HCQ, and maintained low disease activity since then. Pregnant in X-2, delivery in June X-1, positive anti-ds-DNA antibody and positive urinary protein in February X, MMF were added. After the antibody level decreased, the patient developed right facial paralysis in July X. She was admitted to the hospital for close examination and treatment, and was judged to have NPSLE. The dose of oral prednisolone was increased and improvement of paralytic symptoms. After discharge from the hospital, facial paralysis remained. anifrolumab was introduced and improvement of paralytic symptoms. [Discussion] NPSLE is considered to be a severe condition originating from SLE, and concomitant use of IVCY is recommended. In this case, the use of IVCY was difficult because the patient wished to have a baby. This case suggests the usefulness of anifrolumab for NPSLE.

P2-102

A case of systemic lupus erythematosus complicated by refractory neutropenia successfully treated with rituximab

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Conflict of interest: None

[Case] A 70-year-old woman with a history of immune thrombocytopenia (ITP), systemic lupus erythematosus (SLE), rheumatoid arthritis, and Sjogren syndrome was admitted for pancytopenia. The administration of prednisolone (PSL) 40 mg/day combined with cyclosporine yielded an improvement in anemia and ITP, whereas neutropenia progressed, reaching 547/μL on day 31. A bone marrow biopsy revealed no evidence of other hematological disorders, and antineutrophil antibody was negative. Belimumab and high-dose intravenous immunoglobulin therapy were ineffective, while the initiation of rituximab (RTX 375 mg/m^2/week, for 4 weeks) on day 43 resulted in a gradual increase in neutrophil count (1747/μL on day 79). Approximately one year later, anti-DNA antibody became positive and severe neutropenia recurred (30/μL). In addition to increasing the PSL dose to 20 mg/day, RTX was restarted. Subsequently, the neutropenia slowly improved. [Clinical Significance] Severe neutropenia is rare in SLE but could be a risk factor for infection. Neutropenia may be caused by increased destruction associated with autoantibodies, decreased bone marrow production, and increased apoptosis, but no treatment strategy has been determined. RTX might be a treatment option for refractory neutropenia in SLE.

P2-103

Single-Center Retrospective Analysis of Anifrolumab Treatment Outcomes in 22 SLE Patients

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Conflict of interest: None

Objective: This study aimed to evaluate the effects of Anifrolumab (ANF), an anti-type I interferon receptor antibody, in patients with SLE through a single-center retrospective analysis. **Methods:** We reviewed 22 SLE patients in the maintenance phase who initiated ANF treatment by September 2023. Baseline demographic data, SLEDAI-2K scores, anti-dsDNA levels, prednisolone (PSL) dose, and adverse events through week 36 were assessed. **Results:** Of the 22 patients, 77.3% were female, with a median age of 45.5 years. Treatment targeted skin (68.2%), joint (27.3%), and fatigue symptoms (27.3%). Three of seven biopsied patients had proteinuria. Baseline anti-dsDNA averaged 107.9 IU/L, with 40.9% positive for anti-Sm antibodies. Initial PSL dose averaged 8.8 mg, and 33.2% had prior belimumab use. By week 36, SLEDAI-2K scores, anti-dsDNA levels, and PSL doses significantly decreased, while C3, C4, and proteinuria remained unchanged. LLDAS rates rose from 0% to 60%. Discontinuation occurred in 31.8% due to herpes zoster (9.1%), respiratory infections including COVID-19 (18.2%), and lack of efficacy (31.8%). **Conclusion:** ANF reduced disease activity and PSL needs in SLE patients with skin, joint, and fatigue symptoms. Long-term studies comparing ANF with other therapies are recommended.

P2-104

Successfully treated by fostamatinib for thrombocytopenia associated with systemic lupus erythematosus

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Conflict of interest: None

[Case] A 36-year-old female. [Clinical Course] She was diagnosed with idiopathic thrombocytopenic purpura when she was 10 years old and was treated with prednisolone (PSL) 5~10 mg. In April 2024, fever and arthritis, thrombocytopenia appeared at the same time. She was diagnosed with systemic lupus erythematosus based on positive anti-nuclear antibody titer (>1:80), anemia, low platelet counts, low C4 counts, and positive for antiphospholipid antibodies. Her platelet counts dropped to 31,000/mm^3, the dose of PSL was increased from 5 mg to 10 mg in June 2024, thus fostamatinib was started for thrombocytopenia, and hydroxychloroquine was started for SLE in July 2024. Platelet counts were recovered in 11 days to over 100,000/mm^3, and symptoms of fever and arthralgia disappeared. Currently, the dose of PSL has been reduced to 7 mg without SLE relapse, including thrombocytopenia. [Clinical Importance] Fostamatinib blocks the activity of the enzyme spleen tyrosine kinase. It was approved for chronic idiopathic thrombocytopenic purpura and its therapeutic efficacy for thrombocytopenia associated with SLE was unclear. We report this case because it was suggestive that the additional use of fostamatinib for thrombocytopenia associated with SLE may minimize the use of glucocorticoid.

P2-105

A case of a successful response to eculizumab in a patient with SLE presenting with refractory thrombotic microangiopathy

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Conflict of interest: None

A 22-year-old man had hair loss for 2 months, edema and low-grade fever for 3 weeks. He was referred to our hospital because of pancytopenia, hematuria, proteinuria, and renal disorder. He was found to have alopecia, sun sensitivity, stomatitis, positive antinuclear antibody, positive anti-dsDNA antibody, low complement level, renal failure, thrombocytopenia, hemolytic anemia, and fragmented red blood cells, and was judged

to have SLE and TMA. Glucocorticoid pulse therapy, high-dose glucocorticoid therapy, IVCY, plasma exchange, and hemodialysis were started, but thrombocytopenia and hemolytic anemia persisted. RTX was added on the 12th day, and finally, he completely lost his hematuria. Withdrawal from red blood cell transfusion and plasma exchange was difficult due to prolonged TMA, and eculizumab (ECZ) was started on the 41st day. After the initiation of ECZ, auturia was observed, platelet count gradually increased, and the number of broken erythrocytes decreased. On the 113th day, she underwent plasma exchange, and on the 116th day, he was weaned from hemodialysis. Although complications such as hemorrhage and infection were observed during the course of her treatment, her general condition improved, and she was discharged from the hospital on the 156th day.

P2-106

The roles of small EVs for B cell differentiation in Systemic Lupus Erythematosus (SLE)

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Conflict of interest: None

[Objectives] The objective of this study is to investigate whether small EVs contribute to the differentiations of Age-associated B cells (ABCs)/ Antibody-secreting cells (ASCs) in SLE. [Methods] 1. Naïve B cells from healthy controls (HCs) were stimulated in vitro with various cytokines to promote ABCs/ASCs. 2. Naïve B cells were stimulated with small EVs, extracted from the plasma of HCs or untreated SLE patients, under the same condition as method 1. 3. miRNAs in small EVs from HCs and SLE patients were evaluated by microarray. [Results] 1. TLR7 and IFNγ induced the differentiation of ABCs and ASCs. 2. Small EVs decreased the proportion of ABCs and increased ASCs. compared to HC-derived small EVs, those from SLE patients significantly promoted the differentiation of ASCs. 3. The principal component analysis showed distinct expressions of miRNAs between HCs and SLE patients. [Conclusion] Small EVs derived from SLE patients significantly promoted the differentiation of ASCs.

P2-107

Role of fatty acid elongase Elovl6 in mice model of systemic lupus erythematosus

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Conflict of interest: None

[Objectives] To clarify the effect of lipid metabolism in pathogenesis of systemic lupus erythematosus (SLE) using its mice model. [Methods] 1) Elovl6 expression in organs of wild-type (WT) mice inducing lupus-like pathology by imiquimod (IMQ) was analyzed by quantitative PCR (qPCR). 2) Immune cell subsets were isolated from spleen in lupus-induced mice by magnetic-cell sorting, and Elovl6 expression was examined by qPCR. 3) Phenotype was evaluated in WT mice and Elovl6 knock out (KO) after the induction of lupus. Functional subset and cytokine production of CD4+ T cells isolated from the spleen and lymph nodes of WT and KO mice were analyzed by flow cytometry and ELISA. [Results] 1) Elovl6 expression was decreased in the liver of IMQ-treated mice compared with untreated control mice. 2) Elovl6 expression was also decreased in splenic CD4+ T cells of IMQ-treated mice compared with control mice. 3) Lupus-like pathology and functional subset variation and cytokine production of CD4+ T cells in IMQ-treated WT and KO mice are now under investigation. [Conclusion] Decreased expression of Elovl6 in liver and splenic CD4+ T cells in IMQ-induced lupus model mice suggested the possibility that alternation of fatty acid metabolism might be involved in the pathology of SLE.

P2-108

Analysis of the Pathogenic Significance of the Transcription Factor T-bet in TLR7 Agonist-Induced SLE Model Mice

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Conflict of interest: Yes

[Objectives] To investigate the involvement of transcription factor T-bet in imiquimod (IMQ) induced SLE model mice. [Methods] C57BL/6 T-bet knockout (KO) mice and wild-type (WT) mice were administered IMQ for 8 weeks. 1) T-bet expression in CD4+ T cells and CD19+ B cells in the spleens of WT mice was analyzed using flow cytometry (FCM). 2) Levels of anti-dsDNA IgG antibodies, urinary protein, renal pathology, and immune complex deposition in the glomeruli were compared between WT and KO mice. 3) Subsets of T and B cells in the spleens of WT and KO mice were analyzed using FCM. CD4+ T cells from the spleens were stimulated in vitro, and cytokine production was analyzed by FCM. [Results] 1) In IMQ-induced WT mice, T-bet expression in CD4+ T cells and CD19+ B cells was higher than controls. 2) 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. 3) KO mice exhibited decreased Tph cells and IFNγ production from CD4+ T cells. No significant differences were noted in B cell subsets. [Conclusion] T-bet may be involved in the development of SLE by regulating CD4+ T cell differentiation, cytokine production, and promoting immune complex formation.

P2-109

A Study of Decreased Treatment Satisfaction in Rheumatoid Arthritis Patients of Different Generations-Characteristics of Pain Symptoms and Unmet Medical Needs-

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Conflict of interest: None

[Introduction] This study compared the characteristics of decreased treatment satisfaction in RA patients across generations. [Methods] A self-administered questionnaire was used to investigate the degree of treatment satisfaction (NRS) and factors contributing to decreased treatment satisfaction in 126 RA patients (59.8±12.3 years old) undergoing outpatient treatment. Patient attributes (age, gender, disease duration, Steinbrocker Class/Stage, CDAI, DAS28-CRP, HAQ) and pain symptoms (site, Pain-VAS, PDAS, PSEQ) were compared between mature and elderly patients. [Results] There were no significant differences in treatment satisfaction, patient characteristics, or pain symptoms between generations, but there were significant differences in pain location ($p<0.05$). Decreased treatment satisfaction was characterized by pain, fatigue, anxiety about deformity, and contractures, which were common to all generations. On the other hand, the mature age group was characterized by inadequate family roles and social participation, and the elderly age group by inadequate activities of daily living. [Discussion] In this study, the influence of different pain symptoms and impaired ability to cope with them among generations was suggested as a factor in the decrease in treatment satisfaction.

P2-110

Study on the proactiveness of health care of rheumatoid arthritis patients living in the community

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Conflict of interest: Yes

Introduction: Active participation in treatment is essential to improve treatment satisfaction and quality of life of rheumatoid arthritis patients. In this study, we investigated the proactiveness of health management among RA patients living in the community. **Methods:** Ninety-one RA patients (59.4±12.8 years) were included in the study to investigate their positive attitude toward health care (PAM-13) and related factors. Patient characteristics (age, gender, disease duration, Steinbrocker Class/Stage, DAS28-CRP, and HAQ) and pain symptoms (Pain-VAS, PDAS, and PSEQ) were evaluated and compared in terms of the level of proactivity toward health management (4 levels). **Results:** PAM-13 classification was done in 30% of patients in the first stage, 26% in the second and third stages, and 18% in the fourth stage. There were no significant differences in patient demographics among the tiers, but there were significant differences in PDAS and PESQ ($p<0.05$). PAM-13 was correlated with DAS28-CRP, Pain-VAS, PDAS, and PSEQ. **Discussion:** This study suggests that residual pain and pain perception may have an impact even when patients maintain good disease activity, and that residual pain should be the subject of rehabilitation therapy to improve the quality of life of RA patients.

P2-111

A Study of Issues in Rehabilitation Medicine for Rheumatoid Arthritis -Intergenerational Comparison of Self-Perceptions of Rehabilitation-Related Job Functions-

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Conflict of interest: None

[Introduction] In addition to the decrease in treatment opportunities, there is concern that the quality of rehabilitation treatment for RA is declining due to the increasing youthfulness of therapists and the concentration of treatment facilities. In this study, we investigated the self-efficacy of clinical skills of therapists working at RA treatment facilities. [Methods] 64 therapists (30.1 ± 7.4) from 4 RA-specialized centers were included. Self-efficacy in RA rehabilitation treatment was quantified by NRS and compared among generations in terms of age, years of clinical experience, and number of RA patients handled per day. [Results] Generational differences were observed in self-efficacy for clinical skills such as evaluation, treatment, and prevention of deformity. Younger generations had a greater sense of urgency regarding inexperience. [Discussion] Rehabilitation therapy has reached a major turning point. The reconstruction of a rehabilitation treatment system that not only improves function and ability, but also contributes to treatment satisfaction and quality of life, and the education of therapists is an urgent issue.

P2-112

Comparison of older rheumatoid arthritis patients and community-dwelling older adults with sarcopenic obesity: A propensity score matching study

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Conflict of interest: None

[Objective] Compared to simple sarcopenia and obesity, sarcopenia obesity (SO) has been reported to be associated with poor functional outcomes. The purpose of this study was to clarify the characteristics of SO in older patients with rheumatoid arthritis (RA). [Methods] RA patients aged 65 to 75 years and community-dwelling older adults were included, and subjects were matched using propensity scores (covariates: age, gender). SO was diagnosed in subjects based on the SO diagnostic criteria in Japan published in September 2024. Statistical analysis compared the prevalence of SO and index value of SO components (body mass index [BMI], body fat percentage, hand grip strength, and BMI-corrected limb skeletal muscle) between RA patients and community-dwelling older adults. [Results] Thirty-one RA patients and community-dwelling older adults were recruited. The prevalence of SO was 6.5% in RA patients and 0% in community-dwelling older adults. RA patients had a significantly higher body fat percentage and lower grip strength than community-dwelling older adults. [Conclusions] The prevalence of SO was higher in RA patients compared with community-dwelling older adults. To improve functional outcomes in RA patients, it may be necessary to address both excess body fat and muscle weakness.

P2-113

Practice of online music therapy for patients with rheumatoid arthritis by using body percussion and 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). Since the COVID-19 pandemic, we switched the activity to online since 2020. In this study, we investigated the effects of online music therapy by using body percussion and chair dance. [Methods] Zoom online meeting system was recruited. Five songs were sung with piano accompaniment, two songs were performed body percussion, and one song was danced sitting in a chair. 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] Six female patients with RA (one 40s, one 50s, three 60s, and one 70s) were investigated. The median of HAQ-DI was 0.188. The results of before/after the activity were; GH 1.5/1.5, pain 2.8/2.5, positive affect of PANAS 22.8/24.2, and negative affect of PANAS 16.5/16.5, and four subscales of ERS were 9.7, 11.2, 10.2, 10.5, respectively, which suggested the improvement of physical and psychological condition in patients with RA. [Conclusions] On line active music therapy by using body percussion and chair dance improves the condition of patients with RA.

P2-114

Development of Assistive Chopsticks for Mild Finger Function Impairments using a 3D Printer - Thick Grip, Leaf Spring Mechanism, and Anti-slip Feature

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Conflict of interest: None

[Objective] Developed assistive chopsticks for upper limb impairments. [Method] Designed using 3D-CAD and printed with PLA using a 3D printer. [Results] Used plastic bento chopsticks without left-right difference. Created a cylindrical grip (9 mm radius, 35 mm length) with a 4.5 mm hollow core, tapered for chopstick angles. Designed a 2 mm thick leaf spring mechanism. Cut the grip cylinder parallel to its long axis to fix the spring. Developed parts to prevent chopstick tips from slipping when closed. Cost was 50 yen, print time 50 minutes, weight 11 g. [Discussion] Mild finger impairments make it difficult to grip thin supports, so we designed the support part with an 18 mm diameter. Installed a 2 mm thick leaf spring in the grip to address issues with releasing chopsticks due to finger deformities and muscle weakness. The spring's strength can be adjusted by thickness and is replaceable. Limited finger movement causes misalignment in pinching actions; a convex-concave fitting mechanism was introduced to prevent slipping. Commercial assistive chopsticks are costly (880-3850 yen); ours cost about 150 yen to make. [Conclusion] Using a 3D printer to create assistive chopsticks for upper limb impairments is beneficial for improving ADL.

P2-115

Development of a Modular Grip-Type Assistive Device for Severe Finger Function Impairments using a 3D Printer - Hook, Point, and Press Parts

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Conflict of interest: None

[Objective] Developed a modular grip-type assistive device for severe finger function impairments. [Method] Designed using 3D-CAD and printed with PLA using a 3D printer. [Results] The grip is cylindrical (30 mm diameter, 80 mm length) with 10 mm circular holes for ventilation. Auxiliary parts are fitted at both ends, with fixed pins designed as headless pins. Created three types of auxiliary parts: hook, point, and press. Variations in size, angle, and length were also made. Additionally, parts for grip bands were developed. The running cost was 200 yen, print time was 5 hours and 40 minutes, and weight was 47 g. [Discussion] Severe finger function impairments often limit daily living activities due to deformities and muscle weakness. We developed an assistive device that grips and bands to the hand, with auxiliary parts connected at the ends. The hook part allows for opening bags or pulling objects through holes. The point part enables the use of a computer keyboard. The press part allows for pressing down vegetables while cutting. This device has various uses, thus improving ADL. Various auxiliary parts can be added based on ideas. [Conclusion] Using a 3D printer to create assistive devices not commonly available in the market appears useful for improving ADL.

P2-116

Development of Assistive Scissors for Moderate Finger Function Impairments using a 3D Printer - Improved Spring Mechanism Parts

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Conflict of interest: None

[Objective] Developed an assistive device for scissors to aid moderate finger function impairments. [Method] Designed using 3D-CAD and printed with PLA using a 3D printer. [Results] Created parts to improve "smart scissors" available at 100-yen shops. Designed parts to fix with zip ties on both ends of the handles. The parts are rectangular (5×2.5×0.8 cm) with rounded surfaces and added holes for zip ties. Running cost was 40 yen, print time 40 minutes, weight 9 g. The parts can be used by gripping the ends ("grip use") or placed on a table and pressing the upper part ("table use"). [Discussion] Upper limb impairments make it difficult to insert fingers into regular scissor handles and open them. Spring-type stick scissors are an option if gripping is possible, but commercial ones have thin handles that are hard to grasp. Designed parts with longer width for three fingers and shorter height for finger hooking. Made the bottom surface rounded for table use. Commercial assistive scissors are expensive (1600-5500 yen), but our parts cost about 150 yen and are half to two-thirds the weight. [Conclusion] Creating assistive scissor devices using a 3D printer is beneficial for improving ADL.

P2-117

Introduction and practice of a consultation room-rehabilitation room information sharing system in early rehabilitation of rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] It is important to establish a system that allows close sharing of medical information between the examination room and the rehabilitation room because anti-rheumatic drugs can cause dramatic physical changes in the early stage of rheumatoid arthritis (RA) onset. [Methods] A shared sheet in the electronic medical record was used as a shared medical record. As information in the examination room, the physician recorded the RA activity and treatment medications on the shared sheet. The physical and occupational therapists (PT/OT) recorded data on joint findings, muscle strength, and range of motion, and planned and practiced rehabilitation based on information from both rooms, and recorded the details on the shared sheet. [Results] The PT/OT were able to introduce rehabilitation and modify the rehabilitation program in accordance with the timing of treatment. Physicians could also check the status of rehabilitation achievement and changes in RA joint symptoms assessed by PT/OT on the shared sheet. [Conclusion] We are able to exchange information instantaneously by introducing a shared sheet between the examination room and the rehabilitation room in the electronic medical record. Collaboration between the two rooms made it possible to provide treatment better.

P2-118

Longitudinal analysis of locomotive syndrome progression and physical function decline in rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] Patients with rheumatoid arthritis (RA) suffer from physical dysfunction, which is a cause of locomotive syndrome (LS). The purpose of this study was to investigate the relationship between physical function and deterioration of LS in RA patients longitudinally. [Methods] A prospective cohort study on frailty in RA patients (Fairy study) was used. The number of patients who did not have LS at the first year was 200. Patient background, disease activity, physical function, and body composition were compared between the progression group that became LS at the second year and the non-progression group that remained non-LS. Associated factors of progression groups were examined in multivariate analysis. [Results] Of the 200 patients, progression/non-progression group was 14%/86%. Age was 63/63 years (P=0.83), DAS28-CRP was 1.94/1.94 (P=0.98), walking speed was 1.23/1.24 m/sec (P=0.78), TUG was 11.1/9.2 sec (P=0.04). Basal metabolic rate was 1030/1058 kcal (P=0.51), total muscle mass was 36/37 kg (P=0.77) and SMI was 6.4/6.4 (P=0.99). Gait speed, 2-step test value, and Sit to Stand-5 test were associated factors. [Conclusion] Maintenance of physical function may contribute to the prevention of progression of LS in RA. It is important to evaluate gait speed and lower limb muscle strength.

P2-119

Association Between Rheumatoid Arthritis and Passive Smoking

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Conflict of interest: None

Background: Smoking is a known risk factor for rheumatoid arthritis (RA). The role of passive smoking, however, remains unclear. This study explored the association between passive smoking, specifically exposure from adult cohabitants, and RA risk. **Methods:** A cross-sectional study was conducted from November 2022 to January 2023, and June 2024, involving 192 RA patients from JR Hiroshima Hospital and 193 healthy individuals. A questionnaire collected information on active smoking, passive smoking exposure in childhood (parental smoking), adulthood (cohabitant smoking), workplace exposure, and periodontal disease history. Multivariate logistic regression analysis was used to identify factors associated with RA. **Results:** Cohabitant smoking during adulthood was more prevalent among RA patients than controls (64% vs. 31%, p<0.0001). Multivariate analysis confirmed adult cohabitant smoking as an independent risk factor for RA (odds ratio 1.98, 95% CI 1.03-3.83). No significant associations were observed with parental smoking, workplace exposure, or designated home smoking areas. **Conclusion:** Exposure to cohabitant smoking in adulthood may increase RA risk. Further studies are needed to clarify how passive smoking influences disease activity in RA patients.

P2-120

The mechanism of the activation of rheumatoid arthritis synovial fibroblasts by histone H3K36 methyltransferase NSD2

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Conflict of interest: None

[Objectives] Epigenetic mechanism dysregulation has been suggested to be associated with the pathogenesis of rheumatoid arthritis (RA). Methylation of histone H3 lysine 36 (H3K36) is positively correlated with active gene transcription. We investigated the mechanism by which H3K36 methylation regulates the activation of RA synovial fibroblasts (SFs). [Methods] SFs were isolated from synovial tissues obtained from RA or osteoarthritis patients during total knee joint replacement. We examined which H3K36 histone methyltransferases (HMTs) were aberrantly expressed in RASFs. We investigated changes in demethylation of H3K36 (H3K36me2) levels and mRNA levels of RA-associated genes upon small interfering RNA-mediated depletion of the identified HMT genes. [Results] H3K36-specific HMT NSD2 was highly expressed in RASFs. Silencing of NSD2 decreased H3K36me2 levels and mRNA levels in matrix-degrading enzyme, cytokine, and chemokine genes in RASFs. [Conclusion] Active transcription of matrix-degrading enzyme, cytokine, and chemokine genes is suggested to be regulated by H3K36me2 via NSD2 in RASFs. Because suppression of NSD2 expression can simultaneously repress the expression of many genes associated with the pathogenesis of RA, NSD2 might be a candidate target of a new therapeutic agent for RA.

P2-121

Analysis of Type I IFN signaling-mediated regulatory T cell dysfunction in elderly-onset arthritis

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Conflict of interest: None

[Objectives] To clarify age-related changes of Tregs in RA patients and GIA mice [Methods] 1) RNA-seq of Tregs from aged and young healthy subjects (HC) and untreated RA patients was performed. 2) Tregs were isolated from young and aged GIA and naïve mice, and their functions were evaluated by suppression assay and cell metabolism assay. 3) CD4+ T cells were isolated from inguinal lymph nodes of GIA and control young and aged mice, and scRNA-seq was performed to analyze the DEGs in Treg clusters. 4) Functional changes in young and aged Tregs induced by IFN-β were evaluated by suppression assay and qPCR. [Results] 1) Aged Tregs were less activated than young ones in RA, and this difference was not detected in HC. In addition, pathway analysis of genes that varied between young and aged RA Tregs showed that IFN-related pathways were enriched. 2) Aged Tregs showed lower inhibitory function and OCR under GIA. 3) Treg clusters from aged mice showed enhanced type I IFN signaling. 4) Treatment with IFN-β resulted in decreased suppressive function of aged Tregs and increased expression of PD-1. [Conclusion] It was suggested that in elderly-onset arthritis, type I IFN signaling in aged Tregs was enhanced and PD-1 expression was elevated, leading to the impaired function.

P2-122

Immune Checkpoint Molecule Landscape in T-cell Subsets: An Exploratory Study of Seropositive and Seronegative Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To identify differences in immune checkpoint molecule expression in T cells between seropositive (SP) and seronegative (SN) RA using mass cytometry. [Methods] We analyzed T-cell subsets from 16 SP-RA and 17 SN-RA patients for 25 markers, focusing on activation (HLA-DR, CD38), apoptosis (Fas), costimulatory (CD28, ICOS, OX40, 4-1BB), and coinhibitory (CTLA-4, PD-1, LAG-3, Tim-3) molecules. Comparative analyses used the Mann-Whitney U test with Benjamini-Hochberg correction (FDR $q < 0.05$). [Results] Key checkpoint molecules showed differential expression: CTLA-4 on Tregs, and 4-1BB on naïve Tregs. In effector memory CD8 cells, CD28, ICOS, PD-1, and 4-1BB levels varied. Naïve T-cell analysis revealed Fas, PD-1, and 4-1BB differences in naïve-CD4 T cells, with 4-1BB also differing in naïve-CD8 T cells and CD4-CD8- T cells. For naïve CD4+ T cells, 4-1BB expression showed a median of 0.27 (IQR 0.35-0.64) in SP-RA and 0.52 (0.67-0.98) in SN-RA, remaining significant after FDR correction ($q = 0.041$). [Conclusion] The differential expression of 4-1BB in naïve CD4+ T cells suggests potential links to metabolic and self-reactivity differences associated with SP-RA and SN-RA pathogenesis, providing new insights into RA pathophysiology.

P2-123

Alteration of CD4+ T cells with aging in arthritis model mice

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Conflict of interest: None

[Objective] To investigate the alteration in the proportion of CD4+ T cell subsets and the function with aging using GPI-induced arthritis (GIA) model mice. [Methods] 1) CD4+ T cells among lymph nodes from young and old GIA day 14 mice were analyzed by scRNA-seq. 2) The proportion and surface molecules of CD4+ Eomes+ T cells among spleens and lymph nodes from young and old GIA and control mice were evaluated by flow cytometry (FCM). 3) The Senescence Associated Secretory Phenotype (SASP) factors produced by CD4+ Eomes+ T cells from young and old GIA day 14 mice were investigated by FCM. [Results] 1) scRNA-seq revealed that *Eomes* was more highly expressed in CD4+ T cells from old GIA mice than young mice. 2) FCM analysis revealed that the proportion of CD4+ Eomes+ T cells in GIA mice was increased compared to control mice, and the difference was more remarkable in old mice. In addition, CCR5 expression was found to be higher in CD4+ T cells with increased Eomes expression. 3) The expression levels of some SASP factors were

altered with aging. [Conclusion] We elucidated that Eomes expression among CD4+ T cells was upregulated in GIA mice. These results raised a possibility that CD4+ Eomes+ T cells may play an important role in the pathology of elderly onset GIA.

P2-124

Analysis of characteristics of patients with difficult-to-treat rheumatoid arthritis

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Conflict of interest: None

[Objectives] The objective of this study is to determine the clinical characteristics and frequency of mode of action (MOA) changes in patients with refractory rheumatoid arthritis (D2TRA). [Methods] Twenty D2TRA patients and 118 non-D2TRA patients treated with biologics and JAK inhibitors (b/tsDMARDs) were included in the study to determine age, gender, disease duration, time to b/tsDMARD initiation, MTX and PSL use, disease activity indicators (DAS28-ESR, CDAI, SDAI), RF, CRP, ESR, and bone mineral density (BMD) of the lumbar spine and femoral neck. [Results] Compared to non-D2TRA patients, D2TRA patients had longer disease duration (24.8±8.4 vs. 18.3±12.7 years, p=0.008), time to b/tsDMARD initiation (11.9±6.0 vs. 10.2±10.8 years, p=0.05), number of b/tsDMARDs used (4.3±1.8 vs 2.0±1.7, p<0.001), DAS28-ESR (3.6± 0.5 vs 2.5±0.9, p<0.001) and RF values (240.3±255.6 vs 116.6±194.8, p=0.009). There were no significant differences in age, gender, MTX or PSL use, or BMD; MOA was changed more frequently in D2TRA patients (38.9% vs. 22.5%). [Conclusion] Patients with D2TRA are characterized by prolonged disease, delayed treatment initiation, high disease activity and RF values, suggesting treatment resistance.

P2-125

Longitudinal Analysis of Central Sensitivity Syndrome in Rheumatoid Arthritis Patients and Examination of Persistence Factors

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Conflict of interest: None

[Objectives] This study aimed to conduct a longitudinal investigation of central sensitivity syndrome (CSS) in rheumatoid arthritis (RA) patients and to identify the clinical characteristics of those in whom CSS does not improve. [Methods] The study involved 220 RA patients who were receiving outpatient treatment at our hospital between 2021 and 2024. Of these, 53 patients were identified as having CSS and were followed for at least six months. The presence of CSS was determined using the Central Sensitization Inventory (CSI), with a CSI score of ≧40. Patients whose CSI score remained ≧40 after one year were classified as the CSS persistence group, while those whose score decreased to <40 were classified as the CSS improvement group. A comparative analysis was conducted between the two groups. [Results] At baseline, there were no significant differences in the number of swollen or tender joints, CRP, ESR, PtGA, PhGA, pain VAS, DAS28 CRP, or CDAI between the two groups. However, CRP was significantly lower in the persistence group (CSS persistence group: 0.34± 0.89 mg/dL, CSS improvement group: 1.99±3.98 mg/dL). [Conclusion] Lower levels of inflammation could be associated with the persistence of CSS in RA patients.

P2-126

Evaluation of the Flare defined on ARD in our institute's cohort dataset

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Conflict of interest: None

[Objectives] To verify disease activity Flare in rheumatoid arthritis (RA) as defined by the Annals of Rheumatic Diseases (ARD). [Methods] We used a cohort dataset of RA patients treated at our hospital. Flare is defined as when the Health Assessment Questionnaire (HAQ) has increased by 0.125 or more compared to 3 months prior, and the Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) are calculated using the cutoff obtained from receiver operating characteristics. The cutoff index (COI) was adopted and compared with the ARD definition. Changes were classified by comparing clinical index values from 3 months before Flare, between groups who experienced Flare (G-Flare) and those who did not (G-nonFlare), and by whether there was a change in the treatment protocol for G-Flare (G-C/G-S); changes over time were compared between groups. [Results] The COI was +4.63 in SDAI and +4.48 in CDAI (ARD definition: SDAI +4.7; CDAI +4.5). Most indicators of G-Flare changed significantly from 3 months ago compared to G-nonFlare. In addition, the change in activity for the G-C was significantly lower than that for the G-S until 1 year after Flare, and HAQ was significantly lower at the final follow-up observation. [Conclusion] The Flare definition was appropriate.

P2-127

Drug Retention Rates of Ozoralizumab in Rheumatoid Arthritis Patients with Chronic Kidney Disease

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Conflict of interest: None

[Background] TNF inhibitors show reduced drug retention rates without methotrexate (MTX) combination therapy. This study aimed to determine whether chronic kidney disease (CKD) serves as a risk factor for discontinuation of ozoralizumab (OZR) therapy. [Objectives] To investigate the impact of CKD on drug retention rates of OZR in patients with rheumatoid arthritis (RA). [Methods] We analyzed 26 RA patients who initiated OZR between April 2023 and July 2024. Patients were stratified into two groups: CKD group (eGFR <60 mL/min, n=10) and non-CKD group (n=16). [Results] The CKD group comprised patients with CKD stage IIIa (n=7), IIIb (n=1), IV (n=1), and V (n=1). Baseline characteristics including gender, age, disease duration, previous bDMARDs/tsDMARDs use, PSL dose, and CRP levels were comparable between groups. However, MTX dose was significantly lower in the CKD group (p<0.05). The 12-month drug retention rates were 37% in the CKD group and 70% in the non-CKD group, showing no significant difference. After adjusting for gender and age, CKD status remained non-significant as a risk factor for OZR discontinuation (HR: 1.79 [95% CI: 0.41-7.80], P=0.44). [Conclusion] CKD was not identified as a significant risk factor for OZR discontinuation in patients with RA.

P2-128

A study of the efficacy and continuation rates of b/tsDMARDs in anti-SS-A antibody positive rheumatoid arthritis patients: the ANSWER cohort study

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Conflict of interest: None

[Objective] The role of anti-SS-A antibodies in rheumatoid arthritis (RA) treatment response remains debated. This study examined the impact of anti-SS-A antibody positivity on treatment efficacy and b/tsDMARDs continuation in RA. [Methods] We retrospectively studied 4,377 RA patients tested for anti-SS-A antibodies who began b/tsDMARDs. Two-year continuation rates were analyzed using survival and Cox proportional hazards models with baseline covariates. Logistic regression assessed if anti-SS-A positivity was linked to achieving low disease activity (LDA). [Results] The anti-SS-A-positive group was younger, predominantly female, had higher RF and ACPA positivity, longer disease duration, and more prior b/tsDMARD use than the anti-SS-A-negative group. Anti-SS-A positivity correlated with a reduced risk of treatment discontinuation (Hazard Ratio, 0.62; 95% CI, 0.40-0.97; p = 0.036). However, it did not significantly predict LDA. [Conclusion] Anti-SS-A antibody positivity was associated with better b/tsDMARD continuation rates but not with LDA achievement. These results suggest anti-SS-A antibodies may indicate treatment persistence, but their role in disease control warrants further study.

P2-129

Clinical Features and Management Approaches for Non-Inflammatory D2T RA

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Conflict of interest: None

[Objectives] D2TRA presents a clinical challenge. This study investigates its clinical characteristics and management. [Methods] We categorized 313 RA patients into 3 age groups (<65, 65-74, >75). Non or low-inflammatory D2TRA defined by CRP<0.14 mg/dL and a PGA-EGA difference>14 mm (n=82, Group A), and those with 0.99>CRP>0.3 and PGA-EGA difference>14 mm (n=69, Group B) were analyzed. [Results] DAS28-CRP, PGA, EGA, and PGA-EGA difference were significantly higher in older age groups. A relationship of PGA=1.17xEGA+14 was observed, with PGA consistently exceeding EGA. Group A showed significantly younger age, earlier onset, and fewer affected joints with lower EGA and PGA values compared to Group B. There were no significant differences in disease duration, serological markers, or medication status. No correlation was found between CRP and PGA distribution in either group. [Discussion] Defining non-inflammatory D2TRA is challenging, but it is characterized by strong subjective complaints and low patient satisfaction despite minimal inflammation, possibly driven by psychological pain. Some features align with inflammatory D2TRA, such as the lack of correlation between CRP and PGA. Management should adhere to T2T strategies, and then addressing psychological and emotional factors.

P2-130

The course of treatment for seronegative rheumatoid arthritis in our hospital

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Conflict of interest: None

[Objectives] To investigate the course of treatment for seronegative rheumatoid arthritis (SNRA) in our hospital. [Methods] The subjects were 22 patients with SNRA who were newly diagnosed in our hospital between April 2021 and March 2024 according to 2010 ACR/EULAR or 1987 ACR classification criteria. Their background and treatment course were analyzed. [Results] Thirteen patients were female and the mean age at diagnosis was 77.0 years. The mean DAS28-CRP was 4.36±4.30, and serum CRP level was 6.1±4.4 mg/dL. Methotrexate was used in 18 cases, salazosulfapyridine in 6 cases, and iguratimod in 1 case. Prednisolone was used in 3 cases. Among 18 patients, DAS28-CRP remission was achieved an average of 23.6 weeks after treatment initiation. DMARDs were reduced after remission in 12 of these patients, and 8 patients achieved drug-free remission after a mean of 112 weeks. One patient with CRP level of 0.70 mg/dL and 3 patients who took 25-79 weeks to achieve remission were able to discontinue DMARDs. [Conclusion] The combination of high CRP levels at diagnosis and early DAS remission within 4 months are considered as predictors of drug-free remission in patients with SNRA. However, it seems possible to attempt to discontinue DMARDs even in patients without these features.

P2-131

A case of rheumatoid arthritis presenting with atlantoaxial subluxation without peripheral arthritis

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Conflict of interest: None

A 43-year-old man was referred to our hospital in X-4 years with intermittent joint pain starting X-9 years prior. Initial blood tests showed CRP at 0.34 mg/dL, RF at 28 IU/mL, and anti-CCP antibody at 254 U/mL. X-rays of hands and feet and musculoskeletal ultrasound revealed no synovitis or bone erosions, suggesting palindromic rheumatism, but his symptoms spontaneously improved, leading to temporary discharge. In January X, he presented with neck and shoulder pain. Blood tests indicated increased CRP, RF, and anti-CCP levels, suggesting polymyalgia rheumatica; he was treated with prednisolone and bucillamine. He returned in September of X with persistent neck pain. Repeated imaging of hands and feet showed no pathological changes; however, cervical X-rays in a flexed position revealed an anterior atlantodental interval of 9.5 mm, diagnosing atlantoaxial subluxation. He was diagnosed with rheumatoid arthritis and treated with methotrexate. [Clinical Significance] Atlantoaxial subluxation, a characteristic spinal manifestation of rheumatoid arthritis, usually appears in long-term cases with high disease activity. It is rarely an initial symptom, underscoring the importance of early diagnosis when atypical symptoms are present, as treatment delays may impact prognosis.

P2-132

Actual use of subcutaneous methotrexate injection for rheumatoid arthritis patients in our hospital

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Conflict of interest: None

[Background] Methotrexate (MTX) is the anchor drug in RA treatment, but many patients cannot take sufficient doses of MTX oral due to adverse events like gastrointestinal symptoms and liver dysfunction. MTX subcutaneous injection (MTX sc) reportedly has fewer adverse events. We examined MTX sc use in our hospital. [Objectives] This study aimed to investigate MTX sc use in our hospital. [Methods] Fourteen patients (all switched from MTX oral) who received MTX sc between September 2022 and January 2024 were evaluated for reasons for switching, MTX sc dose, CDAI at 12 weeks, and discontinuation. [Results] The mean age was 47.9 years, 10 (71%) were female, mean disease duration was 7.6 years, 5 (35%) on b/tsDMARDs, 6 (42%) on csDMARDs, and 3 (21%) on glucocorticoids. The median MTX oral dose was 8 mg/week. Reasons for switching were GI symptoms and fatigue in 9 (64%), intensification in 4 (28%), and hepatic disorder in 1 (7%). Discontinuation reasons were GI

symptoms in 2, injection reactions in 2, and fear of injection in 1. The CDAI of 9 patients improved from 16.9 to 4.4 at 12 weeks (P=0.002). [Conclusion] MTX sc may be an effective option for patients with GI symptoms, liver dysfunction, and inability to use or increase the dose of MTX oral in terms of treatment intensification.

P2-133

Efficacy and safety of subcutaneously administered methotrexate in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives and Methods] Methotrexate (MTX) is the most recommended drug for the treatment of rheumatoid arthritis, but patients often experience side effects such as gastrointestinal (GI) symptoms and liver dysfunction. Subcutaneous MTX (scMTX) is considered to have fewer side effects than oral MTX, so we report the efficacy and safety of 25 patients who switched from oral MTX to scMTX at our hospital from February 2023 to September 2024. [Results] The reasons for switching to scMTX were GI symptoms in 15 patients, hepatic disorder in 5 patients, and insufficient response to oral MTX in 5 patients. The reasons for discontinuation of scMTX were GI symptoms (3 cases), hepatic disorder (1), insufficient efficacy (1), stress for injection (5), and cost burden (1). GI symptoms were relieved in 12 of 15 patients, whereas hepatic disorder was not improved in 4 of 5 patients. In 2 of 5 patients with insufficient response, disease activity was reduced by switching to scMTX even at the same dose as the oral MTX. [Conclusion] ScMTX reduced the GI symptoms of oral MTX, but the effect on liver dysfunction was not clear. In some cases, the change to scMTX reduced disease activity despite the same dose. These results suggest that the change from oral MTX to scMTX may be a useful option.

P2-134

A Background Study of Rheumatoid Arthritis (RA) Administered Subcutaneous Methotrexate (SC MTX)

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Conflict of interest: None

[Background] Experience with subcutaneous methotrexate in the treatment of rheumatoid arthritis is gradually increasing, but the appropriate patient profile is not clear. [Objectives] To clarify the appropriate patient profile for SC MTX. [Methods] We retrospectively evaluated 26 RA patients newly treated with SC MTX at our department from April 2023 to October 2024. [Results] There were 5 males and 21 females, and the mean age at induction was 56.5 years. Twelve patients had SC MTX as the first drug used in their treatment. Of the 14 patients with a history of oral drug use, 7 switched due to side effects and 7 for treatment intensification. At 4 months after induction, the continuation rate on the Kaplan-Meier survival curve was 69.9%. 6 patients overcame nausea side effects by switching to SC MTX. 5 of the 10 discontinued patients had difficulty continuing due to nausea. 2 of them were switched from 2 mg and 4 mg/week doses, but gave up induction due to increased nausea at the 7.5 mg dose. [Conclusion] SC MTX may be suitable for patients with nausea who have difficulty in receiving a sufficient dose of MTX. On the other hand, caution should be exercised regarding the possibility of inducing nausea with even the lowest doses of SC MTX.

P2-135

Efficacy of subcutaneous methotrexate injections in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Methotrexate (MTX) plays a central role in the treatment of rheumatoid arthritis (RA), but oral MTX formulations can cause gastrointestinal disorders and reduced efficacy. Here, we report 17 cases in which MTX was switched to subcutaneous MTX due to these limitations. [Methods] The study subjects were RA patients who had experienced side effects or insufficient efficacy with oral MTX and were treated with injectable MTX. There were 2 males and 15 females, with an average age of 51 years, disease duration of 7.6 years, oral MTX dose of 9.3 mg/week, and treatment period of 6.4 years. The reasons for switching to injectable MTX were reduced efficacy in 4 cases and side effects in 13 cases. [Results] The MTX injection dose was 7.9 mg/week, and of the 13 cases of side effects, symptoms and abnormal test results improved or disappeared, except for one case of liver damage. In addition, the test and disease activity before and after switching to the injectable formulation were SDAI: 8.3±1.8→6.2±1.5, demonstrating the effectiveness of switching. [Conclusion] In cases where oral MTX formulations are ineffective or have side effects such as gastrointestinal symptoms or liver dysfunction, switching to a subcutaneous formulation is useful for optimizing MTX therapy.

P2-136

Comparative study on the introduction of methotrexate (MTX) in oral and subcutaneous formulations for early-stage rheumatoid arthritis patients

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Conflict of interest: None

Objective: MTX can be administered orally (oMTX) or subcutaneously (scMTX). This study compares the differences in patient background and efficacy between the two formulations. **Methods:** We examined 25 newly diagnosed rheumatoid arthritis patients who started MTX between 2022 and 2024, analyzing patient demographics, disease activity before and after initiation, MTX dose at week 24, and the rate of biologic introduction. **Results:** The oMTX group included 20 patients (6 men, 14 women, mean age 66), and the scMTX group had 5 patients (3 men, 2 women, mean age 70), with no significant age or gender differences. The median DAS28-ESR at diagnosis was 4.71 [4.34, 5.38] for oMTX and 6.30 [6.02, 6.57] for scMTX, indicating higher disease activity in the scMTX group. After 24 weeks, the median DAS28-ESR was 2.99 [2.47, 3.71] in oMTX and 3.25 [2.81, 3.58] in scMTX, with remission rates of 35% and 20%, respectively, showing no significant difference. However, the median MTX dose at week 24 differed significantly, with 10.0 mg for oMTX and 15.0 mg for scMTX. Seven oMTX patients advanced to biologic therapy, while no scMTX patients did. **Conclusion:** scMTX was more often selected in cases of higher disease activity, suggesting that adequate MTX monotherapy dosing can be effective even in such cases.

P2-137

High dose subcutaneous MTX can improve rapid radiographic progression in first phase therapy

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Conflict of interest: None

[Objectives/Methods] The recently introduced MTX subcutaneous injection formulation in Japan is reported to have fewer gastrointestinal symptoms and more clinical efficacy than oral formulations. However, there are little reports about improvement of joint destruction. [Results] Of the 24 cases, 7 were restricted from increasing MTX doses due to some side effects. Additionally, 7 cases had worsening RA. Other 10 cases had worsening RA +adverse events about oral MTX. The average dose of oral MTX was 8.6 mg per week, and folic acid was used at an average of 2.4 mg per week. The average volume of the subcutaneous injection MTX formulation was 9.4 mg per week at the start of administration and 12.5 mg at 6 months, with 10 cases using the maximum amount (15 mg syringe). The DAS28-ESR improved from 4.2 before administration to 3.0 ($p<0.05$), 3.1, 3.1 at 1, 3, 6 months ($p<0.01$). Moreover, gastrointestinal symptoms, hair loss, and liver dysfunction improved. Especially, 5 pa-

tients with rapid radiographic progression markedly inhibited joint destruction by high dose (15 mg/week) subcutaneous MTX. [Conclusion] We firstly demonstrated high dose s.c. MTX is effective to reduce RRP. We firstly demonstrated high dose s.c. MTX is effective to reduce RRP.

P2-138

Comparison of Patient Satisfaction Between Methotrexate Subcutaneous Injection Syringe and Pen

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Conflict of interest: None

Objective: Methotrexate subcutaneous injection syringes (scMTX-SY) were approved in September 2022, and administration to rheumatoid arthritis (RA) patients started. In February 2024, the injector was redesigned to a pen-type (scMTX-PEN), featuring a non-visible needle tip and simplified injection technique, deemed highly useful for patients. This study evaluated the impact of switching from scMTX-SY to scMTX-PEN on patient injection experiences. **Methods:** RA patients on scMTX-SY were surveyed using a Visual Analog Scale (VAS) to assess changes in fear, pain during injection, device satisfaction, and continuation intentions upon switching to scMTX-PEN. Surveys were conducted four weeks post scMTX-SY introduction and four weeks after switching to scMTX-PEN. **Results:** Twenty patients participated in the survey. While 80% experienced fear with scMTX-SY, 90% reported no fear with scMTX-PEN. Additionally, 60% expressed dissatisfaction with scMTX-SY, while none did with scMTX-PEN. Moreover, 80% did not want to continue using scMTX-SY, but all preferred continuing with scMTX-PEN. Despite no changes in the drug's properties, injection pain VAS scores significantly reduced from 72 to 28. **Conclusion:** scMTX-PEN, with high patient satisfaction, is expected to enhance treatment adherence.

P2-139

The early therapeutic effect of subcutaneous methotrexate (MTX) in MTX-naïve patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] We investigated the early therapeutic effects of MTX subcutaneous injection (MTX sc) in MTX-naïve rheumatoid arthritis (RA) patients. [Methods] Thirteen MTX-naïve RA patients who were treated with MTX sc and were followed up for 12 weeks were included. Treatment efficacy, and complications were evaluated up to 12 weeks. Treatment efficacy was evaluated using pain VAS and disease activity at 4 and 12 weeks after treatment. [Results] There were 9 females and 4 males, with an average disease duration of 29.5 months, and an average age at the start of sc MTX treatment of 57.5 years. All patients started with 7.5 mg/week of sc MTX, the dose was increased as appropriate. No complications requiring drug suspension occurred during the administration period, but one patient was transferred to another hospital after 4 weeks. The other 12 patients continued MTX sc until 12 weeks, and the average dose at 12 weeks was 12.1 mg/week. Pain VAS scores at 4 and 12 weeks of treatment significantly decreased. The average disease activity of DAS-CRP, SDAI, and CDAI improved significantly at 4 and 12 weeks of treatment. [Conclusion] MTX sc could be controlled pain and disease activity without serious complications. MTX sc was considered to be useful in the initial treatment of RA Phase 1.

P2-140

The analysis of the clinical efficacy and safety of baricitinib for Japanese patients with rheumatoid arthritis (NAOE study)

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Conflict of interest: None

[Objectives] This study evaluated the efficacy and safety of baricitinib (BAR) in patients with rheumatoid arthritis (RA) in Niigata Prefecture, Japan. [Methods] We retrospectively analyzed 192 patients with RA (39 men, 153 women) who were administered with BAR from October 2017 to October 2023. We assessed patient characteristics, treatment response, continuation rate, and adverse events at 52 weeks after the administration. [Results] The mean age was 66.0±13 years, and the mean disease duration was 13.4±11.4 years. Of the patients, 77% were RF-positive, 76% were positive for anti-CCP antibodies, and 9.9% were double negative. CDAI, DAS28-ESR, and serum MMP-3 levels significantly decreased. Events leading to BAR discontinuation were ineffectiveness in 35 patients, adverse events in 10 patients (disseminated zoster, epicarditis, vertigo, the onset of dermatomyositis, colon diverticulitis, death from pneumonia, urticaria, anemia, ileus, mood discomfort in 1 patient each, and unknown in 1 patient. [Conclusion] BAR significantly reduced RA disease activity and had a high continuation rate. Serious adverse events were rare, and good efficacy and safety in the clinical setting were confirmed.

P2-141

Changes in spinal balance including upper cervical spine, bone mineral density, and bone metabolism markers during 5 years of continuous treatment with baricitinib in 19 patients

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Conflict of interest: None

[Objective] We investigated the relationship between BAR treatment and spinal balance and osteoporosis in 19 patients who had been continuously treated with baricitinib (BAR) for 5 years. [Methods] We investigated the relationship between BAR administration, SVA, Atlantodental interval (ADI), Ranawat value, bone mineral density, and changes in bone metabolism markers during the first 5 years after BAR administration. Patient background at the start of treatment was as follows: average age: 74.4 years, disease duration: 7.2 years, SVA: 50.6 mm, ADI: 1.0 mm, Ranawat value: 15.4 mm, femoral neck YAM value: 72.1%, urinary NTX: 39.1nM BCE/mM/Cre. [Results] After 5 years of BAR treatment, disease activity improved to remission to low disease activity with mean DAS28ESR: 2.4, CDAI: 3.8, SDAI: 4.3, mean SVA: 60.3 mm, ADI: 1.1 mm, Ranawat value: 14.8 mm, YAM value: 76.1%, Urinary NTX: 29.6 nM BCE/mM/Cre, eGFR: 72.8 mL/min/1.73 m^2. After 5 years of continuous BAR treatment the number of patients with SVA > 95 mm, which is a concern for ADL impairment, increased by 1 case. The mean YAM and urinary NTX values improved. [Conclusion] Continuation of BAR treatment with controlled disease activity may improve spinal balance, bone mineral density, and bone quality.

P2-142

Evaluation of Persistence in Baricitinib-Treated Rheumatoid Arthritis Patients in Japan: A Prospective Observational Cohort Study (interim analysis)

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Conflict of interest: Yes

[Objectives] To evaluate the persistence of baricitinib (Bari) treatment of rheumatoid arthritis (RA) patients (pts) over 12 months (M) and effectiveness based on disease activity (DA) and PRO in a Japanese real-world setting. [Methods] Data (such as CDAI) was collected at Bari initiation (BL) and post-BL visits (1/3/6/12/18/24M) from Japanese adult Bari-naive RA pts. The primary endpoint is 12M persistence. This presentation shows the data collected from BL to 12M. [Results] The mean age of 353 analyzed pts was 63.4 years; 79% were female; 65.7% had a history of bDMARDs use. The mean BL CDAI and Pain-VAS were 20.03 and 48.4 mm. 12M persistence was 70%, with 106 pts discontinued. Main reasons for discontinuation (DC) were primary nonresponse (35 pts, 9.9%), secondary loss of response (23 pts, 6.5%), and adverse event (AE) (10 pts, 2.8%). Mean changes from BL in CDAI and Pain-VAS at 1/3/6/12M were -9.77/-11.68/-11.75/-13.12 and -15.7/-21.5/-19.7/-19.4 mm. [Conclusion] Pts' background was similar to that in postmarketing surveillance study in Japan. 12M persistence was 70%. The main reason for DC was ineffectiveness and the number of DC due to AE was low. Similar to clinical trials, early improvement on DA and PRO, and its persistence were observed in a real-world setting.

P2-143

Analysis for the efficacy of Filgotinib in patients with RA

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Conflict of interest: Yes

[Objectives] To elucidate the efficacy and safety of Filgotinib for RA patients. [Methods] 40 patients of RA, 25 females and 5 males, with average age of 58.6 years, 37 cases of 200 mg and 3 of 100 mg for Filgotinib, with average disease duration of 10.9 years, MTX 32.5%, PSL 17.5%, 7 for naïve and switch for 33 cases, 87.5% positive of RF, 80% positive for CCP antibody were analyzed for DAS28 (CRP), and RF at baseline and 24 weeks. Continuation rate was analyzed with Kaplan-Meier method for 48 weeks. [Results] DAS28 (CRP) was decreased significantly from 4.93 at baseline to 2.39 at 24W. RF was also significantly decreased from 212 IU/ml to 133 IU/ml. Remission rate was 67% at 24W. Continuation rate was 93.2% at 48W and DAS28 (CRP) at correlated with continuation. [Conclusion] Filgotinive is effective and safe in real world clinical level for RA.

P2-144

Treatment outcomes of Filgotinib in patients with rheumatoid arthritis at our hospital

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Conflict of interest: None

[Objectives] Examining the treatment outcomes of Filgotinib used for RA. [Methods] We examined 20 RA cases treated with Filgotinib. Cases were followed for an average of 16±9.8 months. [Results] The average age was 72.9±9.3 years; disease duration was 21.4±17.4 years. Stage classification: III in 3 cases, IV in 10 cases. Mean DAS28-ESR score was 5.2±1.6 (high disease activity in 8 cases, moderate in 11). Mean RF value was 362±572 (IU/ml), mean MMP3 value was 279±255 (ng/ml). 15 cases started with 100 mg/day, 5 with 200 mg/day. 15 cases started without MTX. 10 cases had coexisting pulmonary diseases like interstitial pneumonia. 13 cases had history of orthopedic surgery. According to JCR guidelines, phase 2 usage in 7 cases and phase 3 in 13. 6 cases had difficult-to-treat RA. 2 cases discontinued treatment within one month. Kaplan-Meier survival analysis, with treatment discontinuation as the endpoint, showed a survival rate of 90%. The recombinant zoster vaccine was administered to 6 cases. One case developed shingles without a vaccination history. [Conclusion] Among Filgotinib-treated cases, half had coexisting pulmonary diseases, 30% had difficult-to-treat RA, and 65% were in phase 3. Despite these challenges, a follow-up period of 16±9.8 months showed a continuation rate of 90%.

P2-145

Two cases of biologic-naive patients with rheumatoid arthritis complicated by interstitial pneumonia treated with filgotinib

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Conflict of interest: None

[Case 1] A 75-year-old woman. At first visit, RF 25, anti-CCP antibody 251, MMP-3 299.3 ng/ml, KL-6 224 U/ml, DAS28-ESR 5.89, SDAI 30.4, and chest HRCT showed NSIP-like interstitial lung disease (ILD). Treatment was started with SASP, and 2 months later, filgotinib (FIL) 200 mg/day was introduced. 12 weeks after the introduction of FIL, echo remission was achieved with MMP-3 31.2 ng/ml, DAS28-ESR 1.89, SDAI 2.03. Echo remission was maintained 48 weeks, and no exacerbation of ILD was observed. [Case 2] A 73-year-old woman. At first visit, RF 168, anti-CCP antibodies 83.3, MMP-3 105.7 ng/ml, KL-6 376 U/ml, DAS28-ESR 5.78, and SDAI was 26.05. Chest HRCT showed NSIP-like ILD and infiltrative shadows suggestive of partially organizing pneumonia. Treatment was started with MTX 6 mg/week, two months later, FIL 200 mg/day was introduced. And 12 weeks later, echo remission was achieved with MMP-3 43.8 ng/ml, DAS28-ESR 2.2, and SDAI 1.04. Echo remission was maintained 48 weeks, and chest HRCT showed disappearance of infiltrative shadows and reduction of reticular and ground-glass opacities. [Clinical Significance] There has been a lot of experience with the use of tofacitinib and baricitinib for RA-ILD, but there are also cases of FIL in which remission was rapidly achieved without exacerbating ILD.

P2-146

A review of the use of filgotinib in rheumatoid arthritis in our department

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Conflict of interest: None

Methods: We analyzed 42 consecutive patients who started filgotinib (FIL) treatment for rheumatoid arthritis (RA) in our department from January 2021 to March 2024. Results: Median age was 70 years, with 81% female patients. 85.7% were ACPA-positive, and 16.7% had comorbid interstitial pneumonia. 73.8% switched from b/tsDMARDs, with 31% from other tsDMARDs. 45.2% used concomitant MTX, and 35.7% used PSL (median dose 6 mg/day). 26.2% started with a reduced FIL dose of 100 mg/day, mainly due to renal dysfunction. 85.7% of patients continued treatment for a median of 13.5 months. 14.3% discontinued after a median of 3.5 months. No serious infections were observed. Among continuing patients, 27.8% used concomitant PSL at the latest observation, with reduced doses compared to initiation. Conclusion: Our hospital's experience suggests that FIL demonstrates high efficacy and continuation rates for RA, with potential for PSL dose reduction.

P2-147

Efficacy and safety of Filgotinib (100 mg) in patient with rheumatoid arthritis in a routine care

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Conflict of interest: None

[Objectives] Filgotinib (FIL) is a JAK inhibitor that has been prescribed in a routine care in Japan since 2020. There are a few studies that have examined the efficacy of FIL begun at one-half dose (100 mg) in Japanese patients with rheumatoid arthritis (RA) in a routine care. In this study, we investigated the long-term efficacy of FIL in Japanese patients with RA. [Methods] RA patients treated with FIL for longer than 1 years were included in this study. We retrospectively reviewed the efficacy (DAS28-CRP), discontinuation of FIL therapy and adverse events. [Results] Fourteen patients were included in this study. Mean age was 74

years old and concomitant methotrexate rates are 64% (2 mg and 4 mg groups, respectively). 6 patients were naïve to biologic DMARDs and JAKi. Mean DAS28-CRP was 4.0 at baseline, and 1.5 at 1 years. The number of patients who withdrew from FIL was three. Serious adverse event is none. [Conclusion] One-half dose (100 mg) of FIL was effective in Japanese patients with RA in a routine care. This study provides support for the possible use of one-half dose of FIL in Japanese patients with RA.

P2-148

Short-term outcomes of Filgotinib in patients with rheumatoid arthritis: a multicenter study

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Conflict of interest: None

[Objectives] This study aimed to investigate the short-term effects of treatment using filgotinib (FIL) treatment in patients with rheumatoid arthritis (RA) in our department. [Methods] Twenty-four RA patients treated with FIL in our hospital and affiliated institutions were enrolled from January 2021 to March 2023. We analyzed the disease activity of RA before FIL administration, 3 months or 6 months after FIL, of 22 patients (8 males, 14 females) who could continue FIL treatment for at least 3 months. [Results] At the initiation of FIL, the median age and disease duration were 72 years old (27-92) and 7 years (0-27), respectively. In addition, positivity of RF in 14 (63.6%) and anti-CCP antibodies in 13 (59%) were seen. Concomitant methotrexate usage was in 9 (40%), and other csDMARDs were used in 6 (27.2%). Seven (31.8%) had a history of previous biologics therapy. DAS28-CRP significantly decreased 3 or 6 months after FIL, from 3.97 to 1.94 and 1.93, respectively ($p<0.001$). There was an improvement in those who had switched from other biologics. The reasons for FIL discontinuation included bronchitis, pneumonia, self-discontinuation, and patient request due to improvement of symptoms. [Conclusion] FIL may improve the disease activity in RA patients early after administration.

P2-149

Comparative Effectiveness of Switching to Alternative JAK Inhibitors, IL-6 Inhibitors, or TNF Inhibitors in Rheumatoid Arthritis Patients with Inadequate Response to Initial JAK Inhibitor Therapy: Insights from the ANSWER Cohort

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Conflict of interest: None

[Objectives] This study evaluated drug retention rates and efficacy of biological agents and JAK inhibitors (JAKi) in rheumatoid arthritis (RA) patients after discontinuation of initial JAKi therapy. While previous reports showed superior drug retention rates for JAKi compared to TNF inhibitors (TNFi), efficacy data are limited. [Methods] We analyzed RA patients from the ANSWER Cohort (2013-2022) who switched to TNFi, IL-6 inhibitors (IL-6i), or other JAKi after discontinuing JAKi. Drug retention rates and CDAI trends were compared over 12 months post-switch, adjusting for background factors including age, sex, disease duration, CDAI, and use of glucocorticoids and MTX. [Results] At baseline, the JAKi group had significantly lower methotrexate use. Drug retention rates for discontinuation due to “inadequate response and adverse events”, “inadequate response”, and “adverse events” showed no significant differences among the three groups (P=0.5, P=0.2, P=0.7). No significant differences in CDAI change over 12 months were observed (P=0.2). [Conclusion] For RA patients with inadequate response to JAKi, TNFi, IL-6i, and other JAKi can all be considered viable treatment options.

P2-150

Comparison of Clinical Outcomes of JAK Inhibitors for Rheumatoid Arthritis by Metabolic Pathway

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Conflict of interest: None

Purpose: We compared and examined the clinical outcomes of cases in which JAK inhibitors were used. Methods: Thirty-six RA patients who were started on JAK inhibitors between 2013 and 2023 were included in the study, with the renal excretion group receiving renally excreted JAK inhibitors (tofacitinib, baricitinib, filgotinib) and the hepatic metabolism group receiving hepatically metabolized JAK inhibitors (smailaf, upadacitinib). There were 24 patients in the renal excretion group and 12 in the hepatic metabolism group. Age at baseline, duration of RA, eGFR, AST/ALT change, methotrexate (MTX) dose, MTX dose rate, prednisolone (PSL) dose, PSL dose rate, and continuation rate were investigated retrospectively. Results: Mean age was 64.1/74.6 years duration of RA was 15.2/13.0 years (renal excretion/hepatic metabolism group), eGFR was 77.8/60.7 (mL/min), MTX dose was 7.8/7.4 (mg/week), MTX administration rate was 59/58%, PSL dose was 4.6/3.5 (mg), and PSL administration rate was 40/33%. AST changed from 23.0/24.0 to 28.3/36.2 (IU/L) after treatment, and ALT changed from 18.9/15.8 to 20.9/28.8 (IU/L) after treatment. Conclusion: Renally excreted JAK inhibitors tended to cause more liver damage than hepatically metabolized JAK inhibitors, but the difference was not significant.

P2-151

Treatment Outcomes of Switching JAK Inhibitors in Patients with Rheumatoid Arthritis: Short-term Results from Our Institution

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Conflict of interest: None

Objective: In Japan, five JAK inhibitors are available for the treatment of patients with rheumatoid arthritis (RA). However, there are limited reports on the clinical outcomes of switching between JAK inhibitors when a change in medication becomes necessary. This study aims to clarify the treatment outcomes of switching JAK inhibitors in RA patients. **Methods:** We evaluated the disease activity in 15 RA patients attending our department who underwent a switch between JAK inhibitors from January 1, 2020, to June 30, 2024. Disease activity was assessed at baseline and at 12, 24, 52, and 104 weeks post-switch. **Results:** Of the 15 cases reviewed, one case discontinued treatment due to lack of efficacy at 16 weeks. 15 patients were followed up at 12 weeks, 14 at 24 weeks, 12 at 52 weeks, and 9 at 104 weeks. Prior to switching, patients had low to moderate disease activity, but at all follow-up periods after the switch, disease activity improved to remission or low levels. **Conclusion:** In RA patients requiring a switch between JAK inhibitors, short-term outcomes following the switch were favorable, suggesting that this strategy may be considered as a future treatment option. However, as these results are based on short-term outcomes, continued follow-up is necessary to evaluate long-term

efficacy.

P2-152

Have we become adept at using JAK inhibitors?

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Conflict of interest: None

[Objectives] With the release of five JAK inhibitors, options for the treatment of rheumatoid arthritis have expanded, but we examined whether these five drugs are being used appropriately. [Methods] We investigated the efficacy of five JKA inhibitors in 42 treatments in 29 patients with rheumatoid arthritis who were administered JAK inhibitors, with efficacy defined as improvement of moderate response or better in DAS28-CRP or DAS28-ESR. [Results] Twenty-nine patients were administered 42 JAK inhibitor treatments. In naïve cases not treated with biologics or JAK inhibitors, the efficacy rate was 82% in 9 of 11 cases, but in switched cases, the efficacy rate was 55% in 17 of 31 cases. In patients with no history of JAK inhibitor treatment, the efficacy rate was 71% in 20 of 28 cases, but in patients with a history of treatment, the efficacy rate was 43% in 6 of 14 cases. Of the five drugs, upadacitinib, which had shown high efficacy, was chosen most frequently in 16 cases, and baricitinib in 11 cases. [Conclusion] A high efficacy rate was achieved in patients who had not previously been treated with biologics or JAK inhibitors. Upadacitinib and baricitinib, which have high efficacy rates, were frequently chosen.

P2-153

Investigation of JAK inhibitor and Freeze-dried recombinant herpes zoster vaccine implementation rates in outpatient pharmacists with inflammatory immune diseases

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Conflict of interest: None

[Objectives] Freeze-dried recombinant herpes zoster vaccine (VC) is recommended for the safe use of Janus kinase inhibitors (JAKI) to prevent the onset of shingles. In our hospital, pharmacists provide information about VC when they suggest JAKI for drug treatment, and we investigated the usefulness of collaboration between physicians and pharmacists regarding VC. [Methods] The subjects were patients who used JAKI from March 2020 to August 2024 at our hospital. The group in which the pharmacist worked with the physician (Pharmacist Outpatient Group) was compared to the group in which the pharmacist did not work with the physician (physician group). The endpoints were VC immunization rates and incidence of shingles. [Results] In the outpatient pharmacist group, 42 of 310 patients using JAKI were inoculated with VC, and 32 (76%) were introduced to VC by pharmacists. In the physician group, 3 (3%) of 94 patients using JAK were vaccinated with VC. The incidence of herpes zoster was 2 (5%) in the pharmacist outpatient group and 0 (0%) in the physician group. [Conclusion] We believe that pharmacists can work with physicians to provide information about VC and make joint decisions about vaccination, thereby enabling the safe introduction of JAKI.

P2-154

Safety and Efficacy of Janus Kinase Inhibitor for Elderly Rheumatoid Arthritis

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Conflict of interest: None

Objectives: We aimed to evaluate the efficacy and safety of janus kinase inhibitor (JAKi) for elderly rheumatoid arthritis (RA) in our department. Methods: We included the patients of elderly RA who was started the treatment with JAKi in our department between January 2014 and October 2023. Elderly RA is defined by the cut-off of 65 years old regardless of the onset age. We retrospectively analyzed general background, disease activities, dosage of prednisolone (PSL) at the baseline and after 52 weeks. Results: Twenty-two patients were included. Among 22 patients, 17 patients (77%) were female. At the baseline, the median age of patients was 75 [73-79] years old, duration of disease was 13 [5-22] years. The most prescribed JAKi was filgotinib (7 patients, 32%). Ten patients (45%) received methotrexate and 14 patients (64%) received PSL. The median DAS28-ESR was 4.4 [3.9-4.8] and the median dosage of PSL was 2.8 [0-4] mg. At the 52 weeks, DAS28-ESR (4.4 [3.9-4.8] vs 2.9 [1.9-3.8], $p<0.01$) was significantly decreased. Three patients (14%) experienced herpes zoster. There were no serious adverse events. Conclusion: JAKi might be one of the safe and effective treatment options for elderly RA.

P2-155

Assessment of Janus kinase inhibitors in patients with rheumatoid arthritis undergoing orthopaedic surgeries

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Conflict of interest: None

[Background] The use of JAK inhibitor (JAKi) for rheumatoid arthritis (RA) is increasing. However, the appropriate perioperative withdrawal period is unclear. [Materials and methods] Of 32 RA patients who received JAKi between January 2013 and March 2024, 5 patients who underwent orthopaedic surgery were included. Age at surgery, duration of disease, operation, types of JAKi, perioperative withdrawal period, and complications were investigated. [Results] The mean age at surgery was 73.6±5.5 years, the mean duration of disease was 21.0±16.6 years, and the mean postoperative follow-up was 15.6±10.0 months. 3 patients underwent total knee arthroplasty, 1 hip bipolar hemiarthroplasty, and 1 total ankle arthroplasty. Upadacitinib was used in 4 patients and Tofacitinib in 1 patient. The mean withdrawal period was 9.4±6.1 days. One patient had recurrent postoperative joint symptoms and one patient had deep vein thrombosis. [Discussion] JAKis are recommended to be withdrawn 3 days prior to surgery for total joint arthroplasty, but there is no consensus on when to resume JAKi withdrawal. In the present study, the patients with the longest total withdrawal period had flare-ups of joint symptoms, but no delayed wound healing or surgical site infection was observed in any of the patients.

P2-156

Efficacy and safety of JAK inhibitor monotherapy for elderly rheumatoid arthritis patients: a single-center retrospective study

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Conflict of interest: None

[Background] The rheumatoid arthritis (RA) patients in Japan are getting older[1)]. "2024 Japan College of Rheumatology Clinical Practice Guidelines for RA" recommends the use of JAK inhibitors for a short period in elderly RA patients. However, there is little evidence for JAK inhibitor monotherapy. [Objective] To evaluate efficacy and safety of JAK inhibitor monotherapy for elderly RA patients. [Method] The data were collected from health insurance claims in our clinic from Oct. 1st, 2023 to Sep. 30th, 2024. The RA patients aged 65 years or older who had a history of prescription of JAK inhibitors and had been performed this therapy for at least 6 months were selected. The patient characteristics, clinical course and occurrence of adverse events were assessed. [Results] 65 cases were included. The therapy was continued in 62 cases (95.4%), and all but two cases have maintained low disease activity or remission. The oldest patient was 97 years old and the longest duration of this therapy was 11 years. [Conclusion] Efficacy and safety of the therapy for elderly RA patients were considered to be acceptable. However, monotherapy might not be selected for severe cases, and it cannot be said that this therapy is effective

for all elderly RA patients. [1] *Int J Rheum Dis.* 2017; 20(7): 839-45

P2-157

Reverse V-Shaped Osteotomy for Ankylosing Rocker-Bottom Foot Deformity in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Foot deformities in patients with RA often were shown from the early stages of the disease. Prolonged disease duration can lead to progressive foot deformities, including ankylosing rocker-bottom foot deformity. This severe deformity often results in infections and pain of callus, causing significant gait impairment and necessitating definitive surgical intervention. In this study, we investigated the outcomes of three cases treated with reverse V-shaped osteotomy of the midfoot. [Methods] We evaluated three RA patients with ankylosing rocker-bottom foot deformity who underwent reverse V-shaped osteotomy. The osteotomy was performed in the midfoot. Radiographic evaluation included preoperative and postoperative calcaneal pitch angle. Clinical outcomes were assessed using JSSF scale and SAFE-Q. [Results] Radiographic analysis showed improvement in the calcaneal pitch angle from -4° to 7°, 10° to 27°, and -2° to 4°, respectively, with disappearance of calluses. The JSSF scale and SAFE-Q scores improved in all patients. [Conclusion] Reverse V-shaped osteotomy appears to be a useful surgical technique for ankylosing rocker-bottom foot deformity in RA patients, providing significant improvements in both radiographic and clinical outcomes.

P2-158

A Short-Term Outcome Study of Forefoot Deformity Correction Surgery with Plate Fixation of the Fifth Metatarsal

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Conflict of interest: None

[Objectives] To report short-term outcomes of forefoot deformity correction with fifth metatarsal plate fixation. [Methods] Subjects were 10 female cases (11 feet) monitored for six months postoperatively, including 3 cases with rheumatoid arthritis (RA) and 7 without. Preoperative and final measurements were compared for HV, M1M2, M1M5 angles, JSSF scale, and SAFE-Q. Procedures on the first metatarsal included proximal closed wedge osteotomy (8 feet), Lapidus (2 feet), and no intervention (1 foot). For the 2nd-4th metatarsals, distal osteotomy was performed on 9 feet and proximal on 2. [Results] Postoperative improvements were noted: HV angle from 47° to 13°, M1M2 from 18° to 5°, M1M5 from 39° to 26°. JSSF RA Foot and Ankle scores rose from 53.5 to 88.5, pain improved from 15 to 30, and deformity from 15 to 25. The Hallux Scale showed improvements in function (27 to 42), shoe comfort (5 to 10), calluses (0 to 5), and alignment (0 to 8). SAFE-Q scores also rose in pain (36.7 to 86.7), physical function (40.9 to 79.5), shoe comfort (25 to 66.7), and overall health (45 to 85). [Conclusion] Short-term outcomes were favorable, showing effectiveness in maintaining the transverse arch and enhancing foot function.

P2-159

A case of polymyalgia rheumatica in which the medial malleolar pseudoarthrosis was healed by revision surgery with combined total ankle arthroplasty

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Conflict of interest: None

[Objectives] We report a case of polymyalgia rheumatica (PMR) in medial malleolar fracture that occurred during total ankle arthroplasty (TAA) was healed by revision surgery with combined total ankle arthroplasty (cTAA). [Medical history] At the age of 78, TAA was performed and a medial malleolar fracture was occured during surgery. At the age of 84, the collapse of the talus by the talar component progressed. CT scans showed a rotational mismatch of the tibial component. Revision surgery with cTAA was performed to correct the rotational mismatch. The medial malleolar pseudoarthrosis was untreated, but bone union was observed during the postoperative course. [Clinical significance and discussion] One of the intraoperative complications of TAA is medial malleolar fracture, which has been reported to occur in 9.7% of cases. Although medial malleolar osteotomy is considered useful for adjusting the tension of soft tissues, cases of severe varus and valgus and cases of medial malleolar nonunion with medial placement of the tibial component have been reported. In this case, the medial malleolar fracture healed by correcting the rotation of the tibial component during reoperation. It was thought that medial malleolar fracture nonunion after TAA suggests a mismatch in rotation.

P2-160

Study of surgical cases for rheumatoid arthritis (study of patients who developed the disease after MTX was approved)

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Conflict of interest: None

[Objectives] To investigate why joint destruction progressed to the point where surgery was required in patients with rheumatoid arthritis who developed the disease after 1999. [Methods] The subjects were 51 patients (6 men and 45 women) who developed rheumatoid arthritis after 1999, at our hospital from 2016 to 2023. Age at the time of surgery ranged from 32 to 90 years old. Medications used were MTX in 46 cases, bDMARDs in 15 cases, and JAK inhibitors in 3 cases. [Results] The surgeries included total joint replacement (47 knees, 3 hips), hand and finger, foot and ankle, and arthroscopic synovectomy in 2 cases. Disease activity at the time of surgery was high in 8, moderate in 18, and low in 25 cases. There were 8 cases in which the diagnosis of rheumatoid arthritis could not be made and the patient was treated for osteoarthritis of the knee. There were 5 cases in which the patient had been evaluated as being in low disease activity, but the deformation of the fingers and foot progressed and surgery became necessary. [Conclusion] Even if low disease activity is maintained, it is important to carefully follow up each joint on a regular basis. Even if images show signs of osteoarthritis, in cases with persistent inflammation, rheumatoid arthritis should always be considered.

P2-161

Investigation of Postoperative Complications in Rheumatoid Arthritis in the Era of Biologics and JAK Inhibitors

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Conflict of interest: None

[Objectives] This study examines postoperative complications in RA surgeries conducted in the era of biologics and JAK inhibitors. [Methods] The study included 286 cases of RA surgeries performed between 2013 and 2023 at three hospitals affiliated with Hamamatsu University School of Medicine. The examined parameters were age, sex, BMI, presence of diabetes, preoperative medications, white blood cell count, neutrophil count, lymphocyte count, hemoglobin, serum albumin levels, eGFR, and Prognostic Nutritional Index (PNI). Postoperative complications analyzed included infections, delayed wound healing (DWH), and postoperative

flare-ups. [Results] Among the 286 cases, 107 patients had used biologics, and 10 had used JAK inhibitors preoperatively. The incidence of complications included 19 cases of infection (6.6%), 45 cases of DWH (15.7%), and 7 cases of postoperative flare-ups (2.4%). Although no significant factors correlated with infections, DWH was more common in foot surgeries. DWH cases tended to have a lower PNI and longer surgical times. A higher proportion of patients who experienced flare-ups had been on JAK inhibitors preoperatively. [Conclusion] DWH appears more prevalent in foot surgeries and may be associated with extended surgical time and lower PNI.

P2-162

Perioperative management of JAK inhibitors in patients undergoing joint arthroplasty

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Conflict of interest: None

[Objectives] We retrospectively reviewed the rheumatoid arthritis (RA) patients who underwent joint arthroplasty to examine the influence of the perioperative use of Janus kinase (JAK) inhibitors on early postoperative complications. [Methods] Five patients controled with JAK inhibitors who underwent seven tolal joint arthroplasty were included in the study. We investigated perioperative management of JAK inhibitors, surgical site infection (SSI), delayed wound healing (DWH), a flare of the disease activity, venous thromboembolism, and other postoperative complications. [Results] JAK inhibitors were withheld for two days prior to the surgery. No SSI and flare-up were identified, while DWH was seen in one patient. [Conclusion] Our study suggest that JAK inhibitors seem to be a safe during the perioperative period of joint arthroplasty. Further study is needed to clarify the appropriate perioperative management of JAK inhibitors.

P2-163

The effect of autoimmune diseases on orthopedic infection-surgery

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Conflict of interest: None

[Objectives] Autoimmune diseases (AIDs) tend to occur infections. Orthopedic infections (OI) are difficult to treat and sometimes fatal. However, there are few reports how AIDs affect the postoperative course on orthopedic surgeries. The purpose of this study was to clarify the effect of AIDs on the postoperative course of OI surgery. [Methods] From January 2010 to October 2023, we collected clinical information of 60 patients; they were performed surgery for OI in our department. [Results] The mean age was 76.3 years, there were 21 men and 39 women. Number of AIDs (n) was described as below; rheumatoid arthritis (11), systemic lupus erythematosus (3), systemic sclerosis (1), psoriasis (1), anti-ARS antibody syndrome (1), Behcet's disease (1), mixed connective tissue disease (1), and no AIDs (41). Comparing AIDs-patients and no AIDs-patients, there were no significant differences in postoperative deaths (p=0.19), length of hospital stay (p=0.55), or postoperative leukopenia (p= 0.11); the AIDs group tended to have less improvement on leucocyte. [Conclusion] In this study, AIDs showed no significant effect on OI surgery. However, AIDs might prevent improvement of inflammation. We would like to confirm this result with a larger case in the future.

P2-164

Evaluation of prevalence rate of arthritis and enthesitis in patients with psoriasis and treatment efficacy using ultrasound

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Conflict of interest: None

[Objectives] The objectives of this study were to assess the prevalence of PsA among psoriasis patients and treatment effect using ultrasound (US). [Methods] This study included 220 psoriasis patients. Synovitis was evaluated using GS-score and PD-score at 1-5MCP, 1-5PIP, 1-5DIP and wrist joint bilaterally. Enthesitis was evaluated using PD-MASEI+E score. [Results] One hundred twenty-five patients had US inflammation. Asymptomatic arthritis and enthesitis were detected in 36 out of 125 patients (28.8%). Multivariate logistic regression analysis revealed that DAS28-CRP (ORs: 0.24, p=0.04) was a risk factor of US inflammation, but PASI (ORs: 0.97, p=0.43) was not. In 18 patients treated with bDMARDs, DAS28-CRP was from 3.4 to 2.6 (p<0.01), GS-score was from 6.9 to 1.5 (p<0.01), PD-score was from 5.3 to 0.9 (p<0.01), PD-MASEI+E score was from 3.0 to 2.0 (p=0.08). In 18 patients treated without bDMARDs, DAS28-CRP was from 3.4 to 2.5 (p<0.01), GS-score was from 4.6 to 3.2 (p=0.18), PD-score was from 3.3 to 2.1 (p=0.29), PD-MASEI+E score was from 2.9 to 2.4 (p=0.50). [Conclusion] Psoriasis patients have asymptomatic arthritis or enthesitis. If PsA treatment was insufficient, clinical symptoms may improve but US inflammation did not.

P2-165

Behavioral difference in liver dysfunction induced by MTX between patients with PsA and RA

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Conflict of interest: None

[Objectives] To clarify the difference and similarity in the behavior of liver dysfunction induced by MTX administration between patients with PsA and RA. [Methods] PsA patients met the CASPAR criteria and age- and sex-matched RA patients met the 2010 ACR/EULAR criteria, who visited our hospital between 2012-2019, were included. Liver enzymes (AST, ALT) and a liver-fibrosis biomarker (Fib-4 Index) were measured at the baseline (0M) and 3 years after the MTX initiation (36 M) and compared. [Results] Nineteen PsA and 19 RA were included. In PsA, the age and the disease duration were 45 and 4 years, 74% male, 26% on glucocorticoid (GC), 63% on NSAIDs, MTX dose 8 mg/week, 16% had dyslipidemia (DL), and 32% fatty liver (FL). In RA, the age and the disease duration were 47 and 3 years, 58% male, 32% on GC, 21% on NSAIDs, the MTX dose 10 mg/week. 5% had DL, and none with FL. At the baseline, AST/ALT levels were higher in PsA compared to RA, and this was also consistent at 36 M. At 36 M, Fib-4/AST showed an increase in RA and PsA, while ALT was elevated in RA and had the tendency in PsA. [Conclusion] Liver enzymes were already elevated in PsA at the baseline. Furthermore, MTX itself can induce liver dysfunction in a same manner across the diseases. Thus, careful monitoring should be necessary.

P2-166

Therapeutic effect of IL-23 p19 monoclonal antibody in psoriatic arthritis

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Conflict of interest: None

[Objective] In this study, we investigated real-world data on the ther-

apeutic effect of IL-23 p19 monoclonal antibody on peripheral lesions of PsA. [Method] We examined 12 cases of PsA treated with IL-23 p19 monoclonal antibody at our hospital. Regarding the efficacy in peripheral lesions, we compared the number of tender joints, the number of swollen joints, pain VAS, patient VAS, physician VAS, CRP, ESR, MMP-3, and changes over time in DAS28, DAPSA, and HAQ with IL-17 inhibitors and TNFα inhibitors. [Results] There were 10 cases of guselkumab and 2 cases of risankizumab, with an average age of 61.9 (38-75). The age of the patients was 6 males and 6 females. The duration of psoriasis was 16.2 (1-45) years, and the duration of PsA was 10.1 (1-22) years, and the PASE was 50.2 (20-67). Regarding the use of each biological agent, 7 cases were the first drug and 5 cases were the second or subsequent drugs. Nine cases had peripheral lesions only, and 3 cases had peripheral and axial lesions. Compared to baseline and 10 months later, improvement was seen with IL-23 inhibitors, IL-17 inhibitors, and TNF inhibitors. [Conclusion] Although the number of cases was small, the effectiveness of IL-23 p19 monoclonal antibody against peripheral lesions in psoriatic arthritis was confirmed.

P2-167

Early Improvement of Pain, Long-Term Disease Control, and Quality of Life Outcomes in Patients With Psoriatic Arthritis Treated with Upadacitinib (Encore)

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Conflict of interest: Yes

[Objectives] To report the improvement (IMP) in pain by baseline (BL) pain severity and the impact of early pain IMP on long-term, stringent disease control targets and patient-reported outcomes in patients (pts) with Upadacitinib (15 mg; UPA15) through 152 week (wk)s. [Methods] In this post hoc analysis, pts randomized to UPA15 in the SELECT-PsA 1 (non-bDMARD-IR) and PsA 2 (bDMARD-IR) were analyzed. Mean pain scores were calculated in pts with mild/moderate and severe BL pain severity (numeric rating scale, NRS). Achievement of MDA, DAPSA low disease activity (LDA), or pain ≦1.5 (NRS) and mean change from BL in SF-36 MCS was calculated. [Results] For pts with severe pain at BL, mean pain scores rapidly decreased to moderate levels in the first 2 wks, with additional reductions by wk 152 in both non-bDMARD-IR (mean: 3.3) and bDMARD-IR (3.8). A larger proportion of pts with early pain IMP achieved MDA, DAPSA LDA, and pain ≦1.5. Additionally, pts with early pain IMPs reported greater IMPs in SF-36 MCS score compared to those without early IMPs. [Conclusion] In non-bDMARD-IR and bDMARD-IR PsA pts, reductions in pain score occurred rapidly and were maintained through 152 wks, regardless of pain severity at BL. More pts with early pain IMPs achieved long-term and quality of life outcomes.

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The efforts of the Psoriasis Center in Yokohama City University Hospital

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Conflict of interest: None

[Objectives] In the treatment of psoriasis, accurate diagnosis, and treatment of comorbidities, including arthritis, are important to achieve treatment goals. We have established the Psoriasis Center to provide comprehensive treatment of psoriasis and to perform face-to-face collaborative outpatient consultations with rheumatologists for diagnosis and assessment of psoriatic arthritis (PsA). This study aimed to identify the clinical characteristics of PsA patients who were diagnosed at the Psoriasis Center. [Methods] Clinical characteristics of 40 newly diagnosed PsA patients from April 2023 to September 2024 were retrospectively analyzed. [Results] The mean age was 58.4 years. The mean time from PsA onset to the diagnosis was 14.1 months, and the mean PASI score was 4.8. The mean number of swollen and tender joints was 1.9 and 1.4, respectively. Imaging findings showed high efficacy with 80% showing changes associated with PsA on ultrasound. Therapeutic intervention was performed for arthritis in 36 patients, followed by further intensive treatment in 5 patients, but 3 patients were applied to the skin, and the course of arthritis was good throughout. [Conclusion] Simultaneous consultation by a dermatologist and a rheumatologist was useful for early diagnosis and intervention of PsA.

P2-169

Efficacy and predictive factors of granulocyte and monocyte adsorption apheresis (GMA/GCAP) in drug-resistant psoriatic arthritis

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Conflict of interest: None

[Objectives] In actual clinical practice, there are many psoriatic arthritis (PsA) in which disease control is difficult. Granulocyte and monocyte adsorption apheresis (GMA/GCAP) is an extracorporeal therapy. In this study, we investigated the efficacy and predictive factors of GMA/GCAP in patients with PsA refractory to various drug therapies. [Methods] 44 PsA patients who received GMA/GCAP between February 2021 and July 2024, those who had not achieved MDA at the time of initial introduction of GMA/GCAP. The efficacy of GMA/GCAP was evaluated using a composite index of disease activity (MDA, DAPSA, ASDAS, BASDAI) before and after the administration of GMA/GCAP. [Results] At the end of the 10 sessions, there was significant improvement in DAPSA, ASDAS, and BASDAI ($p<0.01$), and the MDA achievement rate was 27.3% (12/44). However, no significant differences were found in any of the background factors or biomarkers in the multivariate analysis. [Conclusion] Despite the limitation of a single-center, 44-patient, 10-week short-term observational study, the MDA achievement rate was 27.3% at 10 weeks. Based on this analysis, GMA/GCAP is a useful treatment for PsA refractory to BIO/JAKi therapy.

P2-170

Are pro-angiogenic factors associated with each domain of lesion in psoriatic arthritis?

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Conflict of interest: None

[Objectives] The A disintegrin and metalloprotease (ADAM) family is a protein expressed on the cell membrane surface. It has been reported that serum ADAM-17 concentrations are high in psoriasis vulgaris and PsA, but its involvement in angiogenesis has not been clarified. In this study, we investigated the relationship between PsA and cytokines and chemokines such as ADAM-17 that are assumed to be involved in angiogenesis. [Methods] The concentrations of serum cytokines and chemokines involved in angiogenesis in PsA, rheumatoid arthritis (RA), and normal subjects were measured by ELISA. Next, we examined whether there was a relationship between the measured cytokines and chemokines and clinical symptoms. [Results] The serum ADAM-17 concentration in PsA and RA was significantly higher than in NL. The serum VCAM-1 concentration in

PsA patients with tendon insertion lesions due to clinical symptoms was significantly lower than in patients without tendon insertion lesions, but no differences were observed in other cytokines and chemokines. [Conclusion] Serum ADAM-17 concentrations were significantly higher in PsA than in NL, but no association was observed with clinical symptoms.

P2-171

The Effects of Antimicrobial Peptide LL-37 on B Cells in Psoriatic Arthritis

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Conflict of interest: None

[Objectives] This study aims to elucidate the effects of the antimicrobial peptide LL-37, which increases in the synovial fluid of psoriatic arthritis, on B cells. [Methods] 1) Using the public scRNA-seq database (GSE200815) of synovium samples from patients with rheumatoid arthritis (RA) and PsA, gene expressions of B cell clusters were evaluated. 2) CD20+CD27+ memory B cells were collected by sorting from peripheral blood mononuclear cells, and cytokine production of TNF and IFNγ from B cells stimulated with LL-37 were examined by ELISA. [Results] 1) A total of 202,203 cells were collected from synovium samples of 4 RA and 5 PsA patients. Among them, 4,249 cells were identified as B cells. Pathway analysis showed that inflammatory cytokine signaling pathways such as the IL-17 signaling pathway and the TNF signaling pathway were more detected in PsA. 2) When memory B cells were stimulated with BAFF and LL-37, TNF production was significantly enhanced compared to the control group. No difference was observed in IFNγ production. [Conclusion] Antimicrobial peptides such as LL-37 might contribute to the production of inflammatory cytokines from B cells. We are now investigating what signaling pathways are activated using bulk RNA-seq.

P2-172

Experience with Upadacitinib in Three patients of Psoriatic Arthritis

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Conflict of interest: None

[Objectives] This report presents three psoriatic arthritis (PsA) patients treated with upadacitinib (UPA) for 2 years. [Methods] We assessed patient background, C-reactive protein, erythrocyte sedimentation rate, matrix metalloproteinase-3, white blood cell count, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, Disease Activity Index for Psoriatic Arthritis, Dermatology Life Quality Index, Japanese Early Arthritis Recognition Program, and PsA Severity Index. Patient 1: A 42-year-old man diagnosed with plaque psoriasis at age 10 developed polyarthralgia at age 31. After initial methotrexate (MTX) treatment at 10 mg/week failed to relieve symptoms, UPA was initiated. Patient 2: A 75-year-old man with plaque psoriasis experienced worsening skin and joint symptoms despite MTX (6 mg/week). Unable to achieve improvement, his treatment was switched to UPA. Patient 3: A 72-year-old woman with scalp and nail psoriasis and dactylitis, diagnosed with PsA, had MTX increased to 8 mg/week without relief. Treatment was switched from certolizumab pegol to UPA due to worsening symptoms. [Results] All patients showed improvements in blood tests, disease activity, and skin lesions. [Conclusion] UPA proved effective in both naïve and switch cases of PsA, maintaining efficacy over 2 years.

P2-173

3 cases of SpA especially PAO mimicking bone marrow metastasis

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Conflict of interest: None

The present report describes three more cases of SpA, which were similar to those reported in JCR2021. [Methods] Three more cases are presented here. Case 1: A man in his 60s with a history of DM was referred to our hospital for suspected metastatic bone tumor due to soft tissue shadows around Th8 and Th9 vertebral bodies on coronary artery CT scan taken by a routine examination for multiple PVCs. Case 2: A woman in her 50s had PPP and PsO and back pain since early April. She was referred to an orthopedic surgeon, and MRI scan revealed a metastatic bone tumor. The FDG-PET showed a less intense lesion than MRI, suggestive of inflammation than metastasis. Case 3: A woman in her 70s, referred for suspected bone metastasis, had MRI lesions at the T1, T5, and T6 vertebral bodies, but FDG-PET showed no evidence of metastasis or primary lesion. Since pustules were observed on the fingers, a diagnosis of spinal lesion associated with PPP was made. [Conclusion] We report three cases of SpA that required differentiation from bone metastatic lesions, and SpA cases must be differentiated from multiple bone metastatic lesions and infections, especially when localized to spinal lesions. The clinical features characteristic of SpA in the surrounding area should not be overlooked.

P2-174

A case of clavicle fracture during treatment for pustular osteoarthritis (PAO)

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Conflict of interest: None

[Case Presentation] A 55-year-old female had been diagnosed with palmoplantar pustulosis for twenty years. Three years ago, she suffered from right sternoclavicular joint (SCJ) pain and saw an orthopedic surgeon. Sternocostoclavicular hyperostosis on a CT scan indicated pustulotic arthro-osteitis (PAO). She had been treated with prednisolone and methotrexate. Since the pain got worse, she was referred to our hospital. High intensity area suggesting inflammation in SCJ was observed on T2-weighted MR image. Although her pain had relieved after iguratimod was added, stretching exercise caused right clavicle pain suddenly. An X-ray revealed fracture on slightly proximal to the middle of right clavicle. Slight dislocation led to conservative treatment. However, LIPUS (low intensity pulsed ultrasound) and allendronic acid was started due to prolonged bone fusion. [Discussion] SCJ ankylosis is likely to make stress concentrated in the middle of the clavicle during any shoulder movement, causing stress fracture easily. Conservative treatment is often selected in previous reports. In this case, stretch exercise rose clavicle fracture and conservative treatment was chosen because of slight dislocation. Treatment of PAO is needed to prevent progression of bone sclerosis or joint ankylosis.

P2-175

SAPHO syndrome with bone destruction of lumbar vertebral endplates: a case report

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Conflict of interest: None

[Background] There is no established treatment for bone and joint lesions in SAPHO syndrome, and reports of lumbar endplate destruction are rare. We present a case of SAPHO syndrome with lumbar endplate destruction successfully treated with adalimumab (ADA). [Case] A woman in her 20s had lower back pain, acne, and sternoclavicular joint pain. Blood tests showed mild inflammation, and CT revealed bone destruction and sclerosis at L3/4, L4/5, and the left sternoclavicular joint. With an ASDAS of 2.05 and BASFI of 3.00, NSAIDs were ineffective, so adalimumab (ADA) was administered. Her back pain disappeared in days, acne improved in a month, and inflammatory markers, ASDAS, and BASFI decreased. Three years later, CT scans showed no further changes. [Discussion] Modic changes (MC) may occur when Propionibacterium acnes, responsible for acne, invades the intervertebral disc. MC caused by this bacterium may promote osteoclast differentiation and activation. In this

case, the combination of osteoclast activation from SAPHO syndrome and bacterial infection likely contributed to bone destruction. [Conclusion] ADA appears effective in treating SAPHO syndrome with lumbar endplate destruction.

P2-176

Two cases of pustulotic arthro-osteitis improved by IL-23 inhibitors

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Conflict of interest: None

Case 1: A 50-year-old woman presented with pustules on her palms and soles, with back pain, anterior chest pain, and DIP joint pain. She was diagnosed with palmoplantar pustulosis (PPP), with a PPPASI score of 11.6. Bone scintigraphy (BS) revealed accumulations in sternocostal (SN) and sacroiliac joints, leading to a diagnosis of pustulotic arthro-osteitis (PAO). IL-23 inhibitors, Guselkumab, gradually improved her skin and joint lesions. BS at 28 weeks showed reductions in accumulation. By 52 weeks, her skin lesions had completely disappeared, with no obvious signs of arthritis on sternum MRI. Case 2: A 50-year-old woman was diagnosed with PPP. She had pain around her sternum at 52. After diagnosis with PAO due to sternoclavicular (SC) arthritis, she was managed with only NSAIDs. Despite minor skin lesions (PPPASI 3), her arthritis progressed, causing bone destruction and sclerosis in SC and SN regions on CT scan. Joint pain was exacerbated with elevated serum MMP-3 levels (316 ng/mL) at 58. IL-23 inhibitors, Risankizumab, resulted in improvements in arthritis on sternum MRI and normalization of MMP-3 levels at 28 weeks. [Clinical Significance] Given the limited reports on the efficacy of IL-23 inhibitors for PAO, we present the case reports with a literature review.

P2-177

A case of psoriatic arthritis showing improvement of both peripheral arthritis and enthesitis with deucravacitinib

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Conflict of interest: None

[Introduction] The efficacy of deucravacitinib in psoriatic arthritis is not clear. [Case] A 39-year-old male patient has had polyarthralgia in his fingers since X-2. He was referred to our department in September, X-1, on suspicion of rheumatoid arthritis. At the time of his first visit to our department, erythema with scaling was observed on his forehead and other parts of his body, which was diagnosed as psoriasis by our dermatologist. The presence of peripheral arthritis and enthesitis was observed and we diagnosed him with psoriatic arthritis. csDMARDs were not effective and deucravacitinib was started. After starting deucravacitinib, he showed rapid improvement not only of the cutaneous manifestations but also of the arthritis and enthesitis. [Conclusion] In this case, deucravacitinib was effective in the treatment of peripheral arthritis and tendon adhesions in psoriatic arthritis.

P2-178

A case of upadacitinib successfully treated psoraitic arthritis with involvement of sternocostoclavicular joint

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Conflict of interest: None

[Case] A 45-year-old woman was diagnosed PsA. First, she was treated with MTX and adalimumab; however, biologics was switched to brodalumab because of worsening of psoriasis. Nevertheless, brodalumab was discontinued due to worsening of psoriasis, as a paradoxical effect. Next, her symptoms improved after switching to MTX and certolizumab pegol, and she continued to receive certolizumab pegol 400 mg/q2w as a monotherapy until her first visit to our hospital. She had worsening anterior chest pain and lumbar back pain, and MRI showed STIR high signal in manubrium of sternum and sternocostal joints. Following to administration of upadacitinib 15 mg/day markedly her anterior chest pain diminished, and MRI also showed improvement in sternocostal arthritis findings. [Discussion and Conclusion] We have experienced a case of PsA presenting anterior chest pain due to sternocostal arthritis in which upadacitinib was effective. Although biologic agents are effective in the treatment of peripheral and axial joints of PsA, there are very few reports of their efficacy in sternocostal joints, Our report suggests that upadacitinib may be an useful treatment option when biologic agents are not available or ineffective.

P2-179

A Case of Psoriatic Arthritis with DIP Joint Repair Achieved through Adalimumab Administration

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Conflict of interest: None

Case: A 65-year-old male patient began treatment for rheumatoid arthritis (RA) in another prefecture in Year X - 7. He first visited our department in April of Year X following a relocation. At the initial examination, tenderness was noted in his fingers, wrists, and elbow joints, along with swelling in the DIP joints of both little fingers. He tested seronegative and presented with rashes on his forearms, leading to a diagnosis of psoriasis by a dermatologist. Sulfasalazine was increased, and NSAIDs were initiated. However, there was no improvement in peripheral arthritis or the rash, so adalimumab administration began in August of Year X. Subsequently, both joint pain and the rash disappeared, and X-rays showed joint repair in the DIP joints of the little fingers. It has now been four years since the initiation of adalimumab, and he has maintained remission without any recurrence of arthritis or rash. Discussion: There are several reports of joint repair with adalimumab administration in RA, but such reports are rare in PsA. In this case, not only were the rash and joint swelling suppressed, but joint destruction was also suppressed and repaired. This suggests that adalimumab administration may have the potential to achieve joint repair in PsA as well.

P2-180

A prospective cohort study of the long-term and short-term prognosis of young patients with systemic lupus erythematosus in Japan, including pregnancy outcomes (PLEASURE-J Study)

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Conflict of interest: None

[Objective] Systemic Lupus Erythematosus (SLE) often affects young individuals, significantly impacting their quality of life (QOL). While treatment advances have improved prognosis, long-term disease activity

and steroid-related side effects remain challenges. Evidence on the long-term prognosis of young SLE patients is limited, and this study aims to create a registry to understand their outcomes in Japan. [Methods] We target SLE patients aged 6 to 40 years, diagnosed within one year, involving 127 facilities nationwide. This open cohort study has a follow-up of over 10 years, with primary outcomes including mortality, hospitalization, and QOL. Pregnant patients transition to a pregnancy cohort for additional data on pregnancy and neonatal development. [Results] To date, 283 cases have been registered from 127 facilities (total follow-up of 1,225 person-years). The pregnancy cohort has 51 cases, and the developmental cohort 19. A system for Research Questions (RQ) allows registered physicians to conduct clinical research, supported academically by the JCR Clinical Research Promotion Committee. [Conclusion] This study is expected to generate valuable evidence on young SLE patients in Japan, with new research opportunities emerging from the pregnancy and RQ systems.

P2-181

Does parenting improve patient reported outcome in patients with systemic lupus erythematosus?: A cross-sectional study from lupus registry of nationwide institution (LUNA) cohort

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Conflict of interest: None

[Objectives] Patients with SLE often experience perinatal flare-ups and difficulties of childcare due to fatigue and dysfunction. We aimed to examine the impact of childbirth and childcare on quality of life (QOL) for patients with SLE who are during treatment. [Methods] This was a cross-sectional study using LUNA registry. We included female patients with confirmed parenting status. The exposure was parenting, categorized for their children's age (including infants [0-5 years], and only school children [6-18 years]). The main outcome was QOL score of lupus patient-reported outcomes (LupusPRO). Multiple regression analysis was performed with patient age, number of children, SDI, living with spouse, and caregiving as confounders. [Results] A total of 631 patients (mean age 42.1 years, mean duration of illness 14.3 years) were included, 67 with infants, 46 with school children only, and 518 without parenting. Patients who gave birth and raised infants during treatment showed significantly better cognitive function scores (memory and concentration) compared to controls (coefficient 11.5, 95% CI 0.4-22.7, p=0.042). [Conclusion] Parenting infants was associated with better cognitive function in patients with SLE who were giving birth and parenting while undergoing treatment.

P2-182

Impact of Rheumatologist Burnout on Patient Trust in Systemic Lupus Erythematosus Care: Findings from the TRUMP2-SLE Study

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Conflict of interest: None

[Objectives] Establishing a good physician-patient relationship is essential for the long-term management of SLE. While we showed that SDM and the personality of attending rheumatologists promote trust, the impact of burnout on this relationship remains unclear. In this study, we examined this association. [Methods] This was a multicenter cross-sectional study involving SLE patients and their rheumatologists participated in the TRUMP2-SLE study. Physician burnout was assessed using the MBI-GS scale and the outcome was patient trust in their physician, measured by an abbreviated version of the Wake Forest Physician Trust Scale. A multiple linear regression analysis was conducted with physicians as the cluster unit, adjusting for potential confounding factors related to both patients and physicians. [Results] A total of 422 patients (female 87.0%, mean age 47 years, mean SLEDAI score of 3.9) and 38 physicians (female 23.7%, mean age 40 years) were participated. Burnout was observed in 27 physicians (71.1%) and was associated with lower levels of patient trust in their rheumatologists (-4.1 points, 95% confidence interval [-7.9, -0.3]). [Results] Rheumatologists' burnout was significantly associated with lower trust among SLE patients.

P2-183

Investigation of the association between fatigue and iron deficiency in patients with systemic lupus erythematosus: a cross-sectional study

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Conflict of interest: None

[Objectives] Fatigue is common in systemic lupus erythematosus (SLE), and non-anemic iron deficiency (NAID) is suspected as a potential cause. This study aimed to examine the association between NAID and fatigue in SLE. [Methods] We conducted a cross-sectional study using SLE multicenter registry (LUNA, 2021-2023). SLE patients without anemia (men: Hb > 13 mg/dL, women: Hb > 12 mg/dL) with variable ferritin and TSAT data were included. Iron deficiency was defined as ferritin < 15 ng/mL, or ferritin < 100 ng/mL with TSAT < 20%. Fatigue was measured by the LupusQOL fatigue score (0=worst, 100=best) and analyzed with a linear regression model adjusting for potential confounders. Subgroup (SG) analysis was performed by sex. [Results] Of the 304 patients, 90.8% were women, mean age was 50 years (SD±12.9), disease duration was 15.9 years, SLEDAI score was 2, median ferritin level was 51 ng/mL [IQR 22, 99.9], and fatigue score was 81.25 [IQR 62.5, 93.75]. 78 patients had NAID. Median fatigue scores were higher in NAID vs. non-NAID (estimate value 79.5 vs. 74.4; adjusted group difference: 5.6, 95%CI [0.23, 10.9], p=0.041). Female SG showed a significant association. [Conclusion] NAID was associated with lower fatigue in SLE, but this did not apper large enough to be clinically meaningful.

P2-184

Characteristics of moon face in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] This study investigated the occurrence and characteristics of moon face in patients with systemic lupus erythematosus (SLE). [Methods] We surveyed SLE patients with a history of steroid therapy at our hospital, evaluating their experiences and current symptoms of moon face. Clinical data were obtained from medical records. [Results] Of the 145 surveyed patients, 123 (84.8%) experienced moon face after starting treatment; 90 showed improvement over time, while 24 still had symptoms at the time of response. Patients with moon face had higher median maximum steroid doses compared to those without it. Patients whose symptoms did not improve were on higher current steroid doses than those whose symptoms did improve. These patients also experienced a decline in health-related quality of life (HRQOL), with no observed differences in non-health-related QOL. No significant differences were found in sex, age at onset, age at survey, disease duration, SDI, or SLEDAI between patients with or without a history of moon face or current symptoms. The steroid dose at improvement was 8 mg of prednisolone equivalent. [Conclusion] Moon face is a common side effect of steroid therapy in SLE patients, especially those with a history of high doses, and is associated with decline HRQOL.

P2-185

A Case of Class V Lupus Nephritis Discovered Without Renal Dysfunction or Proteinuria

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Conflict of interest: None

Background: A female patient in her 40s presented with Raynaud's phenomenon and finger swelling in Year X-5, visiting our clinic in April of X-4. SLE was diagnosed based on antinuclear and anti-Sm antibodies, leukopenia, and hypocomplementemia. Initial treatment with vasodilators targeted circulatory symptoms. Joint symptoms emerged later, leading to hydroxychloroquine initiation (200 mg/day). Around X-2, intermittent mild microscopic hematuria appeared. Despite normal eGFR and absence of proteinuria, worsening hypocomplementemia prompted a renal biopsy in July of X. Results: Optical microscopy showed spike formation, pinhole lesions, and basement membrane double contours with slight endocapillary hypercellularity. Electron microscopy revealed subepithelial deposits, membrane thickening, foot process effacement, and virus-like particles. After confirming Class V lupus nephritis, treatment with MMF and belimumab was initiated without glucocorticoids, as renal function remained stable. Clinical Significance: Silent lupus nephritis occurs without renal dysfunction or urinary abnormalities, typically presenting as Class I or II. This case of Class V lupus nephritis with podocyte injury but without proteinuria represents a rare presentation, warranting discussion with literature review.

P2-186

A case of AYA generation with systemic lupus erythematosus presenting with silent lupus nephritis

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Conflict of interest: None

[Introduction] Childhood-onset systemic lupus erythematosus (cSLE) is associated with severe lupus nephritis (LN), and silent LN may show severe LN on renal pathology. For this reason, biopsy tends to be considered aggressively in cSLE. [Case Report] A 16-year-old female presented with erythema, and SLE was suspected based on the positive antinuclear antibodies and hypocomplementaemia. At the initial presentation, only a skin rash appeared, but within one week, edema, livedo racemosa, and pleural effusions and ascites appeared. She was positive for anti-dsDNA antibodies and was diagnosed with SLE. Urinalysis showed only mildly abnormal finding. Skin biopsy did not identify vasculitis, however, she was clinically presumed to have lupus vasculitis. The photomicrographic examination revealed mild enlargement of the mesangial matrix, however, immunostaining demonstrated a full house pattern, and electron microscopy examination revealed marked deposition of immune complexes. The patient was treated with prednisolone, mycophenolate mofetil and hydroxychloroquine. [Discussion] The renal pathology was useful for treatment selection in silent LN. We report this case to discuss about the indication of renal biopsy for silent LN in the Adolescent and Young Adult age group.

P2-187

A case of lupus vasculitis presenting with purpura and abnormal sensation in both lower limbs

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Conflict of interest: None

Case: 61-year-old female **Chief complaint:** Hypoesthesia in the lower legs **Present illness**: The patient started oral mesalazine for ulcerative colitis in year X-6. Six months ago (X-6 months), she developed hypoesthesia in both lower legs, and one month ago (X-1 month), she visited our outpatient clinic. Livedo reticularis was observed on both lower legs. A nerve conduction study suggested findings of mononeuritis multiplex. Blood tests revealed an antinuclear antibody (ANA) titer of 1:1280 and positive anti-DNA antibodies, raising suspicion of drug-induced lupus or lupus vasculitis. Mesalazine was discontinued, and the patient was admitted to our department in year X. A skin biopsy from the left thigh showed full-thickness necrotizing vasculitis in a small muscular artery. She was diagnosed with lupus vasculitis and started on prednisolone (40 mg/day), leading to improvement in her symptoms. **Discussion:** Lupus vasculitis typically occurs in younger patients with a long disease duration, making this case atypical. Additionally, drug-induced lupus caused could not be ruled out. There are few reports of histologically confirmed necrotizing vasculitis in systemic lupus erythematosus (SLE). We will review the literature regarding lupus vasculitis and mesalazine-induced drug-induced lupus.

P2-188

A case of systemic lupus erythematosus with necrosis of the digits

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Conflict of interest: None

Case: 24-year-old woman, diagnosed with systemic lupus erythematosus (SLE) in X-7 based on Raynaud's phenomenon, haemopenia, positive antinuclear antibody, positive antiphospholipid antibody and positive anti-RNP antibody; in September X-1, purpura on the lower legs appeared and skin biopsy showed leukaemic vasculitis. Subsequently, hypocomplementaemia developed, anti-ds-DNA antibodies rose and the patient was admitted to hospital. Prednisolone, mycophenolate mofetil plus belimumab were introduced, followed by sudden onset of colour irregularities and pain in the fingers and toes. Contrast-enhanced CT and MRI showed arterial occlusion in the fingers and toes, which was judged to be vasculitis symptoms associated with SLE. The patient was treated with steroid pulse therapy, antithrombotic therapy and vasodilators, but there was no improvement, so cyclophosphamide intravenous cyclophosphamide (IVCY) was added, and the progression of necrosis was suppressed. Clinical significance: It is rare for patients with SLE to present with a blood flow disturbance leading to necrosis of the digits. In this case, the presence of cutaneous vasculitis and the severity of SLE suggested vasculitis as the cause, and IVCY therapy prevented the progression of the disease.

P2-189

A case of lupus vasculitis with rapidly progressive limbs necrosis due to COVID-19 infection during SLE flare-up

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Conflict of interest: None

[Case] A 29-year-old woman who was diagnosed with MCTD (SLE-like) due to Raynaud's phenomenon, finger swelling, and positive anti-U1-RNP antibody and anti-ds-DNA antibody 15 years ago, was maintained low disease activity with PSL 2 mg and HCQ 200 mg. From December 2023, complement levels decreased, anti-RNP and anti-dsDNA antibodies increased and Raynaud's phenomenon worsened, and numbness and pain appeared in the upper and lower limbs. After COVID-19 infection in January 2024, the limbs necrosis progressed rapidly. Vasodilators, m-PSL pulses, IVCY, and MMF did not improve the condition, and the patient was transferred to our hospital in February 2024. Numbness and pain in the limbs suggested mononeuritis multiplex, antiphospholipid antibodies were negative, and ischemic necrosis due to lupus vasculitis was suspected. The progression of necrosis was suppressed by simple plasma exchange, continuous heparin infusion, and IVIg. [Discussion] We reported a case in which endothelial damage due to lupus vasculitis and thrombotic tendency s due to COVID-19 infection lead to rapidly progressive limb ischemia. SLE patients who are positive for anti-U1RNP antibodies are prone to endothelial cell damage, and careful monitoring is required if Raynaud's symptoms worsen.

P2-190

A case of systemic lupus erythematosus diagnosed following severe lower limb ulcers

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Conflict of interest: None

A 60-year-old male had experienced photosensitivity symptoms for two years but had not been to the hospital. Three months ago, ulcers appeared on his lower limbs, showing little improvement, which led him to visit our hospital. Multiple round ulcers were noted on both lower limbs, with the largest lesion being a deep ulcer on the dorsum of the left foot, approximately 60 mm in size, with tendon exposure. Although he was a former heavy smoker, no significant arterial stenosis was found in lower limb arterial ultrasound and contrast CT. Blood tests showed a positive anti-ds-DNA antibody level of 27 IU/mL and negative anti-phospholipid antibodies. A biopsy of the ulcer on the dorsum of the foot showed no clear signs of vasculitis. However, a biopsy of the erythematous area on the cheek revealed findings consistent with an acute rash of systemic lupus erythematosus (SLE), leading to a comprehensive diagnosis of lower limb ulcers due to SLE. treatment with oral prednisolone and hydroxychloroquine was initiated. Following the treatment intervention, the ulcer lesions showed gradual improvement. Skin ulcers are rarely seen in SLE cases not complicated by anti-phospholipid syndrome. When lower limb ulcer lesions are noted, SLE should be considered as one of the differential diagnoses.

P2-191

A Case of Systemic Lupus Erythematosus Complicated by Cold Agglutinin Syndrome

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Conflict of interest: None

A 69-year-old male presented with photosensitivity for 4 years. In October of year X, he experienced dizziness and was found to have anemia (Hb: 6.5 g/dL) at a local clinic. Suspecting systemic lupus erythematosus (SLE), he was referred in late November. Based on the 2019 EULAR/ACR classification criteria, he scored 15 points, confirming SLE. Hemolytic anemia was noted, with a positive direct Coombs test. Specific testing revealed IgG negative and C3d positive, with a cold agglutinin titer of 512. A positive direct agglutination test led to the diagnosis of cold agglutinin syndrome. He also experienced seizures, indicating central nervous system lupus. Treatment included steroid pulse therapy and cyclophosphamide pulse therapy, followed by a tapering dose of prednisolone starting at 60 mg/day. There were no recurrences of seizures, anemia improved, and the cold agglutinin titer decreased. While autoimmune hemolytic anemia occurs in about 10% of SLE cases, the combination with cold agglutinin syndrome is rare. In this case, the cold agglutinin titer became negative with SLE treatment, confirming it as cold agglutinin syndrome associated with SLE.

P2-192

A case report of SLE and Sjögren's syndrome complicated by Ehlers-Danlos syndrome

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Conflict of interest: None

We report a case of a 47-year-old woman with the main complaints of loss of appetite and weight loss due to taste disorder. She was admitted to our department due to pancytopenia, decreased complement levels, and high titers of antinuclear antibodies, and was diagnosed with SLE and Sjögren's syndrome (Sjs). Shortly after the start of treatment, she developed an iliopsoas hematoma, and repeated bleeding required multiple hemostatic procedures. Even after becoming an outpatient, she continued to have intermittent symptoms such as multiple varicose veins in the lower limbs, cerebral aneurysms, multiple internal bleeding, rectal prolapse, and uterine prolapse. She was subsequently diagnosed with Ehlers-Danlos syndrome (EDS), but genetic testing did not reveal any pathological mutations corresponding to known disease types, making it unclassifiable. Both SLE and EDS have been noted to cause vascular fragility, but in EDS, bleeding sites are not compressed by surrounding tissues, so hematomas can easily form due to bleeding, and hemostatic procedures may be required. There have been no reported cases of SLE or Sjs combined with EDS, but there are reports that the incidence of EDS is high in Sjs, and it may be one of the complications to watch out for in autoimmune diseases.

P2-193

A case of early-onset hydroxychloroquine retinopathy with abnormally high hydroxychloroquine blood level

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Conflict of interest: Yes

Background: Ophthalmic screening for hydroxychloroquine (HCQ) retinopathy is performed yearly after initiation in Japan. Among three cases from Japan in which retinopathy occurred in less than 5 years, one had abnormally high blood levels, but at a dose of 6.7 mg/kg/day and had CKD stage G3. The association of high HCQ blood level and the development of HCQ retinopathy is still controversial. Case: A 52-year-old Japanese female patient with SLE started HCQ at a dose of 3.8 mg/kg (200 mg/day). 3 years and 6 months later, ophthalmologic examination revealed a decrease in sensitivity of visual field test and obscuration of EZ line on SD-OCT, and she was diagnosed with HCQ retinopathy. Whole blood level at discontinuation was 2393 ng/ml. Clinical Significance: The optimal blood concentration of HCQ in the treatment of SLE is reported to be 750-1,200 ng/mL. In this case, despite the low dose and lack of risk, the patient developed retinopathy less than 5 years after initiation, and HCQ blood levels revealed abnormally high. This suggests that blood levels may be important as a risk factor in early-onset cases. Several associations between blood levels and drug metabolism genes have been reported, suggesting that genetic predisposition may result in abnormally high blood levels.

P2-194

A case of intractable acute generalized exanthematous pustulosis caused by hydroxychloroquine

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Conflict of interest: None

[Introduction] Acute generalized exanthematous pustulosis (AGEP) is a severe cutaneous adverse reaction characterized by multiple aseptic pustules with a fever. We report a case of systemic lupus erythematosus (SLE) that developed AGEP by hydroxychloroquine (HCQ) and was difficult to treat. [Case] A 43-year-old woman had been diagnosed with SLE 13 years previously, and treated with prednisolone (PSL) at a dose of 5 mg/day in the last 10 years. HCQ was started on day Y, because of hair loss and mild proteinuria. On day Y+22, she complained of erythema and HCQ was discontinued. However, her erythema worsened, and she had a high fever. Skin biopsy was performed and the histopathological analysis showed some intraepidermal pustules with neutrophil infiltration. On day Y+43, she was treated with PSL at a dose of 60 mg/day. On day Y+51, cyclosporine (CyA) was started. Her erythema improved gradually. Based on the clinical course, she was diagnosed with AGEP. [Conclusion] Antibiotics are the most common cause of AGEP. However, HCQ is also associated with AGEP. Most cases improve with discontinuation of the offending drug, but some cases require additional treatment, such as CyA. HCQ is recommended for all SLE patients, but it is necessary to be care about a cutaneous adverse reaction.

P2-195

Seronegative Systemic Lupus Erythematosus with a Challenging Diagnosis

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Conflict of interest: None

[Case] A woman in her 40s began experiencing Raynaud's phenomenon six years ago. Five years ago, she presented with a nephrotic syndrome, prompting a renal biopsy. Immunofluorescence revealed C1q staining along capillary loops and mesangium, while light microscopic examination showed minimal change disease and acute tubular necrosis. Immunosuppressive therapy with prednisolone (PSL) led to remission. Six months ago, the patient experienced a recurrence of proteinuria, accompanied by decreased complement levels, necessitating a second renal biopsy. This time, immunofluorescence displayed C1q and IgM staining along the capillary loops and mesangium, and electron microscopy identified high electron-dense deposits in the mesangial area and virus-like particles within endothelial cells, indicative of lupus nephritis. Treatment with PSL, hydroxychloroquine, mycophenolate mofetil, and belimumab was initiated, resulting in remission without relapse. [discussion] This case was diagnosed in the context of decreasing complement levels and a second renal biopsy following the recurrence of proteinuria. However, the initial renal biopsy did not yield disease specific findings, and specific SLE antibodies remained negative throughout the course, rendering this an atypical and insightful case.

P2-196

A case of systemic lupus erythematosus with antinuclear antibodies changing from nuclear to cytoplasmic pattern during the course of rheumatoid arthritis

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Conflict of interest: None

Case: A 59-year-old woman was diagnosed with rheumatoid arthritis (RA) in 2007. She was being treated with methotrexate. She noticed fever in March of this year. As pneumonia was suspected, antibiotics were used, but fever continued. In June, she developed edema and proteinuria, which led to the suspicion of involvement of a systemic autoimmune disease. She visited our department for further examination. She was diagnosed with systemic lupus erythematosus (SLE) and lupus nephritis (LN) based on erythema, leukopenia, thrombocytopenia, anti-DNA antibody, and proteinuria. The patient was treated with glucocorticoids, belimumab, and hydroxychloroquine. In this case, antinuclear antibodies (ANA) were x160 until March, and the staining pattern was homogeneous and speckled. In June, the nucleoplasm was negative, and cytoplasmic was observed. At the same time, anti-DNA antibodies by RIA and EIA were also positive, furthermore, ribosomal P were positive by Line Blot (Euroimmune). [Discussion] SLE is an autoimmune disease that produces a variety of autoantibodies. When SLE concurrent and anti-cytoplasmic antibodies are induced, ANA pattern may change significantly. It was also suggested that staining of the nucleoplasm may have been difficult to observe due to anti-cytoplasmic antibodies.

P2-197

A case of SLE with new autoantibodies acquired due to drug neglect

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Conflict of interest: None

It has been reported that autoantibodies for SLE gradually turn positive before the onset of SLE, and that more specific antibodies turn positive immediately before the onset of SLE, and that new autoantibodies are difficult to acquire after the onset of SLE. A 20-year-old female developed SLE due to a skin rash at the age of 11 and was treated in the pediatrics department of a local general hospital. In May of year X, she was referred to our department after entering university and moving. At the time of referral, she was receiving treatment with belimumab, tacrolimus, and prednisolone, and the disease was well controlled. In August of the same year, she stopped visiting the outpatient department without any contact. In March of year X+1, she visited our emergency department complaining of joint pain and fever. She was diagnosed with a relapse of SLE based on fever, joint pain, white blood cell count, decreased complement, and increased anti-dsDNA antibodies. In addition, rescreening of autoantibodies revealed that anti-Sm antibodies, anti-U1-RNP antibodies, and anti-SS-A antibodies, which had previously been negative, had turned positive.

P2-198

A case of anti-eIF2B antibody-positive systemic sclerosis complicated by refractory myocarditis

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Conflict of interest: None

[Case] A 49-year-old woman presented to our department with complaints of arthralgia and skin hardening in her hands and fingers for the past two months. She was diagnosed with systemic sclerosis (SSc) based on skin hardening, Raynaud's phenomenon, arthritis, and interstitial pneumonia (IP). She was positive for anti-eIF2B antibodies (Abs) but negative for other Abs associated with SSc. She was treated with four courses of RTX 550 mg/body/week and PSL 30 mg/once every two days. The fever resolved, and the inflammatory response was reduced, but CK, CK-MB, and troponin I remained elevated, and myocarditis was diagnosed. The patient had no symptoms, electrocardiographic changes, or abnormal wall motion on echocardiography. MMF 1500 mg/day and TAC 8 mg/day were added due to treatment refractoriness, and laboratory markers of myocarditis decreased after two months. PSL 5 mg/day, MMF 1500 mg/day, and TAC 8 mg/day are continued without relapse. [Conclusion] Anti-eIF2B Abs are associated with diffuse cutaneous SSc. Anti-eIF2B Abs are known to be frequently associated with IP, but there are no reports of myocarditis. In this case, myocarditis refractory to immunosuppressive agents was complicated during the treatment of SSc. We report a rare case of anti-eIF2B Ab-positive SSc.

P2-199

A Case of Sick Sinus Syndrome Associated with Myocardial Involvement During Treatment for Interstitial Pneumonia in a Patient with Systemic Sclerosis and Rheumatoid Arthritis Overlap Syndrome

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Conflict of interest: None

A 67-year-old woman was diagnosed with RA 16 years ago and had been treated with MTX and adalimumab (ADA). Two years ago, she developed Raynaud's phenomenon and skin sclerosis, presenting progressive skin sclerosis and digital ulcers. Chest CT revealed interstitial pneumonia with a NSIP pattern, leading to a diagnosis of systemic sclerosis (SSc) and RA overlap syndrome with positive anti-U1-RNP antibody. MTX and ADA were discontinued, and tocilizumab 162 mg/w was started. Two months later, she developed dyspnea, and chest CT showed worsening NSIP, resulting in hospitalization for acute exacerbation. Glucocorticoid pulse therapy, followed by 30 mg/day of prednisolone, was administered. On admission, ECG showed a left anterior fascicular block, but on the 11th day, she developed bradycardia (30 bpm). Further evaluation confirmed sick sinus syndrome (SSS). Cardiac MRI showed delayed enhancement in the inferior wall, likely due to SSc-related myocardial involvement, contributing to SSS development. [Clinical Significance] The coexistence of arrhythmias as a myocardial manifestation of SSc is not uncommon; however, cases of SSS with myocardial fibrosis identified by cardiac MRI are rare, making this case a valuable contribution to the literature.

P2-200

A 15-year-old girl patient with anti-PM-Scl75 antibody and anti-PM-Scl100 antibody positive overlap syndrome complicated by interstitial pneumonia and muscle weakness

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Conflict of interest: None

Introduction: The usefulness of autoantibodies in clinical practice has attracted attention in idiopathic inflammatory muscle diseases. Case: A 15-year-old girl appeared to have pain in her right fingers for past 5 years and both hands stiffness, lower leg edema and plantar pain had persisted for 1 month. Vital signs were normal. She gained 2 kg in three months. The fingers of both hands were swollen, and the range of motion was limited due to tenderness and swelling of the PIP and DIP joints. No disease specific skin rash and muscle grasping pain had occurred. Grip strength dropped to 8 kg on both sides. The laboratory data showed blood cell count was normal, CRP0.92 mg/dL CK2619 IU/L ALD73.5 ANA5120x. Moreover, autoantibodies of anti ssDNA (115 AU/mL), antiPM-Scl75 (immunoblotting procedure 3+) and anti PM-Scl100 (2+) were positive, as compared with anti MDA-5 anti ARS antibodies were negative. Considering future fertility, cyclophosphamide was not used. The patient improved by mycophenolate mofetil (MMF) and tacrolimus followed by MPT 3 cools. Conclusion: It has been reported that interstitial pneumonia is often associated with PM-SSc autoantibody-positive overlap syndrome in adult patients. However, there are few reports of pediatric cases, and it is desirable to accumulate cases.

P2-201

Three cases of mixed connective tissue disease with trigeminal neuropathy

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Conflict of interest: None

Case 1: A woman in her 20s with Raynaud's phenomenon, polyarthralgia, and positive antinuclear antibody was referred to our department. One and a half years later, she developed abnormal sensation on the left face and was diagnosed with trigeminal neuropathy and mixed connective tissue disease (MCTD). Case 2: A woman in her 50s was referred to our department because of stiffness in her fingers and abnormal sensation on the left face. She was positive for anti-U1-RNP antibody. Six months later, Raynaud's phenomenon began to appear, and she was diagnosed with MCTD. Case 3: A woman in her 40s had a history of paresthesia and dysgeusia at the apex of the tongue, and then hypesthesia and abnormal sensation extended from the bilateral cheeks to the lower jaw. Three months later, Raynaud's phenomenon appeared, and she was referred to our department because she was positive for anti-U1-RNP antibody and diagnosed with MCTD. Discussion: We have seen three cases of MCTD with trigeminal neuropathy. In patients with trigeminal neuropathy preceding Raynaud's phenomenon, as in cases 2 and 3, the search for autoantibodies and careful follow-up were considered necessary. Effective treatment has not yet been established and more cases are needed.

P2-202

A case of anti-Ku antibody-positive myositis complicated by systemic lupus erythematosus during a relapse of idiopathic inflammatory myopathy

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Conflict of interest: None

[Case] A 28-year-old female. Four years prior, she was diagnosed with idiopathic inflammatory myopathy (IIM) by proximal muscle weakness, elevated CK, electromyographic discharges with histopathology of myositis. She was treated by prednisolone (PSL) and intravenous immunoglobulin (IVIg), resulting in improvement. However, she discontinued treatment for two years and then she presented with fever, myalgia, arthralgia, and Raynaud's phenomenon. Examination revealed polyarthritis and proximal muscle weakness. Laboratory tests confirmed elevated CK, positive anti-dsDNA and anti-U1-RNP antibodies, hypocomplementemia, increased pulmonary artery pressure and active myositis by MRI. She was diagnosed with systemic lupus erythematosus (SLE) complicated by IIM and pulmonary hypertension. She was treated by 1 mg/kg PSL, mycophenolate mofetil, tacrolimus, and IVIg. Anti-Ku antibody was confirmed by A-Cube. [Clinical Significance] Anti-Ku antibodies are associated with overlap syndromes involving scleroderma and myositis, classified into two subtypes: one with elevated CK and the other with positive anti-dsDNA antibody and glomerulonephritis. The phenotypic shift in a single case is rare. MxA expression in this case, unusual in anti-Ku-positive myositis, suggests a link to the coexisting SLE.

P2-203

Clinical Characteristics and Treatment Challenges in Rhupus: A Comparative Study with RA and SLE

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Conflict of interest: None

[Objectives] Rhupus is a rare condition combining systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). This study explores its clinical features and treatment strategies compared to RA and SLE. [Methods] A retrospective analysis was conducted on 24 patients from Kinki University Hospital (2009-2024) meeting both RA (EULAR/ACR 2010) and SLE (SLICC 2012) criteria, compared with 941 RA and 312 SLE patients. [Results] The average age was 40.6 years, with 91.6% female. RA preceded SLE by 27.9 months. RF and anti-CCP antibodies were positive in 91.6% and 62.5%. Key scores included DAS28-CRP (5.3 ± 1.2) and SLEDAI (7.2 ± 3.1). Common symptoms included cytopenia (41.6%), rash (25%), and hypocomplementemia (25%). Methotrexate was used in 66.7% of cases, with IL-6 inhibitors used more often than TNF-α inhibitors. Around 70.8% used multiple biologics, and 54.1% were difficult-to-treat (D2T), more than in RA (17.2%). Radiographic progression was seen

in 41.6%. Hydroxychloroquine (66.7%) and glucocorticoids (87.5%) were widely used, with 87.5% achieving low-dose glucocorticoid therapy. [Conclusion] Rhupus patients have more treatment-resistant joint symptoms than RA, requiring more complex management.

P2-204

A Case of Mixed Connective Tissue Disease preceded by multiple renal stones associated with incomplete distal renal tubular acidosis

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Conflict of interest: None

[Case] A 65-year-old woman presented with finger stiffness and wrist pain for six months. She was diagnosed with mixed connective tissue disease (MCTD) based on Raynaud's phenomenon, polyarthritis, elevated myogenic enzymes, and a positive anti-U1-RNP antibody. She had a 20-year history of surgeries for renal ureteral stones, and multiple stones were found in both kidneys upon her hospital visit. Although there were no signs of acidemia, hypokinemia, dysacidemia, or hypercalciuria, a stone analysis from a lithotripsy performed two years ago showed calcium hydrogen phosphate (83%) as the main component. Incomplete distal renal tubular acidosis (idRTA) was suggested, and potassium citrate and sodium citrate hydrate were prescribed for stone prevention. The patient was negative for anti-SS-A antibodies, ruling out secondary Sjögren's syndrome. [Discussion] idRTA is a subclinical disorder that can cause recurrent urinary stones without typical lab findings like metabolic acidosis or hypokinemia. While Sjögren's syndrome is known background condition, there are no reports of idRTA complicating MCTD. In this case, idRTA is suspected as a complication of MCTD and may have contributed to long-term urinary tract infections (UTIs) while preceding various MCTD symptoms.

P2-205

A case of anti-RuvBL1/2 antibody-positive overlap syndrome with treatment resistance but remission

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Conflict of interest: None

[Case] 31-year-old female [Case Presentation] 11 months before, She became of limitation of range of motion. Seven months, limitation of range of motion in the upper body and neck. Three months, facial swelling and was referred to our department because systemic scleroderma suspected. She was observed m-Rondman TSS 41, telangiectasia, and grasping pains in the proximal muscles. Examination of the organs, pulmonary, cardiovascular, renal, or gastrointestinal lesions weren't found, but elevated myogenic enzymes, abnormal MRI signals, and myogenic changes on electromyography were observed, diagnosis of coexisting inflammatory myositis. Induction of remission with rituximab and steroids, and skin stiffness improved, but resistant to myositis with symptoms and high CK levels. Refractory to high-dose intravenous immunoglobulin therapy, and discharged home on the 73rd day of her illness after a response to methotrexate therapy. Later, anti-RuvBL1/2 antibody titer of 223.6 (Index value, normal value<10) was confirmed. [Clinical Significance] Anti-RuvBL1/2 antibody the specific antibodies known the overlap between SSc and DM/PM, and resistant to cutaneous sclerosis, myositis and interstitial pneumonia. It is rare antibody about 1% in myositis, we report this case as treatment remission.

P2-206

A case of systemic scleroderma with pneumatosis cystoides intestinalis markedly treated with hyperbaric oxygen therapy

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Conflict of interest: None

The patient, a 71-year-old woman, was diagnosed with systemic sclerosis (diffuse type) in March 20XX-7, based on diffuse skin sclerosis, periungual bleeding, anti-Scl-70 positivity, interstitial pneumonia, and GI motility disorders. She began treatment with prednisolone (PSL) 30 mg/day and high-dose cyclophosphamide, later adding nintedanib (NTD) and mycophenolate mofetil (MMF). By April 20XX, her regimen was PSL 5 mg/day, NTD 200 mg/day, and MMF 1500 mg/day. Chest X-ray showed free air under the diaphragm, and CT confirmed pneumatosis cystoides intestinalis (PCI). Minimal improvement was noted with fasting alone, so oxygen therapy (5 L/min) was initiated, leading to significant recovery. PCI, a rare condition with multilocular, gas-filled cysts in the intestinal wall, was first reported in Japan in 1901. Recent advances in imaging have increased case reports, now exceeding 600. When intraperitoneal free air is observed, PCI should be considered alongside intestinal perforation. High-concentration oxygen therapy, which may displace nitrogen in the intestine and have antimicrobial effects, should be considered if fasting and motility agents fail.

P2-207

A case of anti-Jo-1 antibody-positive polymyositis that developed with systemic lupus erythematosus-like symptoms against the background of systemic sclerosis that had been self-neglected

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Conflict of interest: None

[Background] The concepts of overlap syndrome and MCTD are known, but an appropriate understanding of the main pathology is required for treatment selection. [Case] A 51-year-old woman who had not been attending regular hospital visits. She was admitted to hospital due to low-grade fever and pain in both shoulders for one month, and difficulty walking due to dyspnea on exertion and proximal muscle weakness. She was diagnosed with PM based on CK 4614 IU/L, high signal areas on STIR images, myogenic changes on EMG, and anti-Jo-1 antibody over 550 U/mL. There were also SSc findings such as skin hardening and shortening of the finger tips due to distal phalangeal bone fusion. Echocardiography showed an RVSP of 49.9 mmHg Low complement levels, ANA (spe) 1280, anti-UI-RNP antibody over 550 U/mL, and positive anti-DNA antibody suggested the possibility of SLE coexistence, but this was not confirmed. PSL 1 mg/kg/day and TAC 4 mg/day was used to induce remission in PM, but this did not improve the condition, and IVIG was added to achieve a positive response. [Discussion] In addition to PM, there were also mixed findings of SSc and SLE-like findings. Even when the findings of one disease are prominent, it is necessary to provide medical care without anchoring bias.

P2-208

Isolated brain stem involvement in posterior reversible encephalopathy syndrome in a Scleroderma Renal Crisis

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Conflict of interest: None

77-year-old man. He has had stiffness in his fingers for 7 months. He started taking 5 mg of prednisolone 1 month ago after being diagnosed with arthritis. He visited the hospital on the day of the convulsions. He had skin sclerosis with an mRSS score of 30, blood pressure of 224/131 mmHg, hemoglobin of 9.1 g/dL, fractured red blood cells, LDH 1,124 IU/L, haptoglobin 1 mg/dL, positive anti-RNA polymerase III antibody, renal dysfunction, high signal in the pons and midbrain on head MRI FLAIR. Systemic sclerosis and associated renal crisis, posterior reversible encephalopathy syndrome (PRES) were diagnosed. Blood pressure was controlled with hemodialysis and captopril. His blood pressure and consciousness improved, and the high signal in the brain stem on the MRI four

days later was improving. Although PRES typically causes damage to the occipital lobe, a report published in 2020 that summarized 556 cases (PMID: 32265829) stated that damage also occurs in the pons (22.3%), brain stem (20.7%), and midbrain (8.6%). In addition, it has been suggested that, compared to occipital lobe-only PRES, abnormal hypertension may play an important role in the development of vasogenic edema in brainstem-only PRES (PMID: 22886172).

P2-209

Case of Systemic Sclerosis with spontaneous resolution of interstitial lung disease during 30 years

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Conflict of interest: None

[Case] A 93-year-old woman, who had Raynaud's phenomenon since X-30, had been visiting previous doctor since X-24. She was diagnosed as limited cutaneous systemic sclerosis because of anti-topoisomerase I antibody, skin sclerosis, reflux esophagitis, and interstitial pneumonia. She was referred to our hospital in X-13. In June X, high-resolution computed tomography (HRCT) showed fibrosis in both lungs, but no worsening compared to 2 months earlier. Retrospectively, KL-6 was low (308 U/mL) and the extent of lung lesions was limited (<20%), but she had advanced risk factors for progression with a score of 6 (non-smoker, 80 years old, %DLco 36.2%) in SADL model, and was eligible for treatment. Her respiratory status and oxygenation were good, so no therapeutic intervention was performed. [Clinical Significance] The patient had remained untreated for 30 years without oxygenation or deterioration of quality of life. Various risk factors for interstitial lung disease associated with systemic sclerosis have been proposed, including SADL model and KL-6 levels in patients who are unable to perform a 6-minute walk. However, when multiple risk factors do not show a certain trend, it is suggested that they may not reflect the pathophysiology of advanced fibrosis.

P2-210

Investigation of an approach to cardiorenal interactions in a case of scleroderma complicated by interstitial lung disease

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Conflict of interest: None

A 67-year-old woman was diagnosed with systemic scleroderma (SSc) positive for anti-Scl-70 antibody in X-2 year. In X-1, Y-1, fingertip ulcer appeared and interstitial lung disease (ILD) worsened. On Y Z, she visited the emergency room for orthopnea, decreased oxygenation. CT showed bilateral pleural effusion, IP exacerbation, intestinal dilatation, pericardial effusion and diffuse wall hypokinesia, and sudden onset of cardiomyopathy, atrial tachycardia (AT), SIBO led to congestive heart failure (HF) associated with SSc. Z+20 Respiratory status improved, discharged. Z+44, she was readmission due to worsening of AT-related HF and AKI, Emergency CHDF was introduced, diagnosed as NRSC (normotensive renal crisis), treated with ACE inhibitors, and placed on maintenance dialysis, died at Z+70 days. Clinical Significance: This patient had a SSc heart during the course of SSc-ILD, further merge NRSC, and struggled with dyspneic symptoms. NRSC is difficult to diagnose early, but in this case, it was difficult because without elevated blood pressure. In addition to SRC, SSc heart is prompt differentiation and initiation of treatment is important. In cases of SSc cardiac complications, it is important to differentiate between HF and NRSC, and the coexistence of both should be kept in mind.

P2-211

maintenance therapy in rapid progressive interstitial lung disease with anti-MDA5 antibodies

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Conflict of interest: None

[Objectives] This study aims to evaluate the treatment and prognosis of patients receiving remission maintenance therapy at Juntendo University Hospital. [Methods] A retrospective chart review was conducted for patients diagnosed with anti-MDA5 antibody-positive RP-ILD who received treatment at Juntendo University Hospital between April 2008 and September 2024. [Results] Of 57 patients diagnosed with anti-MDA5 antibody-positive dermatomyositis or clinically amyopathic dermatomyositis, 49 had RP-ILD. Two were excluded due to ongoing induction therapy, and six were excluded due to transfer to other facilities. During follow-up, seven patients died from interstitial lung disease, four from malignancies, one from sepsis, one from iliopsoas hemorrhage, and one from progressive supranuclear palsy. Among 27 patients undergoing remission maintenance therapy, six (22%) achieved drug-free remission, five achieved glucocorticoid (GC)-free remission with immunosuppressants, and 16 required both GC and immunosuppressants. [Conclusion] In this study, 22% of patients with anti-MDA5 antibody-positive RP-ILD receiving remission maintenance therapy achieved drug-free remission. The factors contributing to drug-free remission remain unclear.

P2-212

Risk Factors for Recurrence in Anti-ARS Antibody-Positive Dermatomyositis: Importance of Initial Steroid Dose and Presence of Other Collagen Disease Complications

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Conflict of interest: None

[Objectives] In anti-ARS antibody-positive dermatomyositis, some patients experience frequent recurrences or difficulty in reducing steroid doses despite immunosuppressive therapy. This study examined the characteristics and risk factors for recurrence. [Methods] A retrospective analysis of 26 cases treated from 2007 to 2024 was conducted, focusing on age at onset, interstitial pneumonia, additional collagen diseases, recurrence status, and initial steroid dosage. [Results] Median onset age was 59 years (IQR: 53.75-67.75). Interstitial pneumonia was present in 88.6% (22/26), with a median initial steroid dose of 60 mg. Recurrence occurred in 50% (13/26), and recurrence timing was similar regardless of collagen disease presence. Among the 9 patients with other collagen diseases, only 1 avoided increased steroid dosing. Recurrence was more frequent in complicated cases ($p=0.017$), while uncomplicated cases with recurrence had lower initial steroid doses ($p=0.047$). [Conclusion] These results suggest that anti-ARS antibody-positive dermatomyositis patients with other collagen diseases are at higher recurrence risk and need close monitoring. For uncomplicated cases, precise initial steroid dosing may help prevent recurrence.

P2-213

Ultra-low dose rituximab may be an option for managing treatment-resistant skin ulcers in MDA5-DM: a case report

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Conflict of interest: None

[Background] Anti-MDA5 antibody-positive dermatomyositis (MDA5-DM) and its interstitial lung disease (ILD) are often resistant to standard immunosuppressive therapy. Ultra-low dose rituximab (RTX) has been reported to be potentially effective while reducing the risk of infection. [Case] 47-year-old female diagnosed with MDA5-DM and ILD. Following initial treatment with steroid pulse therapy, intravenous cyclophosphamide, and intravenous immunoglobulin, the patient achieved remission with prednisolone (6 mg/day), mycophenolate mofetil (2500 mg/day) and cyclosporine (125 mg/day). However, skin ulcer recurred and anti-MDA5

antibody titer increased in few years. Various additional treatments including plasmapheresis, hydroxychloroquine, and baricitinib were administered, but none of them were sufficiently effective. Eventually, ultra-low dose RTX (100 mg every 3 months) was initiated, and skin ulcers got stable again. [Clinical Significance] RTX promotes B cell apoptosis and reduces the number of autoreactive plasma cells, thereby slowing disease progression. The low dose regimen is supposed to minimize the risk of infection, a common side effect of RTX. This case demonstrates that ultra-low dose RTX may be an effective treatment option for treatment-resistant skin ulcers in MDA5-DM.

P2-214

Pathological Study of Muscle Tissue of Anti-ARS Antibody-Positive Dermatomyositis Presenting as Focal Myositis

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Conflict of interest: None

[Background] We experienced a case of anti-ARS antibody-positive myositis with a clinical picture of focal myositis lacking systemic symptoms of typical anti-ARS antibody syndrome, so we report here the case with pathological considerations. [Case description] A 45-year-old woman with no significant medical history. She came to our hospital because of heat, pain, and erythema in her right upper extremity for the past six months. Physical examination revealed erythema and tenderness on the flexed side of the right upper arm. Blood tests showed no elevation of CK, CRP, or sedimentation rate, and positive autoantibodies for ARS antibody (PL-12), anti-SS-A/Ro-52 antibody, and anti-CCP antibody. MRI, needle electromyography, and muscle biopsy revealed inflammatory myositis as anti-ARS antibody syndrome. [Discussion] Pathologically, lym [phocytic infiltration was observed in the intramuscular sheath, mainly around blood vessels in the perimuscular membrane. Immunohistochemical staining showed a predominance of CD20- and CD4-positive lymphocytes, not inconsistent with anti-ARS antibody syndrome. [Conclusion] This is the first reported case of focal myositis preceding systemic symptoms in anti-ARS antibody syndrome.

P2-215

Prophylactic effect of trimethoprim-sulfamethoxazole on infections in idiopathic inflammatory myopathy

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Conflict of interest: None

[Objectives] Idiopathic inflammatory myopathy (IIM) is commonly treated with glucocorticoids and other immunosuppressants. Therefore, trimethoprim-sulfamethoxazole (TMP/SMX) is often used to prevent *Pneumocystis jirovecii* pneumonia. We evaluated the efficacy of TMP/SMX in preventing severe infections in IIM. [Methods] This retrospective, single-centre study included 91 patients diagnosed with IIM. The occurrence of severe infections during the follow-up period was evaluated. Cox regression analysis was used to identify risk factors for severe infection, with significant variables from the univariate analysis further evaluated in a multivariate analysis. [Results] Nineteen patients developed severe infections during the observation period. Patients with severe infections were significantly older. A higher proportion of them had rapidly progressive interstitial lung disease and were positive for anti-MDA5 antibodies. In the multivariate analysis, older age and higher serum creatinine level were associated with an increased risk of severe infection. TMP/SMX use was associated with a decreased risk of severe infection. [Conclusion] TMP/SMX is effective for preventing severe infections in patients with IIM who underwent remission induction therapy.

P2-216

Predictive Factors for Glucocorticoid-Free Remission in Patients with Idiopathic Inflammatory Myopathies

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Conflict of interest: None

[Objectives] To investigate predictive factors for glucocorticoid (GC)-free remission in patients with idiopathic inflammatory myopathies (IIMs). [Methods] A cross-sectional analysis was conducted comparing patients who discontinued GC during the remission period with those who continued it. [Results] Thirty patients (female 21, mean age 66.5±23.3) were enrolled. The autoantibody profile was as follows: anti-ARS (n=17), anti-MDA5 (n=3), anti-TIF1-γ (n=3), anti-SRP (n=1), and unknown (n=6, including 2 with anti-cytoplasmic antibodies). Excluding 5 patients who either did not use systemic GC for remission induction or were tapering GC immediately after onset, 21 out of 25 patients discontinued GC. The median duration of GC use was 32 months (IQR 20-58). Two predictors of GC-free remission were identified: age of onset less than 74 years (p= 0.0012) and absence of progressive fibrosing interstitial lung disease (PF-ILD) (p=0.0012). [Conclusion] The findings suggest that the predictive factors for positioning GCs as “bridging therapy” in IIMs are an age of onset less than 74 years and the absence of PF-ILD.

P2-217

Association between Negative Seroconversion of Anti-MDA5 Antibodies and Long-Term Remission in Patients with Dermatomyositis-associated Interstitial Lung Disease

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Conflict of interest: None

[Objective] To examine the relationship between anti-MDA5 seroconversion and clinical outcomes of dermatomyositis-associated interstitial lung disease (DM-ILD). [Methods] We retrospectively analyzed 29 anti-MDA5+DM-ILD patients treated at our institution from January 2004 to August 2024, each with at least two anti-MDA5 measurements using the MESACUP™ anti-MDA5 test, taken over a year apart as per the treating physician’s discretion. Remission was defined as stable disease for ≧3 months on <10 mg/day prednisolone equivalent; relapse was renewed activity requiring therapy escalation. [Results] Of the 29 patients, 28 achieved remission, 27 glucocorticoid-free remission (GFR), and 10 drug-free remission (DFR) at medians of 210 [range: 44-1537], 736 [213-3797], and 2074 [777-3638] days from treatment initiation, respectively. The time to first seroconversion was 1328 [218-4155] days. At the last observation, seroconversion rates were 0% (0/2) in non-GFR, 71% (12/17) in GFR, and 100% (10/10) in DFR. There were 8 relapses in 5 patients, including 1 after achieving GFR. There were no relapses after achieving DFR or seroconversion. [Conclusion] Anti-MDA5 seroconversion occurred in majority of DM-ILD cases observed for over a year and was linked to long-term GFR, DFR, and relapse-free survival.

P2-218

Identifying Two Pathways to Poor Prognosis in Patients with Anti-MDA5 Antibodies: Insights from Prognostic Factor and Cytokines Analysis

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Conflict of interest: None

[Objective] To identify the pathways from cytokine abnormalities to

mortality via prognostic factors in patients with anti-MDA5 antibodies. [Methods] Prognostic factors were identified using Cox regression and Kaplan-Meier methods. Prognostic factor groups were identified using PCA, factor, and cluster analyses. The association between cytokine levels and prognostic factors was examined using PCA, correlation, and path analyses. A prognosis-prediction model was developed using prognostic factors from the different groups. [Results] Thirty-five patients were included in this study, of whom 3l had RP-ILD, and 14 died. We identified WBC, γ-GTP, LDH, CRP, ferritin, KL-6, SP-D, and CT score as prognostic factors, in addition to von Willebrand factor and thrombomodulin. Two prognostic factor groups were found: Group 1 included WBC, CRP, KL-6, SP-D, CT score, and Group 2 included ferritin, LDH, and γ-GTP. Both groups independently contributed to mortality. Group 1 was associated with IL-6, and Group 2 was related to IL-6, IL-10, and IP-10, and indirectly with TNF-α. A model using CRP (Group1) and γ-GTP (Group2) achieved an AUC of 0.84. [Conclusions] These two pathways lead to poor prognosis in patients with MDA5 Ab-positive dermatomyositis, each characterized by cytokine abnormalities.

P2-219

Clinical Characteristics of Anti-SS-A/Ro Antibody-Positive Cases in Inflammatory Myopathies

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Conflict of interest: None

Objective: To clarify clinical characteristics of inflammatory myopathy patients positive for anti-SS-A/Ro antibodies. **Methods:** A retrospective study was conducted on 58 inflammatory myopathy patients treated in our department from January 2016 to October 2024. Clinical features at onset were compared between anti-SS-A/Ro antibody-positive and negative groups. **Results:** Among 58 patients, 14 were antibody-positive, 41 negative, and 3 unknown. Analysis on 55 patients (14 positive vs. 41 negative) showed no significant differences in onset age (53.00±16.36 vs. 56.59±18.44 years, p=0.522) or gender (71.4% vs. 70.7%, p=1.000). The positive group had significantly higher CK levels (4324.07±4054.97 vs. 1732.00±1850.16 U/L, p=0.002). Anti-SRP antibodies were more common in the positive group (28.6% vs. 2.4%, p=0.012), while anti-ARS antibodies were lower (0.0% vs. 30.0%, p=0.024). There were no significant differences in anti-MDA5, anti-TIF1-γ, or anti-Mi-2 antibodies. Immune-mediated necrotizing myopathy was also more frequent in the positive group (28.6% vs. 2.4%, p=0.012). Rates of interstitial pneumonia, cardiac involvement, or malignancy showed no significant differences. **Conclusion:** A potential link between anti-SRP antibody-positive necrotizing myopathy and anti-SS-A/Ro antibody was suggested.

P2-220

Clinical Feature of Autoantibodies Associated with Systemic Sclerosis/Dermatomyositis by A-Cube

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Conflict of interest: None

[Objectives] Dermatomyositis (DM)/Polymyositis (PM)/Systemic sclerosis-specific autoantibodies are useful for treatment strategy and prognosis. We aimed to evaluate the clinical characteristics of autoantibodies detected by the A-Cube test, which can detect DM/PM/Systemic sclerosis-related autoantibodies that cannot be measured by insurance-covered tests. [Methods] Seventeen patients who had attended our hospital between January 2022 and September 2024 and had undergone A-Cube testing were included. The age, sex, diagnosis, symptoms, laboratory findings, treatment and course were retrospectively investigated. [Results] Of the 17 patients, 8 had PM/DM. Five patients had Systemic sclerosis. Overlap syndrome was detected in 4 cases. Autoantibodies detected were PL-7, PL-12, EJ, KS, Zo, c1NA, SAE, Ki, SRP, Ku, RNAP III, hUBF, Th/To, p80-coilin, SSSCA1, RuvBL1/2, eIF2B. There was one death due to malignancy (SAE/cN1A/Ki positive) and one death due to alveolar hemorrhage (SSSCA1/eIF2B/Ki positive). [Conclusion] SSSCA1/eIF2B/Ki antibody may have poor prognosis. There have not been many reports of autoantibody cases using tests not covered by insurance, and we report this valuable data here. Further accumulation of cases is needed in the future.

P2-221

A multi-case study exploring high-dose intravenous immunoglobulin (IVIg) therapy for steroid-resistant idiopathic inflammatory myopathy (IIM)

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Conflict of interest: None

IVIg is considered an effective treatment for steroid-resistant IIM. We reviewed the clinical characteristics of IIM patients treated with IVIg in our department. We collected medical records of eligible IIM patients between 2011 and September 2024. A total of 7 cases with 3 males and 4 females were included, 3 dermatomyositis, 2 polymyositis, and 2 immune-mediated necrotizing myopathy. The mean age at first onset was 64.1±11.4 years. Myositis-specific antibodies were anti-SRP positive in 2 cases, anti-MDA-5 positive in 2 cases, anti-Mi2 positive in 1 case, anti-mitochondrial antibody positive in 1 case, and antibody negative in 1 case. The mean prednisolone (PSL) dosage at the first dose of IVIg was 45.0± 17.8 mg/day. Other immunosuppressive drugs were tacrolimus in 7 patients and cyclophosphamide in 2 patients. The therapeutic outcomes were favorable response in 2 cases, recurrence in 3 cases, and death in 2 cases. All relapses, including 3 patients, occurred after 2023. The PSL mean dose at the time of recurrence was 6.0±1.7 mg/day. All recurrent cases received an increased PSL dose and were forced to discontinue IVIg therapy due to lack of supply of IVIg. Stable supply of IVIg should be maintained so that steroid-resistant IIM patients can continue to receive low-dose PSL.

P2-222

Hospitalization during the clinical course in patients with elderly-onset idiopathic inflammatory myopathies

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Conflict of interest: None

[Objective] We investigated hospitalization characteristics during the clinical course in patients with elderly-onset idiopathic inflammatory myopathies (IIM). [Methods] The medical records of 111 patients in outpatient care, who were initially diagnosed with IIM and achieved remission after initial treatment in our hospital, were reviewed. Of these patients, hospitalization and its causes were investigated and compared between patients in whom IIM was diagnosed at more than 65 years (elderly) and less than 65 years (young). [Result] Of the 111 patients, 36 were included in the elderly group (mean 72 years, 17 women), while hospitalization was experienced in 62, of whom 26 were in the elderly group. Of those with hospitalization, deterioration of IIM was observed in 67 (26.9%) in the elderly group and 5 (19.2%) in the younger group. Hospitalization ascribable to malignancy and infections were more frequently observed in the elderly group (8 [30.8%] and 5 [19.2%], respectively) than in the young group (4 [11.1%] and 0, respectively), [Conclusions] Our study suggests that hospitalization during the clinical course of elderly-onset IIM may be predominantly attributed to malignancy and infections compared to its young generations.

P2-223

Development of ANCA-associated Vasculitis with Diffuse Alveolar Hemorrhage Following Autologous Hematopoietic Stem Cell Transplantation for Systemic Sclerosis

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Conflict of interest: None

A 52-year-old man was referred to our department with progressive skin thickening in his fingers. He was diagnosed with diffuse cutaneous systemic sclerosis (SSc), complicated by interstitial lung disease (ILD) and small intestinal bacterial overgrowth. Treatment with mycophenolate mofetil and tocilizumab was initiated; however, his ILD continued to progress. Autologous hematopoietic stem cell transplantation (auto-HSCT) was performed and successfully halted the progression of organ damage due to SSc. Six years after HSCT, he presented with exertional dyspnea and hemoptysis. Diffuse ground-glass opacities were observed predominantly in the lower lungs, and bronchoalveolar lavage revealed bloody fluid. Serum PR3-ANCA was elevated, resulting in a diagnosis of diffuse alveolar hemorrhage (DAH) due to ANCA-associated vasculitis. Treatment with glucocorticoid and rituximab led to rapid improvement. It should be noted that a variety of autoimmune phenomena can emerge after HSCT. Even in severe cases of DAH, favorable outcomes may be achievable with accurate diagnosis of the cause and prompt immunosuppressive therapy. When respiratory symptoms arise post-HSCT, DAH should be considered, and thorough evaluation is essential to assess new-onset autoimmune diseases as a potential cause.

P2-224

A pediatric case of HLA-B51/A26-positive primary central nervous system vasculitis showing improvement after infliximab

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Conflict of interest: None

[Introduction] GC and IVCY have been reported as treatments for PACNS, but there are also cases that are dependent or resistant to these treatments. [Case Presentation] A 14-year-old girl was admitted to our hospital with fever and short-term memory impairment. Brain contrast MRI showed ring-like enhancement with edema in the bilateral thalamus. Methylprednisolone pulse therapy was administered, but symptoms did not improve and brain MRI findings worsened. A brain biopsy was performed from the contrast-enhanced area of the left thalamus to differentiate from tumorous diseases. Pathological examination revealed lymphocytic vasculitis. The patient was diagnosed with PACNS. Although IVIg and IVCY were administered, the patient became drowsy and the MRI findings worsened. Rituximab was also administered, but this had little effect and the patient went into a coma. There had been no clinical symptoms suggestive of Behçet's disease, and no increase in cerebrospinal fluid IL-6, but the patient had HLA-B51 and A26. Infliximab resulted in afebrile and an improvement in brain MRI findings, but the patient's consciousness remained impaired. [Discussion] Rituximab has been reported most frequently as a biological agent for PACNS, and there have been few reports on TNF inhibitors.

P2-225

A Case of RF-Positive Eosinophilic Granulomatosis with Polyangiitis Presenting with Diverse Symptoms, with Cerebrovasculitis Successfully Treated by Methotrexate

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Conflict of interest: None

[Case] A 43-year-old woman developed bronchial asthma at X-15M, which was controlled with inhaled and oral steroids. At X-6M, she self-discontinued PSL, resulting in acute heart failure and nephritis. She was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) based on an hypereosinophilia and positieve MPO-ANCA, with myocarditis and nephritis. She received high-dose PSL following mPSL pulse therapy, with subsequent improvement. At X-2M, she experienced headache and fever with increased eosinophils. Mepolizumab (MEP) was added, which controlled the eosinophilia, but inflammation persisted. Azathioprine was added soon, but she developed headache and fever due to cerebrovasculitis. Intravenous cyclophosphamide (IVCY) was added, and she was referred to our hospital. IVCY was continued, and PSL was increased, showing partial response. However, cerebrovasculitis was persistent. As the cumulative dose of IVCY exceeded 5 g at X+4M, methotrexate (MTX) was introduced, leading to resolution of cerebrovasculitis symptoms. She remained relapse-free while tapering PSL. [Conclusion] Cerebrovasculitis was resistant to PSL and IVCY, showing a remarkable response to MTX. While some reports suggest MTX efficacy in RF-positive cases, comprehensive studies are lacking.

P2-226

A case of eosinophilic granulomatosis with polyangiitis in which mepolizumab was administered first and cholecystectomy was performed because suppurative cholecystitis could not be ruled out

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Conflict of interest: None

Case: An 56-year-old female presented with a three-month history of distal limb paresthesia. Initial blood tests at a local clinic showed peripheral eosinophilia, leading to her referral to our hospital. Given her asthma history, elevated eosinophils, and multiple mononeuropathy, she was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). CT imaging revealed cholelithiasis and gallbladder wall thickening, with elevated serum procalcitonin suggesting possible suppurative cholecystitis. Mepolizumab was administered as initial treatment, followed by laparoscopic cholecystectomy by the Department of Gastroenterological Surgery. Postoperatively, high-dose corticosteroids were initiated. Pathological findings of vasculitis were shown in the removed gallbladder. Discussion: Although EGPA can involve eosinophilic cholecystitis, histopathologically confirmed cases remain rare. There are currently no definitive biomarkers to differentiate suppurative from eosinophilic cholecystitis, and treatment decisions are generally left to physician discretion. In this case, we report the use of mepolizumab, a relatively safe therapeutic option, as an initial treatment approach for EGPA with cholecystitis.

P2-227

A Case of IgA Vasculitis Complicated by Severe Diffuse Alveolar Hemorrhage Successfully Treated with Immunosuppressive Therapy

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Conflict of interest: None

[Case] A 61-year-old woman had sore throat one month before admission, which resolved in a few days. Two weeks later, she presented with palpable purpura and pain in both lower legs. A skin biopsy confirmed leukocytoclastic vasculitis. She was admitted due to new onset of lower abdominal pain, acute renal injury, proteinuria, hematuria and patchy ground-glass opacities in both lungs on computed tomography (CT). On day 3, she developed cough with hemoptysis and CT showed crazy paving pattern. A renal biopsy indicated proliferative glomerulonephritis with IgA and C3 deposition, confirming IgA vasculitis. Bronchoscopy with bronchoalveolar lavage showed diffuse alveolar hemorrhage (DAH). She received pulse methylprednisolone on day 4 and plasma exchange on day 7. However, she developed hypoxia and required mechanical ventilation on day 8. Cyclophosphamide pulse therapy was initiated, leading to respiratory improvement and she was extubated on day 18. Her skin rash and re-

nal function improved and she was transferred for rehabilitation on day 100. [Clinical Significance] DAH associated with IgA vasculitis is extremely rare and highly lethal particularly in adult-onset cases with no established treatment. Early introduction of immunosuppressive therapy may have saved this patient's life.

P2-228

Elderly ANCA-associated vasculitis with significant response to rituximab-Avacopan combination therapy: Two case reports

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Conflict of interest: None

Background: The ADVOCATE trial demonstrated Avacopan's superiority over glucocorticoids (GC) in achieving sustained remission at 52 weeks in patients with ANCA-associated vasculitis (AAV). There is limited evidence on its efficacy and combination therapy in elderly patients. This report presents two cases of elderly AAV patients treated with Avacopan after remission induction with Rituximab (RTX). **Case 1:** A 72-year-old female with microscopic polyangiitis (MPA) complicated by interstitial pneumonia, rapidly progressive glomerulonephritis (RPGN), and mononeuritis multiplex. She received two doses of RTX, but further administration was halted, resulting in persistent renal dysfunction. After Avacopan initiation, her renal function improved, and no symptom relapse was observed despite GC tapering. **Case 2:** A 67-year-old male with granulomatosis with polyangiitis (GPA) complicated by RPGN and otitis media associated with AAV (OMAAV). He received four doses of RTX; however, he had recurrent OMAAV and persistent renal dysfunction. Avacopan administration improved his otitis media and renal function with no relapses. **Discussion:** The combination of RTX and Avacopan resulted in favorable outcomes. Further studies are needed to investigate long-term safety and efficacy in older populations.

P2-229

Treatment and prognosis in patients with polyarteritis nodosa

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Conflict of interest: None

[Objectives] Polyarteritis nodosa (PAN) has variable treatment responses, with disease progression that can be fatal. This study aimed to investigate the treatment, disease course, and prognosis of PAN. [Methods] We retrospectively analyzed the medical data from eight patients diagnosed with PAN between September 2010 and September 2024. [Results] The male-to-female ratio was 1:3, with a median age of onset at 68 years. The frequencies of major symptoms were as follows: general symptoms (63%), arthralgia/myalgia (75%), skin symptoms (63%), renal involvement (13%), peripheral neuropathy (25%), gastrointestinal involvement (25%), and cardiac involvement (13%). The five-factor score (FFS) and Birmingham Vasculitis Activity Score (BVAS) at the initial visit were 1.5 and 7 points, respectively. The initial prednisolone (PSL) dose was 42.5 mg/day, and 88% of patients received immunosuppressive drugs. For patients refractory to or intolerant of immunosuppressive agents, biologic agents were used in four cases and Jak inhibitors in two, allowing subsequent PSL reduction. Two patients died within two years; these patients had baseline FFS $\geqq$ 3 and BVAS $\geqq$ 12. [Conclusion] High FFS is associated with poor prognosis in PAN, emphasizing the need for tailored treatment in high-risk cases.

P2-230

Eosinophilic granulomatosis with polyangiitis complicated by rapidly progressive limb necrosis associated with peripheral arterial disease

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Conflict of interest: None

The patient is a 75-year-old male diagnosed with peripheral arterial disease (PAD) in 20XX-20. In November 20XX, he was referred to our hospital due to petechial hemorrhage on the dorsal surface of his foot and polyneuritis, with laboratory tests revealing eosinophilia and elevated inflammatory markers. Although MPO-ANCA and PR3-ANCA were negative, a skin biopsy indicated necrotizing vasculitis with eosinophilic infiltration, leading to a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). Upon admission, there were no necrotic lesions on the fingers or toes. However, within one week, rapidly progressive necrotic changes were observed, prompting high-dose glucocorticoid therapy and intravenous cyclophosphamide. The lesions worsened until rituximab was added on day 22, resulting in a suppression. EGPA is often associated with cutaneous manifestations, though reports of necrosis are rare. Mechanisms for skin ulceration include immune response activation, endothelial cell damage, thrombus formation. In this case, necrosis was likely due to blood flow failure caused by vasculitis, in addition to existing PAD. Early therapeutic intervention is crucial for patients with EGPA who have PAD due to the risk of rapid progression of blood flow insufficiency.

P2-231

A case of multidisciplinary treatment of polyarteritis nodosa presenting with necrosis of the fingers, successfully controlling the progression of the disease

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Conflict of interest: None

[Case] An 85-year-old woman. [Chief complaint] Pain in the fingers. [History of current illness] In October of X-1, Raynaud's phenomenon, slight fever had developed. In March of X, the patient developed pain in the fingers, which gradually worsened. Skin biopsy from the livedo reticularis demonstrated small vasculitis of the subcutaneous pancreatic tissue. Abdominal contrast CT revealed multiple areas of poor nephrography, and abdominal angiography revealed irregular stenosis of the left renal artery. The patient was diagnosed with polyarteritis nodosa (PAN). Prednisolone at 1 mg/kg/day was started, and the systemic symptoms improved, but the cold sensation and blackening of the fingers progressed. Prostaglandin preparations and steroid pulse therapy were performed. For intensified treatment, intravenous cyclophosphamide therapy and high-dose immunoglobulin therapy were added. Vasodilators, hyperbaric oxygen therapy, near-infrared therapy, and antithrombotic drugs were used to treat peripheral circulatory failure. The inflammatory response normalized on the 51st day and we confirmed there was no progression of finger necrosis. [Clinical Significance] In order to prevent the early progression of necrosis caused by PAN, multidisciplinary treatment is recommended.

P2-232

A case of IgA vasculitis with steroid refractory peripheral neuropathy improved by Intravenous Cyclophosphamide Pulse Therapy

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Conflict of interest: None

[Case] 20s female [Chief complaint] purpura, abdominal pain [History of present illness] The patient had purpura on the lower legs and abdominal pain. Although she had no renal problems, skin biopsy showed leukocytoclastic vasculitis with IgA deposits, and endoscopy showed mucosal erosion and ulcerations. She was diagnosed with IgA vasculitis. Purpura was improved by rest and Non-Steroidal Anti-Inflammatory Drugs, but abdominal pain and arthralgia got worse, and prednisolone 50 mg/day was started with blood-coagulation factor XIII. Numbness of the upper limbs appeared on the 2nd day in hospital, and nerve conduction study on the 12th day showed multiple mononeuropathy. For neuropathy, steroid pulse and intravenous cyclophosphamide pulse therapy (IVCY) were added. Neuropathy, abdominal pain and arthralgia improved after 6 cycles of IVCY. Steroid is being tapered off. [Clinical Significance] Peripheral neuropathy is rare in IgA vasculitis. In this case, peripheral neuropathy was refractory to steroid, requiring more intense treatment. There were some reports about IVCY effectiveness for abdominal pain and nephritis, but the effectiveness for neuropathy has not been reported. We report a case that 6 cycles of IVCY improved peripheral neuropathy. We'll discuss this issue with the literature.

P2-233

A Case of Eosinophilic Poly-Angiitis Granulomatosis with PSL-Free Using Mepolizumab for Glucocorticoid Resistance

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Conflict of interest: None

[Clinical Significance] Eosinophilic polyangiitis granulomatosis (EGPA) is a vasculitis of small arteries that is included in ANCA-associated vasculitis and responds to high doses of glucocorticoids. We have experienced an EGPA patient in which mepolizumab (MEP) was introduced at our hospital and PSL-Free was achieved. [Case] A 79-year-old woman with a history of bronchial asthma onset at the age of 50 was referred to our rheumatology division with her symptoms of peripheral neuropathy of both lower legs, urticaria rash, peripheral edema of the extremities, and eosinophilia (26,208 per microliter). Then, she was started with a PSL of 0.5 mg/kg body weight (30 mg/day) in consideration of age; however, there was no improvement. On the 7th day, judging that the patient was refractory to existing treatment, the dose of PSL was increased to 40 mg/day and combined use of MEP 300 mg every 4 weeks. After that, the PSL gradually decreased and ended on the day 236. In addition, the interval was extended to MEP 300 mg is extended every 5 weeks from day 242, and her condition was keeping well for more than one year; moreover, further extensions of the injection interval are planned.

P2-234

A case of drug-induced liver injury due to avacopan improved by mycophenolate mofetil

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Conflict of interest: None

[Case] A 74-year-old woman was admitted to our hospital with fatigue and anorexia. Five years prior to admission, she was admitted to our hospital with fever, multiple pulmonary nodules and renal failure. She was diagnosed with granulomatosis with polyangiitis (GPA) based on bronchoscopy findings of necrotizing granulomatous vasculitis and elevated serum myeloperoxidase-antineutrophil cytoplasmic antibody. She improved on induction remission therapy with prednisolone (PSL) and rituximab. Finally, she was maintained on 3 mg/day of PSL without worsening disease activity. She had started avacopan 3 months before hospitalisation due to worsening disease activity. A week before admission, she experienced fatigue and anorexia. She visited our hospital as her symptoms gradually worsened. At the time of this admission, blood tests showed severe liver injury and since other diseases were ruled out, she was diagnosed with drug-induced liver injury (DILI) secondary to avacopan. Avacopan was therefore discontinued, glucocorticoid doses were increased and ursodeoxycholic acid was administered; however, the liver injury did not resolve until after mycophenolate mofetil was started. It was therefore suggested that mycophenolate mofetil may be effective in treating DILI caused by avacopan.

P2-235

A case of propylthiouracil-induced ANCA-associated vasculitis successfully treated with glucocorticoid and avacopan

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Conflict of interest: None

A 73-year-old woman referred to our hospital because of fever and purpura. She had been taking propylthiouracil (PTU) for hyperthyroidism 1 years ago. Purpura was observed on her face, arms, legs, and buttocks. Laboratory findings showed C-reactive protein (CRP) was 15.8 mg/dL, creatinine was 1.05 mg/dL, myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) was 8.1 IU/mL. A drug lymphocyte stimulation test for PTU was positive. Urinalysis showed persistent proteinuria. Chest CT showed interstitial pneumonia in both lungs. A skin biopsy revealed inflammatory cell infiltrate in dermis and fat lobules. Based on these findings, the patient was diagnosed with PTU-induced ANCA-associated vasculitis (AAV). PTU was discontinued, and CRP levels decreased; however, fever, purpura, and renal dysfunction persisted. She received prednisolone 0.5 mg/kg/day and avacopan. After 4 weeks, clinical symptoms improved, MPO-ANCA levels decreased, and proteinuria improved. Drug-induced AAV typically does not involve severe organ damage and improves with the discontinuation of an offending drug. In this case, severe organ damage occurred, and combination therapy with glucocorticoid and avacopan was highly effective. We report clinical features of PTU-induced AAV and literature review.

P2-236

A Case of Microscopic Polyangiitis Mimicking Anti-Jo-1 Antibody Positive Myositis

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Conflict of interest: None

Case: A 68-year-old woman presented with a-month history of fever, polyarthralgia, and limb weakness, leading to gait disturbance. Blood tests showed anti-Jo-1 antibody positivity, and chest CT indicated interstitial pneumonia, suggesting anti-ARS syndrome. Physical Examination: Swelling and tenderness in finger and wrist joints, with muscle weakness (neck 4, deltoid 3/3, iliopsoas 2/2, anterior tibialis 2/2). Decreased sensation in ulnar nerve areas, lower legs, and purpura on toes were noted. Laboratory Findings: CK 18 U/L, aldolase 5.8 U/L, creatinine 0.4 mg/dL, CRP 12.48 mg/dL, MPO-ANCA >300 U/mL, proteinuria (2+), hematuria (2+), and glomerular RBCs. MRI showed thigh STIR hyperintensity; EMG indicated myogenic changes in left proximal muscles. Nerve tests showed reduced CMAP and absent SNAPs in relevant nerves. Skin biopsy showed vasculitis, and kidney biopsy indicated crescentic glomerulonephritis, while right biceps biopsy was negative for myositis Clinical Course: Diagnosed with microscopic polyangiitis, she was treated with steroids and rituximab. Symptoms improved, and she transferred for rehabilitation on day 40. Clinical Significance: Despite high specificity, anti-Jo-1 antibody can yield false positives, requiring differential diagnosis in atypical cases.

P2-237

A case of microscopic polyangiitis presenting with fever of unknown origin and duodenal ulcer

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Conflict of interest: None

A 76-year-old man was found immobile at home and was brought to our hospital. Blood tests showed an increased inflammatory response, and chest CT showed granular shadows in the lungs. Antibiotic treatment was started for bacterial pneumonia, but he was referred to our department because his blood test showed a high MPO-ANCA level of 112 IU/mL. At the same time, he developed a duodenal ulcer, and reevaluation of the pathological specimen showed vascular destruction due to inflammatory cell infiltration. The patient met the classification criteria of the ACR/EULAR, and was diagnosed with microscopic polyangiitis (MPA). Treatment with high-dose prednisolone and methotrexate was started. The patient progressed without recurrence of symptoms and was transferred to another hospital. Although the symptoms of MPA in this case were not typical, the high MPO-ANCA level and pathological findings of the duodenal ulcer allowed us to make a diagnosis. It is important to remember that gastrointestinal ulcers caused by fever of unknown origin are not only stress ulcers, but also small and medium-sized vasculitis.

P2-238

A Case of Recurrent Granulomatosis with Polyangiitis Proven by Pleural Histopathology

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Conflict of interest: None

[Case] A 43-year-old male presented with nosebleeds and ear pain 2 years and 4 months before admission. He had elevated serum CRP (4.5 mg/dL), PR3-ANCA (157 U/mL), and mastoid effusion on CT. He was clinically diagnosed with granulomatosis with polyangiitis (GPA) and started on prednisolone (PSL) 40 mg/day and azathioprine. His symptoms, CRP, and PR3-ANCA improved, allowing PSL tapering. However, upon reducing PSL to 14 mg/day, he developed recurrent nosebleeds, chest pain, and PR3-ANCA elevation (18.1 U/mL). CT revealed right pleural thickening with little effusion, and pleural biopsy showed marked inflammatory cell infiltration in arterial walls and necrotizing granulomas, confirming active GPA. He also had arthralgia and tongue ulcers, prompting glucocorticoid pulse therapy, intravenous PSL (75 mg/day), and rituximab for GPA recurrence. Eight days after admission, he developed sudden abdominal pain. Abdominal CT showed free air, and emergency surgery confirmed peritonitis from perforated small intestinal ulcers likely related to GPA. He later experienced hematemesis due to multiple duodenal ulcers based on endoscopy and ultimately died. [Discussion] This case is the first report demonstrating the pathological characteristics of pleural lesions in GPA.

P2-239

A Case of Microscopic Polyangiitis without Specific Organ Damages Definitely Diagnosed by Muscular Biopsy

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Conflict of interest: None

[Case] A 79-year-old male presented with fatigue, fever, and lower limbs edema 3 months before his admission. He visited a nearby hospital and was suspected of pyelonephritis by CT findings and a CRP elevation of 10.7 mg/mL. As antibiotics were not effective and MPO-ANCA was 67.1 IU/mL, he was transferred to our hospital. On admission, we observed weakness in his femoral muscles without tenderness. Although his CK levels were normal, MRI showed high intensities on STIR in his thigh muscles, and CT revealed interstitial lung disease of usual interstitial pneumonia pattern. For a definitive diagnosis, we performed a biopsy from his right thigh, including skin, subcutaneous fat, fascia, and the vastus lateralis muscle. The biopsy revealed fibrinoid necrosis and inflammatory cell infiltration in small vessels, confirming microscopic polyangiitis. We administered 0.5 mg/kg prednisolone (PSL) and weekly rituximab due to his exhaustion by sustained inflammation. Following treatment, his manifestations improved rapidly, allowing to taper the PSL. [Discussion] In patients with systemic inflammation and positive MPO-ANCA, a muscle biopsy can provide a definitive diagnosis of vasculitis, especially when specific organ damages are absent but there are inflammatory changes in muscles by MRI.

P2-240

A case of tubulointerstitial damage accompanied by fever and weight loss diagnosed as microscopic polyangiitis and treated with avacopan

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Conflict of interest: None

[Case] 77 years, Female [Cheif complaint] Fever [Current medical history] She had a fiver over 2 weeks, and visited her previous doctor and was found to have loss of weight and had elevated CRP and MPO-ANCA levels. CT scan, upper gastrointestinal endoscopy, and occult blood in stool were performed, but no abnormalities were found. Urinalysis findings suggested renal tubular damage, a renal biopsy was performed and findings showed tubulointerstitial nephritis with peritubular capillary (PTC) inflammation. After treatment induction with PSL 20 mg and discharge, avacopan was introduced while reducing the dose of PSL, and remission has been maintained. [Clinical Significance] Current Japanese diagnostic criteria used to MPA state that the main symptoms are (1) rapidly progressive glomerulonephritis, (2) pulmonary hemorrhage or interstitial Interstitial pneumonia, (3) organ symptoms other than the kidney and lung, and eihter definite diagnosis and probable diagnosis requires the satisfaction of 1 or more of these items. On the other hand, MPA is known to be complicated by tubulointerstitial damage such as PTC inflammation. In this case, we report a diagnosis of MPA based on interstitial nephritis accompanied by PTC inflammation, and the treatment was effective.

P2-241

A case of MPO-ANCA-related vasculitis that combines glomerular nephritis and tubular interstitial nephritis with temporal arteritis

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Conflict of interest: None

The patient was a 68-year-old woman with a history of ulcerative colitis, meningioma, and depression. She had pain when swallowing, neck pain, pain near the temples, fever, and persistent severe inflammation. Antibiotic treatment was ineffective. She developed tenderness in the temporal artery, pain in the entire head, and numbness in both legs, so PSL 40 mg (1.0 mg/kg) was started. A temporal artery biopsy revealed necrotizing arteritis. A renal biopsy revealed crescentic glomerulonephritis, tubulointerstitial nephritis, and necrotizing vasculitis of the interlobular arteries. Based on the pathological findings of positive MPO-ANCA, the patient was diagnosed with ANCA-associated vasculitis, and rituximab was administered. This is a rare case of ANCA-associated vasculitis with simultaneous widespread vasculitis, pathologically proven inflammation of medium-sized vessels at the temporal artery level, interlobular arteries of the kidney, and glomeruli and interstitium. There have been few reports of ANCA-associated vasculitis associated with temporal artery lesions and small-vessel vasculitis, so we summarize the literature on ANCA-associated vasculitis associated with temporal artery lesions.

P2-242

Dynamic contrast-enhanced MRI was useful in two cases of antineutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: None

[Background] Reports on the usefulness of dynamic contrast-enhanced (DCE) MRI for muscle lesions in antineutrophil cytoplasmic antibody-associated vasculitis (AAV) are limited. Here, we report two AAV cases in which DCE MRI was useful. [Case 1] A 77-year-old woman developed fever, upper limb muscle pain, and lower leg edema, along with elevated CRP levels and MPO-ANCA positivity. DCE MRI of the lower legs showed dot-like contrast enhancements within the muscle. Muscle biopsy revealed fibrinoid necrotizing vasculitis, leading to a diagnosis of microscopic polyangiitis. Prednisolone (PSL) was started, resulting in clinical improvement, and resolution of DCE MRI findings. [Case 2] A 68-year-old man experienced fever and lower leg muscle pain. He had a history of asthma and eosinophilia and was accompanied by nasal polyps, obstructive airway lesions, and palpable purpura. DCE MRI of the lower legs revealed dot-like contrast enhancements within the muscle. Skin biopsy from the purpura showed fibrinoid necrotizing vasculitis. He was diagnosed with eosinophilic granulomatosis with polyangiitis. PSL treatment led to symptom improvement and resolution of DCE MRI findings. [Clinical Significance] DCE MRI may be useful for detecting muscle lesions and evaluating disease activity in AAV.

P2-243

A Case of CRP-Negative Microscopic Polyangiitis

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Conflict of interest: None

[Case] An 81-year-old woman. She had noticed proteinuria for about a month, visited a clinic, and was referred to our department due to renal dysfunction. She had lower leg edema. Blood test showed CRP 0.14 mg/dL, Cr 1.88 mg/dL, MPO-ANCA 153 U/mL. Urine test Urinary occult blood 3+, urinary protein 2+. Chest CT showed interstitial pneumonia. Renal biopsy was performed. Crescentic glomerulonephritis was observed, and the patient was diagnosed with ANCA-associated vasculitis (AAV). Treatment was started with prednisolone (PSL) 30 mg and rituximab 500 mg 4 times/month, and proteinuria improved. The steroid dose was reduced to 10 mg or less within 3 months of starting treatment. [Discussion] This is a case of interstitial pneumonia and crescentic glomerulonephritis, although fever and inflammatory reactions were negative. There have also been reports of crescentic glomerulonephritis due to microscopic polyangiitis with low or negative inflammatory reactions, so vasculitis must be kept in mind when dealing with renal dysfunction accompanied by hematuria.

P2-244

A case of MPA with extensive gastrointestinal lesions requiring massive blood transfusion successfully treated with RTX

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Conflict of interest: None

[Case] A 73-year-old woman was admitted to hospital in July X-1 because of coughing. A ground glass shadow was observed on CT. After admission, haematemesis and hematochezia occurred, and multiple ulcers were found during upper and lower endoscopy. She had acute kidney injury, and a high PR3-ANCA level, suggesting MPA. mPSL pulse therapy and PSL 60 mg/dL were initiated, but the anemia did not improve, and massive blood transfusion was administered. The endoscopic findings did not improve, so she was referred to our department. After the addition of RTX, it was possible to gradually reduce the transfusions. Repeated endoscopic examination confirmed scarring of the ulcer, and pneumonia and acute kidney injury also improved. Maintenance therapy was then performed by regularly administering RTX, and no recurrences have been observed. [Discussion] Gastrointestinal haemorrhage due to AAV is a relatively rare but serious complication. In this case, extensive ulceration of the upper and lower gastrointestinal tract was observed, and hemostasis by endoscopy and arterial embolisation was difficult, requiring massive blood transfusion. The evidence for treatment choice for gastrointestinal haemorrhage due to AAV is insufficient, but it suggests that RTX may be effective.

P2-245

Successful treatment of severe pulmonary-renal syndrome using early multidisciplinary intervention including plasma exchange (PE) and rituximab (RTX) prior to definitive diagnosis

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Conflict of interest: None

A 58-year-old woman was admitted to another hospital with deteriorating renal function (Cre 5.31 mg/dL). Following the development of pleural effusion and hemoptysis, she required mechanical ventilation and was transferred to our facility. Laboratory investigations revealed severe anemia and worsening renal function (Cre 7.27 mg/dL). V-V ECMO was initiated due to refractory respiratory failure. Based on the clinical presentation and laboratory findings, pulmonary-renal syndrome was suspected. Treatment with mPSL 1000 mg/day and CHDF was initiated. Daily PE was commenced on day 3 and continued for seven days, with RTX (375 mg/m^2) administered on day 4. The patient was transitioned to mPSL 60 mg/day on day 5. Subsequently, PR3-ANCA testing revealed elevated levels (1680 U/mL), confirming ANCA-associated vasculitis with a BVAS of 26 points. Allowing successful weaning from V-V ECMO on day 8 and mechanical ventilation on day 12. Renal replacement therapy was discontinued on day 21. After completing four doses of RTX, the patient's BVAS decreased to 8 points. Clinical Significance: Pulmonary-renal syndrome carries a poor prognosis and requires differential diagnosis. This case demonstrates that therapeutic intervention prior to definitive diagnosis can lead to successful outcomes.

P2-246

A case of multiple cerebral infarctions immediately after the start of MPA treatment

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Conflict of interest: None

[Case] An 85-year-old woman. Her generalized edema worsened, and her pleural effusion and enlarged heart were observed on X-ray. Although her heart failure improved with diuretics, she was referred to our department because ANCA-associated vasculitis was suspected due to positive MPO-ANCA. A renal biopsy revealed crescentic glomerulonephritis and tubulointerstitial nephritis, and the diagnosis of microscopic polyangiitis (MPA) was made, and treatment was started with 1 mg/kg prednisolone (PSL). However, 2 days after the start of treatment, the head MRI showed multiple cerebral infarcts in multiple vascular territories without obvious stenosis of major arteries. Rituximab was introduced in combination with warfarin as the cause of multiple cerebral infarctions due to hypercoagulability caused by initiation of PSL and vasculitis, and the patient has since progressed without recurrent cerebral infarctions. [Discussion] The patient had multiple cerebral infarctions, and the differentials were vasculitis, infectious infarction, intracardiac shunt, Trousseau's syndrome, and coagulation abnormality. The case of this patient who developed immediately after the start of MPA therapy is rare, and we report it here with some discussion of the literature.

P2-247

Report of two cases of ANCA negative ANCA associated vasculitis with alveolar hemorrhage

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Conflict of interest: None

[Objective] ANCA-associated vasculitis (AAV) is a small-vessel vasculitis characterized by ANCA positivity in serum. However, if ANCA is negative serologically but meets the criteria for ANCA-associated vasculitis, it is called ANCA-negative ANCA-associated vasculitis. We report two cases in which the patient was ANCA-negative but was diagnosed with ANCA-associated vasculitis. [Case 1] 72-year-old man. He was rushed to our hospital due to fever and worsening respiratory condition. He presented with hemoptysis, so bronchoscopy was performed and he was diagnosed with alveolar hemorrhage. Due to renal function decline AAV was suspected, and steroid pulse therapy and cyclophosphamide pulse (IVCY) therapy were administered. He was then weaned from the ventilator. Currently, remission is maintained with prednisolone (PSL) 5 mg/day. [Case 2] 66-year-old man. He visited our hospital due to fever and difficulty moving. After that bloody sputum appeared. As in case 1, alveolar hemorrhage was diagnosed by bronchoscopy and treated by steroid pulse and IVCY therapy. The patient is progressing well, too. [Discussion] The ANCA positivity rate is said to be about 70% for MPA, 80-90% for GPA, and 50% for EGPA. We will discuss ANCA-negative ANCA-associated vasculitis through the case of our hospital.

P2-248

Four cases of ANCA-associated vasculitis presenting with pulmonary myocardial syndrome

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Conflict of interest: None

[Objectives] Pulmonary muscle syndrome (PMS) was proposed as a variant of microscopic polyangiitis (MPA) characterized by interstitial pneumonia and myositis symptoms [Birnbaum 2007]. Although there are several case reports of PMS, the characteristics of PMS have not been fully elucidated. We aimed to investigate clinical characteristics of pulmonary myocardial syndrome in a city hospital. [Methods] Patients with ANCA-associated vasculitis (AAV) admitted in our department between April 2012 and October 2024 were screened. We defined PMS as cases having both interstitial pneumonia and muscle symptoms with high-intensity lesions with T2-weighted magnetic resonance imaging. [Results] Among 73 AAV cases, four had PMS. All cases were MPO-ANCA positive and classified as MPA. All cases had rheumatoid factor and normal CK levels. No glomerulonephritis was observed during the observation period of a median of 708.5 days (range 159-3531) after treatment. [Conclusion] PMS in AAV was associated with rheumatoid factor but not with glomerulonephritis. We concluded that PMS was considered as a unique type of AAV.

P2-249

A case of drug-induced liver injury possibly caused by avacopan in a patient with microscopic polyangiitis

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Conflict of interest: None

Case: A 68-year-old man was diagnosed with microscopic polyangiitis (MPA) based on necrotizing crescentic glomerulonephritis 2 months ago. Prednisolone (PSL) 60 mg and intermittent pulse intravenous cyclophosphamide (CY) 500 mg/2 weeks were initiated 56 days ago, followed by the addition of avacopan (AVA) 35 days ago. 14 days ago, AVA was discontinued due to mild liver damage, ALT 64 U/L. Jaundice developed and worsened. he was admitted for further evaluation. There was no history of alcohol consumption. T-Bil 18.6 mg/dL, ALT 118 U/L, ALP 471 U/L, antinuclear antibody <40. All hepatitis virus markers were negative. No calculi were identified on ERCP, and bile culture was negative. Liver biopsy was perfoemed, and histology revealed portal tract inflammation with eosinophilic hepatocyte necrosis. AVA had a RECAM-J 2023 score of 11, indicating a possible drug-induced liver injury (DILI). CY and AVA were discontinued, and PSL was continued. Jaundice gradually improved, and the ALP level decreased. Discussion: AVA was associated with a 5.4% incidence of DILI in the ADOVOCATE trial. A higher incidence was observed in a subsequent Japanese study of AAV patients. These findings suggest that Japanese patients with AAV may have a higher susceptibility to avacopan-induced liver injury.

P2-250

A case of MPO-ANCA positive medium-sized vasculitis limited to the spleen after R-THP-COP therapy for diffuse large B-cell lymphoma (DLBCL)

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Conflict of interest: None

[Case] An 80-year-old female achieved remission 5 years ago following R-THP-COP therapy for DLBCL. She presented with fever and elevated CRP one month ago. CT and bone marrow biopsy showed no abnormalities. PET-CT showed increased FDG uptake only in the spleen. Suspecting a relapse of lymphoma, laparoscopic splenectomy was performed. Necrotizing vasculitis was observed in the central artery in histopathology. At the same time, MPO-ANCA was positive. While she had hearing loss and renal dysfunction for a long time. There were no other organ lesions. She was diagnosed with medium-sized vasculitis limited to the spleen with MPO-ANCA positivity. Her fever persisted after surgery. Remission induction therapy with RTX and PSL was started. She was transferred to the other hospital for rehabilitation. [Discussion] Most of the reports of autoimmune diseases paradoxically developing after RTX show skin and respiratory involvement 2 weeks to 3 years after RTX, but there are a few cases that develop several years after RTX administration. It remains unclear whether her vasculitis is related to RTX, but the atypical manifestations of localized vasculitis of the spleen with MPO-ANCA positivity make this case noteworthy. We report this case with a literature review.

P2-251

A Case of Polyarteritis Nodosa Possibly Associated with Minocycline Use

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Conflict of interest: Yes

[Case] A 61-year-old man was prescribed minocycline (MINO) for folliculitis for the past year. About a month ago, he noticed lower leg edema, joint pain, and scrotal pain. Initially diagnosed with epididymitis, he was kept under observation, but symptoms persisted. He developed a high fever (40°C) daily and consulted a referral physician, revealing an inflammatory response (CRP 2.0 mg/dL) and dilation of the testicular vein on CT, but the fever's source remained unclear. He visited our department a week ago; cellulitis was noted, and joint ultrasound revealed polyarthritis. FDG-PET detected FDG uptake in joints and testes, leading to admission for detailed evaluation. Skin biopsy indicated fibrinoid necrosis in medium-sized arteries, diagnosing polyarteritis nodosa (PAN). Suspecting MINO involvement, it was discontinued, but disease activity continued. Prednisolone (40 mg) treatment led to rapid improvement, and he was discharged in stable condition. [Conclusion] For PAN with skin, joint, and testicular involvement, confirming a minocycline history is essential.

P2-252

A case of HCV-associated polyarteritis nodosa treated with immunosuppressive therapy and direct-acting antiviral drugs

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Conflict of interest: None

Background: It has been reported that 20% of vasculitis in patients with chronic hepatitis C virus (HCV) infection were polyarteritis nodosa

(PAN), which is reported as HCV-related PAN. Chronic HCV infection can be cured with direct-acting antivirals (DAA), but there are few case reports of concurrent DAA in the treatment of HCV-PAN. Case: A 68-year-old woman. She developed bilateral edema in lower extremities and plantar pain, fever, and numbness in both hands and fingers. Nerve conduction test and CT angiography revealed peripheral neuropathy and wall irregularities in renal artery, celiac artery, and superior mesenteric artery. On admission, the patient had drop foot. She was diagnosed as HCV-associated polyarteritis nodosa (HCV-PAN) and treated with high-dose glucocorticoid therapy including pulse therapy, cyclophosphamide pulse therapy, and intravenous immunoglobulin. Although there was no liver fibrosis in response to chronic HCV infection, the patient was concurrently treated with the direct-acting antiviral drug glecaprevir in consideration of the possibility that it might be a contributing factor in the pathogenesis of PAN. Clinical Significance: Use of DAA may be considered in the management of HCV-PAN.

P2-253

A case of cryoglobulinemic vasculitis complicated by Sjögren's syndrome and IgM monoclonal gammopathy of undetermined significance (IgM-MGUS), effectively treated with intravenous immunoglobulin (IVIg) for peripheral neuropathy arising after treatment initiation

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Conflict of interest: None

A 51-year-old woman with a several-year history of reticulopapular lesions on her legs presented to our hospital in April, Year X, due to leg ulcers that had developed a month prior. Based on positive cryoglobulin, low complement, proteinuria, and histology of small vasculitis on skin biopsy, cryoglobulinemic vasculitis (CV) was suspected. She underwent a renal biopsy, which revealed immune complex-mediated membranous proliferative glomerulonephritis and mild lymphocytic infiltration of the tubular interstitium, findings consistent with CV. She was diagnosed with Sjögren's syndrome (SS) and IgM monoclonal gammopathy of undetermined significance (IgM-MGUS), which were considered the background for cryoglobulinemia (Cg). She was treated with prednisolone 30 mg and rituximab, leading to improvements in her urinary and skin findings. However, she developed foot drop and wrist drop. As steroid pulse therapy proved ineffective, intravenous immunoglobulin (IVIg) was administered, which improved of peripheral neuropathy. In this case, prominent vasculitis symptoms suggested that type II Cg with SS was the main background. The efficacy of IVIg for CV has not been established. This case is considered to be a valuable case in which IVIg was effective for peripheral neuropathy of CV.

P2-254

A case of IgA vasculitis associated with JAK2 mutation-positive polycythemia vera

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Conflict of interest: None

[Introduction] The combination of IgA vasculitis (IgAV) and myeloproliferative neoplasia (MPN) is rare, and to the best of our knowledge, there is only two cases have been reported. In this study, we report a case of IgAV diagnosed during the course of JAK2V617F mutation-positive polycythemia vera (PV). [Case] A 69-year-old woman. She was noted to have hematocytosis and was diagnosed with PV based on positive JAK2V617F mutation and bone marrow findings. She was treated with hydroxycarbamide (HYD), but 3 days after, she developed swelling of the dorsalis pedis on both sides. HYD was discontinued, but she subsequently developed watery stools, purpura on the extremities, and hematuria and proteinuria, and was referred for suspected vasculitis. CT scan revealed intestinal edema, and EGD and CS revealed multiple ulcers. Since bloody stools and acute kidney injury occurred and was diagnosed with IgAV based on the results of a skin biopsy, she was administered mPSL pulse therapy, IVCY, and coagulation factor XIII replacement therapy. [Discussion] There have been no reports that provide a detailed mechanism for the onset of JAK2 mutations and IgAV. Since there are previous reports similar to this case, a relationship between the two diseases is suspected.

P2-255

A case of thrombotic microangiopathy caused by anti-GBM antibody disease

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Conflict of interest: None

[Case] 56-year-old woman [Chief complaint] Low platelet count [Clinical Course] The patient was admitted to her previous hospital on July 14, X year after being diagnosed with renal insufficiency. On July 21, a renal biopsy was performed, which revealed crescentic glomerulonephritis and high anti-GBM antibody titer. On July 23, hemolytic anemia and thrombocytopenia were observed, and thrombotic microangiopathy (TMA) was suspected. The patient was transferred to our hospital for close examination. The patient had anemia, thrombocytopenia, low haptoglobin and high LDH, and was considered to have prolonged microangiopathic hemolytic anemia. Her general condition was good, and he was treated with hemodialysis and antihypertensive medication. After transfer, her hemolytic anemia and platelet count improved, and she was discharged from the hospital on November 5. This is a case of TMA secondary to anti-GBM antibody disease. Vascular endothelial damage caused by anti-GBM antibody disease is assumed to be a possible cause of TMA, and although there have been several reports, we report this case because it is considered a rare condition.

P2-256

A Long-term Follow-up Case of a Triple Positive for Anti-GBM Antibody, MPO-ANCA, and PR3-ANCA: Clinical Course of Initial Anti-GBM Antibody-Associated Renal Lesions and Relapsing ANCA-Associated Vasculitis

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Conflict of interest: None

An 83-year-old woman with hypertension, hyperlipidemia, and stable hypothyroidism presented with a month-long history of anorexia and leg edema. Her serum creatinine rose from 0.76 mg/dL to 3.91 mg/dL at a local clinic, showing 3+ hematuria and 3+ proteinuria, leading to her referral. At our hospital, creatinine was 4.48 mg/dL, eGFR 7.8 mL/min, CRP 5.9 mg/dL, anti-GBM antibody 345 U/mL, PR3-ANCA 18.5 IU/mL, MPO-ANCA 153 IU/mL, and proteinuria 2.9 g/gCr. Imaging revealed mild pleural effusion. Renal biopsy found 5 globally sclerosed glomeruli and 40 with cellular crescents, with linear IgG deposits along the glomerular capillaries. Steroid monotherapy was initiated due to poor renal prognosis. No pulmonary or neurological symptoms emerged, and antibodies became negative within six months. Prednisolone (PSL) was tapered off after 1.5 years, but MPO-ANCA levels rose to 45.7 IU/mL with fever, requiring PSL reintroduction for an ANCA-associated vasculitis relapse, stabilized at 5 mg. Triple positivity for ANCA and anti-GBM antibodies is rare, with little data on long-term outcomes. Initially driven by anti-GBM nephritis, MPO-ANCA became the recurrent factor, offering insights into this rare case.

P2-257

A case of cutaneous arteritis induced by cholesterol crystal embolism

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Conflict of interest: None

[Case] A 73-year-old woman with no history of cardiovascular treatment. She had fatigue, painless small erythema, intermittent fever, polyarthralgia, edema, and weight gain. The laboratory data showed an elevated inflammatory response, no findings suggestive of organ damage, and MPO and PR3-ANCA were negative. Skin biopsy showed necrotizing arteritis of medium-sized vessels, which led to suspicion of cutaneous arteritis. However, the contrast-enhanced CT showed Shaggy Aorta, so we examined again the same specimen and it revealed needle-shaped fissures in the lumen of vessels. She was diagnosed with cholesterol crystal embolism (CCE) and secondary arteritis. She was started treatment with steroid and antihyperlipidemic drug. [Discussion] CCE is a disease in which atherosclerotic plaques in large blood vessels broken down by some mechanism, causing cholesterol embolization in organs throughout the body. In particular, renal and skin lesions are frequently reported, but often systemic symptoms as vasculitis are also seen. In this case, the symptoms and pathological findings were consistent with cutaneous arteritis, but the presence of Shaggy Aorta revealed that it was arteritis induced by CCE. We experienced a suggestive case in the diagnosis of vasculitis.

P2-258

Possible infant onset primary Sjögren's syndrome: A case report

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Conflict of interest: None

[Case] A 6-year-old girl was referred to our hospital because of periodic fever, low saliva production since infancy. Her maternal grandmother and her great grandmother had Sjögren syndrome (SS). Ophthalmological examination revealed no signs of dry eyes. A gum test showed 3 ml in 10 minutes. Anti-SS-A and anti-SS-B antibodies were both negative, IgG level was 1179 mg/dl, and rheumatoid factor was negative, antinuclear antibody was 40x (spe, cyto). There was no evidence of sarcoidosis, IgG4-related disease, or infectious disease (HCV, HTLV-1, HIV, EBV). Ultrasound showed enlarged bilateral submandibular glands and uneven echo brightness, salivary gland scintigraphy (99mTc04-) revealed decreased uptake in both submandibular glands and decreased response to acid loading, and MRI revealed apple trees appearance in both parotid glands. Labial minor salivary gland biopsy revealed focus score 3. Based on these findings, the patient was determined to be a possible SS (Clinical practice guidance for SS in pediatric patients (2018)). [Discussion] Oliveira et al. reported a 2-year-old girl with primary Sjögren's syndrome. Our patient might have had onset at a younger age. [Clinical Significance] We report a patient with very early onset primary sialadenitis.

P2-259

A case of primary Sjogren's syndrome with pleural effusion

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Conflict of interest: None

Case Summary: She was hospitalized with left pleural effusion, which was exudative with positive ANA speckled and nucleolar patterns at 5120x. She was readmitted in March due to fever, with exudative pleural effusion detected again. She improved with furosemide and tolvaptan but experienced dyspnea and fever a week after discharge, leading to bilateral pleural effusion and referral for further evaluation due to positive ANA. **Hospital Course:** The patient had similar exudative pleural effusion twice before, with positive RF and anti-SS-A antibodies, leading to a diagnosis of Sjögren's syndrome (SjS) with pleuritis. Prednisolone (PSL) 40 mg (0.8 mg/kg) was started on the 9th hospital day, reducing pleural effusion. PSL was tapered to 30 mg on the 37th hospital day, and she was discharged. Two months later, pleural effusion recurred when PSL was tapered to 20 mg. Cyclophosphamide pulse therapy (IVCY) 500 mg was administered monthly for six sessions, and PSL was tapered without recurrence of pleural effusion. **Clinical Significance:** Primary SjS with pleural effusion is recognized and often responds well to steroids. When treatment is challenging or early steroid tapering is desired, additional treatments like IVCY should be considered.

P2-260

A Case of Sjogren's Syndrome Accompanied by Chronic Eosinophilic Pneumonia

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Conflict of interest: None

An 80-year-old female underwent lumber interbody fusion. A few weeks after the operation, she developed a low-grade fever and shortness of breath. Administration of antibiotics was started, but she was not improved. The department of pulmonary medicine was consulted for the examination. Given her significantly elevated anti-nuclear body, anti-SS-A, and anti-SS-B, we were consulted for possible primary Sjogren's syndrome as her underlying condition. She revealed to have sicca symptoms for several years, and physical examination showed dryness in the oral cavity. Schirmer's test was positive for both eyes and ectocornea injury was revealed. Thus, she was diagnosed as primary Sjogren's syndrome. Chest CT showed diffuse ground-glass opacity in the right lung. Bronchoalveolar lavage was performed and cell differential showed 31.8% eosinophils. This led us to the diagnosis for chronic eosinophilic pneumonia. Methylprednisolone was started and her condition was improved. Sjogren's syndrome is associated with various pulmonary diseases. The most common manifestation is nonspecific interstitial pneumonia, followed by bronchiolitis and usual interstitial pneumonia. There are few reports of Sjogren's syndrome with chronic eosinophilic pneumonia, and we report the case comparing with others.

P2-261

Sjögren's syndrome manifesting as protein losing gastroenteropathy

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Conflict of interest: None

A 50-year-old woman who had been affected by Sjögren's syndrome went to a hospital to receive a treatment of hyperlipidemia, and turned out to have hypoalbuminemia. She consulted our hospital, and there were signs of inflammation, proteinuria or cancer. Although she had no abdominal pain, diarrhea, pitting edema or pleural and ascitic fluid, we considered a possibility of protein losing gastroenteropathy. Redness and edema were found from the end of ileum to colon by endoscopies, and there was a sign of inflammation but no specific findings by pathology. 99mTc-HAS-D scintigraphy demonstrated protein losing from colon. She was diagnosed as having protein losing gastroenteropathy with Sjögren's syndrome. Prednisolone (PSL) at a dose of 35 mg/day relieved hyperlipidemia and she has been in good general condition after commencement of azathioprine in addition to PSL. Protein losing gastroenteropathy sometimes concurrent with collagen disease, but rare with Sjögren's syndrome. PSL and immunosuppressant are used for treatment. If patients don't have abdominal pain, diarrhea, pitting edema or pleural and ascitic fluid, we should consider protein losing gastroenteropathy with Sjögren's syndrome when we see hypoalbuminemia for unknown reason.

P2-262

A case of Sjogren's syndrome complicated by immune thrombocytopenic purpura

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Conflict of interest: None

[Case] 65-year-old woman [chief complaint] oral mucosal hemorrhage [medical history] The patient was diagnosed with Sjogren's syn-

drome (SS) in 2012 based on oral examination, ophthalmologic examination, and serum examination. In January 2024, she showed gradual thrombocytopenia. In May, her platelet count was 6000/μL, and she was admitted to the hospital because of intraoral bleeding and hemorrhagic spots all over her body. [Progress] After close examination, a wide variety of elevated IgG levels, including PAIg in particular, were found in addition to the hypergammaglobulinemia mentioned above. After the exclusion of other diseases, a diagnosis of immune thrombocytopenic purpura (ITP) was made. The patient had severe thrombocytopenia and was treated with dexamethasone 20 mg/day. On the third day, her platelet count improved, but two weeks later, her platelet count decreased to 6000/μL. Dexamethasone was administered again, and PSL 15 mg/day was added as post-therapy to control the platelet count. [Consideration] When the primary disease is collagen disease, the possibility of relapse is high, and treatment based on conventional PSL and post-therapy should be considered. In this report, we describe a relatively rare case of ITP secondary to SS and discuss the literature.

P2-263

Eltrombopag and Rituximab successfully improves steroid-refractory thrombocytopenia in a patient with Sjögren's syndrome

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Conflict of interest: None

[Case] The patient was diagnosed with primary Sjogren's syndrome due to parotid swelling and purpura at 13. Recently, pain from parotid swelling was observed. Platelets were maintained usually around 80,000. Petechiae and hematuria have been observed since X-4, and she visited the hospital on X. She was urgently admitted because of thrombocytopenia of 2,000. She was treated with high-dose globulin therapy and a moderate dose of steroids, and her platelet count gradually improved, so she was discharged. On day X+21, platelets decreased again to 2,000, and she was readmitted for a high-dose globulin therapy plus steroids, along with rituximab and eltrombopag. Platelet normalized and have been maintained for a long time. Steroids were tapered off, but she continues to take small doses of eltrombopag. She is going to be tapered off near future. [Clinical Significance] Mild to moderate thrombocytopenia is occasionally observed in patients with primary Sjögren's syndrome, but platelet loss to the point of requiring treatment is rare. In such cases, the first line of treatment is steroids, but this she was steroid-resistant, and a combination of rituximab and eltrombopag as second-line treatment has maintained remission. Moreover she no longer has recurrent parotid gland swelling.

P2-264

A case of IgG4-related disease with pericardial effusion and marked elevation of serum IgG4

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Conflict of interest: None

[Case Presentation] A 66-year-old male complained of breathlessness and was found to have pericardial effusion. Pericardial drainage only temporarily relieved his symptoms, and diuretics were required to manage his condition. He was referred to our hospital because of the marked elevation of serum IgG4. Chest X-ray also showed left pleural effusion. Hypocomplementemia and elevation of soluble IL-2 receptors were noted, while M-protein was negative. FDG-PET showed FDG accumulation in the lacrimal and submandibular glands, mediastinal, hilar, and periaortic lymph nodes, and the left pleura and pericardium. Biopsies of a submandibular gland and a mediastinal lymph node yielded findings consistent with IgG4-related disease. We considered the pleuritis and the pericarditis to be involved in IgG4-related disease. Treatment of prednisolone 50 mg/day decreased pleural and pericardial effusion, eliminated the need for diuretics, and improved serum abnormality. [Clinical Significance] A few cases of IgG4-related disease with pleuritis or pericarditis have been reported. In this case, despite a marked elevation of serum IgG4, a good response to standard immunosuppressive therapy was obtained. We discuss the clinical characteristics of IgG4-related disease complicated by pericardial effusion.

P2-265

Three Cases in Which Salivary Gland Ultrasound Led to the Suspicion of IgG4-Related Disease

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Conflict of interest: None

The definitive diagnosis of IgG4-related disease (IgG4-RD) requires a biopsy, but non-invasive salivary gland ultrasound (SGUS) can provide useful diagnostic clues. Key findings on ultrasound include "hypervascular nodular hypoechoic areas" or "reticular hypoechoic areas transitioning to normal deeper regions". This report presents three cases where SGUS raised suspicion for IgG4-RD. **Case 1:** An 86-year-old male with bilateral submandibular masses and a serum IgG4 level of 178 mg/dL. Retroperitoneal fibrosis was observed on contrast CT, and SGUS showed hypervascular nodular hypoechoic areas. **Case 2:** A 74-year-old male with bilateral submandibular masses and a serum IgG4 level of 2090 mg/dL. SGUS showed hypervascular reticular hypoechoic areas. **Case 3:** A 77-year-old female with bilateral submandibular masses, dry eyes, and a positive anti-SS-A antibody test, requiring differentiation from Sjögren's syndrome. SGUS revealed hypervascular nodular hypoechoic areas. Biopsies were performed on all three cases to assess the correlation between pathological and ultrasound findings, and the changes in ultrasound before and after treatment were compared. SGUS, being non-invasive and convenient, shows potential as an alternative to biopsy.

P2-266

Angioimmunoblastic T-cell lymphoma difficult to differentiate from proliferative subtype of IgG4 related disease

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Conflict of interest: None

A 70-year-old female developed fever and wheezing four months prior, followed by eyelid swelling two months before admission. Eosinophilia and renal dysfunction were observed, and the patient was referred to our hospital. Blood tests showed eosinophil count 8778μL, CRP 0.59 mg/L, IgG 5667 mg/dL, IgG4 3640 mg/dL, sIL-2R 3762 U/mL, CH50 <10 mg/dL. CT scan revealed generalized multiple lymphadenopathy, enlarged bilateral kidneys, and thickened bronchial wall, and PET-CT showed FDG accumulation in lymph nodes, lacrimal gland, salivary gland, bilateral kidneys. Lip biopsy, renal biopsy, and axillary lymph node biopsy were performed. She was started on PSL 45 mg for IgG4-related disease. Pathology revealed prominent IgG4-positive plasma cells in the minor salivary glands, and angioimmunoblastic T-cell lymphoma (AITL) was diagnosed in the axillary lymph nodes. Kidney biopsy showed a severe infiltration of lymphocytes and eosinophils in the tubular interstitium, with some lymphoma cells. CHOP therapy was initiated for AITL. Two phenotypes of IgG4-related diseases, proliferative and fibrotic subtypes, have been reported. This case presented with organ involvement and immunological abnormalities consistent with the proliferative subtype, and we discussed its differentiation from AITL.

P2-267

~~**IgG4-related disease complicated by cutaneous vasculitis: a case report**~~

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~~Conflict of interest: None~~

Withdrawn

~~A 73-year-old woman presented with bilateral eyelid swelling in December of the previous year. In May, MRI revealed lacrimal gland enlargement, and elevated serum IgG4 levels were detected. She subsequently developed salivary gland swelling. A biopsy of the left submandibular gland confirmed IgG4-related disease (IgG4-RD), a form of Mikuliez's disease. Glucocorticoid therapy was planned, but in early July, she developed palpable purpura on both legs, leading to a skin biopsy and hospitalization. Blood tests revealed elevated CRP and decreased complement levels, and CT showed organomegaly involving the salivary glands, liver, spleen, and kidneys. Treatment with 30 mg of prednisolone led to rapid resolution of purpura and gradual reduction in gland and organ enlargement. Skin histopathology revealed vasculitis with histiocytic and lymphocytic infiltration, endothelial swelling, and vascular destruction, without IgG4-positive plasma cells. It is rare for IgG4-RD to be complicated by vasculitis affecting vessels other than large vessels. We report a rare case of IgG4-RD complicated by cutaneous vasculitis, with a review of the literature.~~

Withdrawn

P2-268

A case of dissecting aortic aneurysm in IgG4-related aortitis

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Conflict of interest: None

Case: A 77-year-old man. 2 years ago, he was diagnosed with parotitis. 6 months ago, he had a persistent sense of discomfort in his chest and abdomen. Blood tests showed CRP 0.45 mg/dL, IgG4 1250 mg/dL, IgG 4180 mg/dL. CT scans showed that the ascending aorta and bilateral common iliac arteries, with mild contrast enhancement of the vessel walls. PET-CT showed FDG accumulation in the aforementioned thickened vessel walls. The pathology of the lymph nodes showed findings that met the definition of IgG4-related disease, so he was diagnosed with IgG4-related aortitis, and treatment was started. Subjective symptoms improved, and the IgG4 level tended to decrease, but a CT scan performed 6 months after the treatment showed that the enhancement in the aortic arch and ULP was observed. We suspected false lumen type dissection, operation was performed. An entry was observed in the aortic arch. The pathology of the aorta showed findings that met the definition of IgG4-related disease. Clinical significance: In IgG4-related aortitis, aortic aneurysms may form aortic dissection. It is difficult to distinguish between aortic dissection due to inflammation and false lumen occlusion in CT scans, and there is a risk of confusion. It is important to evaluate the patient with this in mind.

P2-269

A Case of Elevated Serum IgG4 Levels and IgG4-Related Pericoronary Arteritis Induced by Repeated SARS-CoV-2 Vaccinations

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Conflict of interest: None

[Case Presentation] A 64-year-old man developed chest pain in late October of year X-1 after his third SARS-CoV-2 vaccine dose (BNT162b2). Around the same time, he was diagnosed with benign prostatic hyperplasia and treated with an alpha-1 blocker, which was ineffective. In January of year X, he experienced another chest pain episode lasting over two hours. Although CK and ECG were normal, coronary CT revealed stenosis in the left anterior descending and septal branches, with soft tissue surrounding the coronary arteries. A contrast-enhanced CT showed a thickened aortic wall and enlarged pancreas, suggesting IgG4-related disease (IgG4-RD). He was diagnosed with IgG4-related pericoronary arteritis and treated with 50 mg/day of prednisolone. CK and troponin T levels briefly rose but normalized, improving his chest pain and urinary symptoms. A prostate biopsy confirmed IgG4-RD. A month later, CT showed reduced soft tissue and improved pancreas size. Analysis of stored serum samples before and after the vaccinations revealed that IgG4 levels, initially normal, rose significantly after the third dose. [Clinical Significance] While IgG4-RD has been reported post-vaccination, this case uniquely tracks IgG4 levels before and after vaccination, offering valuable insights.

P2-270

Autoimmune acquired Factor V Deficiency Complicated by IgG4-related Disease

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Conflict of interest: None

An 89-year-old man noticed purpura on both lower legs. Blood tests showed abnormal coagulation with platelets count 182 000/μl, PT ratio 3.1, and APTT 89.1 seconds. Clotting factor activity and antibody tests showed FV activity of 5%, FV inhibitor levels of 1 Bethesda Unit, and anti-FV antibody levels of 324.9 AU/ml. We diagnosed him with autoimmune- acquired FV deficiency (AiFVD). Blood tests showed IgG 4241 mg/dl, IgA 686 mg/dl, IgM 46 mg/dl, and IgG4 806 mg/dl, and CT showed enlarged bilateral parotid, bilateral submandibular, and left inguinal lymph nodes. A left inguinal lymph node biopsy showed IgG4-positive plasma cell infiltration, 70% IgG4/IgG-positive cells, and 70/HPF IgG4-positive cells. We diagnosed IgG4-related disease. We treated his AiFVD with 30 mg/day prednisolone. Six days later, blood tests showed a normal APTT and negative FV inhibitor levels. His purpura disappeared, and his coagulopathy normalized. We reduced the dose of prednisolone every two weeks. There was no recurrence of coagulation abnormalities or high IgG4 levels. AiFVD is a very rare disease, and only a few cases complicated by IgG4-related disease have been reported. We have reported the results of analysis of anti-FV antibody levels.

P2-271

Two cases considered to be IgG4RD-related bone and joint lesions

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Conflict of interest: None

Bone and joint lesions are rarely seen in IgG4-related disease (IgG4RD), there have been reports of cases with such. We have experienced two cases who were treated for rheumatoid arthritis (RA), but the pain and swelling of the joints persisted. A biopsy of the lips revealed the pathological features of IgG4RD. Case 1: Female in her 70s. 12 years ago she was diagnosed RA. 7 years ago, IgG4 1220 mg/dl, abdominal lymph nodes swelling, suspected IgG4RD, but no other organ lesions were found. A synovial biopsy of the elbow joint did not provide a diagnosis. Hypercalcemia, thought to be due to bone destruction, was observed, and denosumab was started. 2 years ago, a salivary gland biopsy showed collagen fibers around acinar cells, and scattered IgG4-positive plasma cells extending radially, suspected IgG4RD. Case 2: Female in her 80s with a history of poliomyelitis, type 1 diabetes, and hypothyroidism. 15 years ago, she was diagnosed RA. 11 years ago, she developed a mass on her lower lip, biopsy suggested IgG4RD. Discussion: In both cases, the inflammatory response was almost negative, strong bone degeneration, and bone scintigraphy showed accumulation. It may suggest changes similar to those in the lips are occurring in the bone and joints, causing destruction.

P2-272

A Case of IgG4-Related Disease in the Left Buccinator Muscle Diagnosed by Four Repeated Biopsies Over Three Years

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Conflict of interest: None

[Case] A male in his 70s developed the left cheek swelling and tenderness three years prior to admission. A biopsy at the previous hospital revealed lymphocytic and histiocytic infiltration, with no evidence of granuloma or malignancy. Two years before admission, as PR3-ANCA was

found to be positive, he visited our hospital. However, there were no significant manifestations suggestive of vasculitis. Additionally, serum IgG4 was 481 mg/dL. A CT scan showed a soft tissue mass in the left cheek, and MRI revealed swelling of the temporalis and lateral pterygoid muscles. A second biopsy revealed no suggestive findings including vasculitis and IgG4-related disease (IgG4-RD). By a third biopsy we could not make a definitive diagnosis. He was subsequently monitored, with no significant change in those findings. However, one year after the last biopsy, his left cheek swelling recurred. CT imaging additively revealed cheekbone osteolysis. A fourth biopsy showed lymphocyte and plasma cell infiltration with fibrosis with enough number and rate of IgG4-positive cells for a definitive IgG4-RD. [Discussion] This is the first reported case of IgG4-RD presenting with a left facial muscle lesion with evaluation of the natural history up to diagnosis, including the histological changes.

P2-273

A case of IgG4-related disease diagnosed incidentally through coronary artery aneurysm detected on chest CT

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Conflict of interest: None

[Case] A 65-year-old man was admitted to neurology in Oct, Year X-1 for acute cerebral infarction. Paroxysmal atrial fibrillation was diagnosed, and anticoagulation therapy began. Chest CT showed a coronary aneurysm. Coronary MDCT, PET-CT, and abdominal CT revealed right lacrimal gland enlargement, pericoronary and periaortic inflammation, and prostate enlargement. His serum IgG4 level was high at 1,160 mg/dL, suggesting IgG4-related disease (IgG4-RD). Review of a prostate biopsy from another hospital showed dense lymphocyte and plasma cell infiltration, with 100 IgG4-positive plasma cells/HPF and an IgG4/IgG-positive cell ratio >80%. Based on these findings, IgG4-RD was diagnosed. Prednisolone (PSL) 40 mg/day was started. A CT in Apr, Year X, while on PSL 12.5 mg/day, showed persistent inflammation, so azathioprine (AZA) 25 mg/day was added. In Oct, Year X, CT while on PSL 6 mg/day and AZA 25 mg/day showed worsening, and rituximab therapy is now considered. [Discussion] Coronary involvement in IgG4-RD is rare, with a prevalence of 1.3-5.0%. Though often incidentally found, coronary lesions can progress to acute coronary syndrome, stressing the need for early diagnosis and treatment. IgG4-RD should be considered in differential diagnosis for pericoronary inflammation or aneurysm.

P2-274

A case of IgG4-related disease with scattered nodular shadows around bilateral kidneys

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Conflict of interest: None

A 67-year-old man, Head CT revealed bilateral lacrimal gland enlargement and serum IgG4 level was high at 1090 mg/dl, so he was suspected of having IgG4-related disease (IgG4-RD). Contrast CT showed bilateral parotid swelling, enlarged multiple lymph nodes, and scattered nodular shadows outside both kidneys. There was no mass or poor contrast effect in the renal parenchyma, which was not characteristic of IgG4-related kidney disease. However, serologic and non-renal imaging findings were very characteristic of IgG4-RD, and a renal biopsy was performed including the nodular lesion. IgG4-positive plasma cells infiltrate with fibrosis were observed within the nodular lesion. There were no IgG4-positive cells within the renal parenchyma, but there were scattered sclerotic glomeruli. Although glomerular lesions were observed, renal function and urinary findings were normal. PSL was started, and all lesions were reduced. In recent years, there have been several cases of IgG4-RD with nodular shadows surrounding the kidneys, and there have been reports of cases of rapidly progressive renal failure due to decreased renal perfusion caused by pressure on the kidneys from the nodular lesions. In this case, because the nodular lesions were localized, renal function may have been preserved.

P2-275

Challenges in a case of IgG4-related disease with coronary arterial lesions, diagnosed after syncope

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Conflict of interest: None

Case: An 84-year-old Japanese male, with repeated episodes of syncope, who was found to have pericardial effusion, was initially referred to the cardiology, and then to rheumatology due to high IgG4 levels. PET-CT showed accumulation in soft tissues mass around the coronary arteries, bilateral submandibular glands, mediastinal lymph nodes, bilateral hilar lymph nodes, ascending aorta, and bilateral common iliac arteries. IgG4-related disease (IgG4-RD) was diagnosed by lip salivary gland biopsy. Cardiac echo showed HFmrEF. In order to treat heart failure, pericardial effusion and aneurysm of the coronary arteries, moderate GC and rituximab treatment was given, then GC was tapered early. IgG4 level, coronary artery CT and B cell 100 percentage were used in combination with common blood test items to follow. Rituximab was going to be scheduled as maintenance therapy in case of possible flares. [Clinical Significance] (1) While having coronary artery lesions and pericardial effusion, this case was diagnosed using less invasive lip biopsy. (2) Coronary aneurysm or cardiac arrest are severe problems of IgG4-RD. After GC and Rituximab treatment, size reduction of the coronary arterial mass was obeserved by VR images of coronary artery CT, also with lower IgG4 levels, semi-quantitatively.

P2-276

A case of IgG4-related autoimmune hepatitis during treatment of eosinophilic polyangiitis granulomatosa

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Conflict of interest: None

[Case] A 59-year-old woman. In March X-2, she was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) and was treated with steroid pulse therapy (IVMP), high-dose prednisolone (PSL), and intravenous cyclophosphamide, which led to remission. In June X-1, Mepolizumab was started. In December of the same year, PSL was reduced to 1 mg/day. In May X, transaminases were mildly elevated. Drug-induced liver injury was suspected, and medication was adjusted, but by September of X year, hepatobiliary enzymes were elevated to AST 293 U/L, ALT 381 U/L, ALP 422 U/L, γ-GTP 1034 U/L. Liver biopsy showed moderate to severe lymphocyte and plasma cell infiltration in the portal area, IgG4-positive cells >10/HPF by IgG4 immunostaining, and IgG4/CD138 positive cell ratio >40%. The patient was diagnosed as IgG4-related autoimmune hepatitis (IgG4-AIH) and started treatment with IVMP and high-dose PSL, which resulted in remission. [Discussion] In IgG4-related disease (IgG4-RD), autoimmune hepatitis is relatively rare. Although serum IgG4 is known to be elevated in EGPA, the relationship between EGPA and IgG4-RD has not been clarified. [Clinical Significance] This is a rare case of EGPA with IgG4-RD. We report this case because of its high clinical significance.

P2-277

A case of IgG4-related epidural inflammatory pseudotumor with residual neurological sequelae after 6-years of treatment

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Conflict of interest: None

A 31-year-old man presented with a 2-month history of motor and sensory dysfunction of lower limbs with several days of bowel and bladder

dysfunction. The thoracic magnetic resonance imaging revealed an epidural mass at the Th2-Th6, and extension around the descending aorta. Methylprednisolone (1000 mg) was intravenously administered for 3 days, and dramatic clinical improvement was achieved. Two months after initial improvement, he noticed the recurrence of symptoms. The thoracic magnetic resonance imaging revealed a growing epidural mass at the T2-T6. The decompression laminectomy of T4 and debulking of the epidural-paraspinal mass was performed, which diagnosed plasma cell granuloma. His symptoms progressively worsened. Two months after operation, histopathological evaluation at another hospital demonstrated IgG4-related disease. He was treated with high-dose prednisolone and immunosuppressive drugs for 6 years with residual neurological sequelae. IgG4-related disease often dramatically responds to systemic corticosteroids. However, it is important to recognize the possibility of serious neurological sequelae in the case of epidural mass, if both surgical and medical interventions are not performed at the appropriate time.

P2-278

A case of eosinophilia with high serum IgG4 levels and hypocomplementaemia, which was difficult to diagnose

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Conflict of interest: None

[Case] 59 years old, male. He had bronchial asthma for three years. Five months ago, generalised itching and a bulging rash appeared, and he was treated with antihistamines, but the symptoms repeatedly worsened and became milder. Two months ago, edema in both lower legs, fever and general malaise appeared, and one month ago, he visited his local physician, who found abnormalities such as proteinuria, increased peripheral blood eosinophil count and hypocomplementaemia, which led to his visit to our hospital. [Clinical Course] The patient was suspected to have IgG4-related disease due to the high serum IgG4 level, hypocomplementaemia and eosinophilia. The possibility of eosinophilic polyangiitis granulomatosa (EGPA) was also suspected based on the clinical course. But, histopathology showed no obvious necrotising granulomatitis or necrotising vasculitis. After admission, the patient's systemic symptoms worsened, so steroid treatment was started as EGPA, and the symptoms improved. [Clinical Significance] There are scattered reports of similar cases and complications of EGPA and IgG4-related diseases, but there is no settled opinion on whether these are combined. We experienced a case with features of these diseases, and report on it based on a histopathological study.

P2-279

A case of death due to intractable infection in a patient with GATA2 deficiency and MEFV mutation

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Conflict of interest: None

[Background] GATA2 gene abnormalities are associated with a variety of blood cell abnormalities, such as monocytopenia and NK cell deficiency, and are also associated with alveolar proteinosis and infectious diseases. MEFV gene abnormalities are the most common genetic mutation in familial Mediterranean fever (FMF). Case: A 45-year-old woman. She was diagnosed with Behcet's disease (BD) at the age of 11. In X-4, she was diagnosed with FMF due to MEFV mutation (E84K) and GATA2 gene mutation (R396Q). Although he continued to receive treatment with GC, ADA, and canakinumab, he was treatment-resistant, and in X-2 he developed NTM lung disease and alveolar proteinosis. A decision was made to perform a hematopoietic stem cell transplant, but in February X-2 he was hospitalized in our hospital due to disseminated MAC disease, and he also developed deep fungal infection due to multiple fungi, and he passed away in April X-2. [Clinical Significance] In this case, the patient's condition rapidly deteriorated due to a combination of immunosuppressive therapy for FMF and immunodeficiency due to GATA2 deficiency, and it was not possible to perform a hematopoietic stem cell transplant. This case demonstrates the need for transplant treatment at an early stage.

P2-280

A case of Schnitzler syndrome successfully treated with colchicine

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Conflict of interest: None

Case: A 83 year-old man was admitted to our hospital for generalized chronic urticaria and fever, which started to manifest 3 years before admission. Blood test revealed elevated inflammatory markers and the presence of IgM-kappa-type monoclonal protein. Bone scintigraphy showed uptakes in the joints and the lumbar spine. Skin biopsy revealed liquefaction degeneration at the dermal-epidermal junction and perivascular infiltration of lymphocytes, eosinophils, and plasma cells in the dermis. The patient was diagnosed with Schnitzler syndrome and received treatment with colchicine, which rapidly improved his symptoms and inflammatory markers. However, colchicine was discontinued due to sudden behavioral changes, which gradually subsided after discontinuation. As fever and urticaria recurred, colchicine was restarted, which rapidly improved the symptoms and inflammatory markers again. The patient has not had behavioral changes after receiving antiepileptic medication. Discussion: Colchicine showed rapid improvement and worsening of fever and urticaria when started, stopped, and restarted in this case. The case indicates that colchicine can be effective regardless of the histopathological presence of neutrophil infiltration in the dermis.

P2-281

Investigation of the clinical features and treatment course of polymyalgia rheumatica in our department

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Conflict of interest: None

We examined the data, treatment methods, and clinical course of 74 patients diagnosed with polymyalgia rheumatica (PMR) at our department for the first time between April 2017 and March 2024. The mean age at onset was 75.5±8.6 years, and the male to female ratio was 1:2. The mean PSL dose at the beginning of treatment was 15.7±4.7 mg. 19 patients (25.7%) were treated with immunosuppressive drugs. The diagnosis was changed to seronegative RA in 11 patients. Of the 63 cases excluding these 11 cases, 4 patients (6.3%) had giant cell arteritis, and 6 patients (9.5%) had malignant tumors. Two cases required hospitalization for treatment. There were 20 cases of relapse (31.7%), with 15 cases of relapse occurring within one year of the initial relapse and 5 cases occurring more than one year after the initial relapse. 6 cases had multiple relapses, and all had an initial relapse of less than 1 year. Many reports suggest that the relapse rate for PMR is around 50%, and in our department, the relapse rate was also around the same level. In this study, there was a tendency for relapse to occur multiple times if relapse occurred early after treatment intervention. If we can prevent relapse occurring early after treatment intervention, we think that the prognosis may improve.

P2-282

A Case of Refractory Castleman Disease with a Giant Axillary Mass

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Conflict of interest: None

[Case] 68-year-old male. He had a mass in his right axilla for 30 years, which had grown to about 8 cm in diameter at the time of his first visit. He had been treated for heart failure for two years but had repeatedly self-interrupted. Cardiomyopathy due to systemic disease was suspected as the cause of his heart failure, then he was referred to the hematology department, and malignant lymphoma was ruled out. He was admitted to the other hospital due to worsening heart failure from around X-3 months and was transferred to our hospital due to suspicion of Castleman disease (CD). After close examination, a diagnosis of idiopathic multicentric CD (iMCD) was made. Treatment with PSL 1 mg/kg/day and TCZ biweekly was started, and the axillary mass was reduced and pleural effusion decreased. The TCZ dose was increased to weekly administration after the mass showed growth in X+2 months. In X+5 months, the largest axilla lymph node mass was surgically removed. Following the excision, the CRP turned negative, and the pleural effusion tended to improve, prompting a return to biweekly TCZ dosing. However, by X+6 months, there was a re-exacerbation of pleural effusion and the enlargement of unresected lymph nodes.

P2-283

Characteristics of difficult-to-treat secondary fibromyalgia patients at our hospital

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Conflict of interest: None

[Objective] To examine the characteristics of patients with secondary fibromyalgia that is difficult to treat. [Methods] Patients with secondary fibromyalgia with uncontrolled pain symptoms were included from 1736 patients with collagen disease who visited our hospital between 10/1/2023 and 9/30/2024. The following items were examined: sex, age, duration of treatment, main disease, symptoms, treatment of collagen disease, treatment of pain, concomitant psychiatric disorders, collaboration with other medical departments, and K-S classification. [Results] 7 patients with secondary fibromyalgia were difficult to treat. Seven patients were female, age 57.6 years, duration of treatment 10.7 years, and the main disease was SLE in 5 cases (SS complication in 3 cases). Symptoms were generalized pain in 4 cases. Five patients were treated with biologics for collagen disease. Pain was treated with neuropathic pain medications in 3 patients. K-S classification: K2.86, S1.57. [Conclusion] Patients with difficult-to-treat secondary fibromyalgia may be more likely to be women who have been treated for SLE for a longer period of time. Pain treatment was not found to be linked to pain clinic or rehabilitation. We believe that multidisciplinary pain treatment is needed in the future.

P2-284

A case of psoriasis with joint symptoms that is successfully treated with a TYK2 inhibitor

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Conflict of interest: None

The case is a 51-year-old man. Diagnosed with psoriasis and psoriatic arthritis since he was at least in his 30s, he was treated with methotrexate at the rheumatology department of a local hospital, but no remission was achieved and he was advised to intensify treatment including biological agents. However, the patient was not satisfied with the explanation and gave up on administering the biological drug. Then, he was referred to a local dermatology clinic. Methotrexate was discontinued because it was judged to be lacking in efficacy and because the patient seemed to have a tendency to refuse it. Apramist was started and continued to be administered. Diarrhea, which was thought to be caused by Apramist, persisted. Therefore, we discontinued Apramist and explained about NSAIDS, reintroduction of methotrexate, and biologics, but they were not introduced due to the risk of infection. Therefore, TYK2 inhibitors approved for psoriasis TYK2 inhibitors are used as immunomodulators in the United States, where they were developed, and are considered to have a lower risk of infection than biological agents. Skin rash occurred two weeks after starting TYK2 inhibitors. The symptoms tended to improve, and the joint symptoms also started to improve after 2 months.

P2-285

A case of hypertrophic pachymenigitis successfully treated with a combination of glucocorticoids and antifungal agents

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Conflict of interest: None

[Case] A 73-year-old woman was suffered from headache and lightheadedness since sinusitis surgery two years ago. She had referred to our otorhinolaryngology department for otitis mediaerosive on the left side two months ago and contrast-enhanced MRI of the head revealed extensive dural thickening on the left side. So, she referred to our department on suspicion of pachymeningitis. She had a chill fever and a blood test showed elevation of serum CRP. Left trigeminal neuralgia and left facial paralysis that worsened over time were also observed. Because a dural biopsy showed no evidence of infection or collagen tissue disease, we started induction therapy with GC as idiopathic hypertrophic pachymeningitis. sCRP improved after induction therapy, but 7 days after treatment, sCRP elevated again and cranial nerve symptoms worsened, so we administered a combination of antifungal agent with GC. After a combination therapy, her symptoms were subsequently improved. [Discussion] The cause of hypertrophic pachymeningitis is reported idiopathic or ANCA-associated vasculitis and Infection is considered less likely. When treating hypertrophic pachymeningitis, it is necessary to consider a wide range of differentials and provide appropriate treatment.

P2-286

The Relationship Between Falls and Sarcopenia in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] This study aimed to investigate the relationship between sarcopenia and falls in patients with rheumatoid arthritis (RA). [Methods] We selected 174 patients from 450 RA patients who underwent muscle strength testing in 2019 and had a CT scan available to measure the cross-sectional area of the psoas muscle at the L3 level (Psoas Muscle Index, PMI). We evaluated the association of muscle mass and strength with the occurrence of falls within 3 years. [Results] There were no significant differences between the fall group (n=54) and the non-fall group (n=120) in terms of age, sex, disease duration, SDAI, CDAI, and DAS28-ESR. No significant associations were found between PMI, bioelectrical impedance analysis (BIA), grip strength, 6-meter walking speed, or the sit-to-stand test and falls within 3 years. Additionally, there were no significant differences in spinal parameters (sagittal vertical axis [SVA], pelvic incidence minus lumbar lordosis, and global tilt) between the two groups. However, in patients with SVA <40 mm, those who did not meet the sarcopenia criteria (AWGS2019) had a significantly higher rate of falls (p=0.04). [Conclusion] In RA patients with SVA <40 mm, failing to meet the sarcopenia criteria is a significant risk factor for falls.

P2-287

Relationship between control of disease activity and sarcopenia in rheumatoid arthritis patients with osteoporosis, analysis of SMI using a bone densitometry device

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Clinic QUEST FOR Rheumatology & WELL-BEING

Conflict of interest: None

[Objectives] To identify factors correlated with sarcopenia in rheumatoid arthritis (RA) patients, we analyzed disease activity, body composition, and exercise habits. [Methods] We studied 55 female RA patients (average age 76.3) receiving bone formation-promoting drugs, analyzing SDAI, BMI, body fat (Fat), SMI, and exercise habits at treatment start and after an average of 29.6 months. Fat and SMI were measured with a bone densitometry device, and weekly exercise time was recorded. [Results] In all 55 cases, at the start of treatment, the values were SDAI: 4.7, BMI: 22.0, Fat: 34.7%, and SMI: 5.21 kg/m^2, while after therapy, they were SDAI: 2.8, BMI: 21.3, Fat: 32.7%, and SMI: 5.44 kg/m^2. In the SMI-increased group (40 cases), SDAI improved, BMI and Fat decreased, and SMI increased by 7.6%. In the SMI-decreased group (13 cases), SDAI improved but both BMI and SMI dropped. There was no significant difference in exercise time between the two groups. [Conclusion] Low SMI values in RA patients are evident. However, prolonged treatment of RA resulted in improved SMI. It was suggested that controlling disease activity is crucial for preventing the progression of sarcopenia.

P2-288

A case of rheumatoid arthritis complicated with lymphomatoid granulomatosis in remission with rituximab

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Conflict of interest: None

[Case] 53 years old, female [Medical history] She developed rheumatoid arthritis at the age of 28 and had been using PSL, MTX, and various biologics. At the age of 48, she visited our outpatient clinic with fever, anorexia, and lymphadenopathy, and a CT scan showed multiple swollen lymph nodes in her trunk. A cervical lymph node biopsy was performed and a diagnosis of OI-LPD was made. The patient was relieved after MTX was discontinued, but later, due to difficulty in controlling arthritis, Upadacitinib was introduced. At the age of 53 years, she had a fever for several months, and a CT scan revealed swollen trunk and axillary lymph nodes and multiple nodular shadows in the lungs. An axillary lymph node biopsy showed findings of granulomatous lymphadenitis with EBER-positive cells. Clinically, the patient was considered to have lymphomatoid granulomatosis as OI-LPD. Upadacitinib was discontinued and the dose of glucocorticoid was increased, but the patient was not in remission, and in addition, her rheumatoid arthritis activity worsened. Rituximab was adopted to treat both rheumatoid arthritis and lymphomatoid granulomatosis, and the treatment was successful. [Discussion] Rituximab is considered to be an effective treatment for rheumatoid arthritis patients with a history of OI-LPD.

P2-289

A case of other iatrogenic immunodeficiency-associated lymphoproliferative disorder that developed due to peripheral neuropathy while being treated with a JAK inhibitor

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Conflict of interest: None

The patient is a 61-year-old man who was diagnosed with rheumatoid arthritis at age 12 and started treatment with methotrexate (MTX). 32 years old, he made his first visit to our department. At age 58, lymphadenopathy and soft tissue mass appeared and MTX was stopped due to suspicion of OIIA-LPD. In January X, numbness in both fingers appeared. In May X, swelling, spontaneous pain, and redness of the left upper arm appeared, and an MRI showed a myopathy. mL, and elevated LDH 695 U/L and sIL-2R 2657 U/ mL. Peripheral blood EBV-DNA was positive at 3.7 logIU/mL. The right submandibular lymph node was also enlarged, and a biopsy was performed at the same site. The patient was diagnosed with high-grade B-cell lymphoma and was started on DA-R-EPOCH therapy, which is currently ongoing. This patient developed OIIA-LPD 2.5 years after MTX was discontinued due to the clinical diagnosis of OIIA-LPD, during treatment with JAK inhibitors, and was suspected to have neurolymphomatosis. We consider this case to be suggestive in the diverse treatment of LPD, and report it here with a discussion of the literature.

P2-290

Safety evaluation of non-steroidal anti-inflammatory drugs (NSAIDs) in the treatment of spondyloarthritis (SpA)

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Conflict of interest: None

[Objectives] NSAIDs are the primary treatment for SpA. Recent data on the long-term safety of NSAIDs is limited, prompting this study to assess their safety through a retrospective review of cases at our hospital. [Methods] We analyzed medical records of patients diagnosed with SpA at our hospital between 2014 and 2023. Baseline characteristics and serial blood test parameters-primarily focusing on renal function-were extracted up to five years after treatment initiation. The study included three groups: 36 patients treated with NSAIDs alone for over one year (N group), 9 patients treated with sulfasalazine (SASP) alone (S group), and 25 patients treated with a combination of NSAIDs and SASP (NS group) [Results] No significant differences were found in age or sex across groups. All groups showed declines in renal function over 1, 3, and 5 years: N group (-4.3/-6.2/-8.6), S group (-4.7/-6.9/-5.8), and NS group (-5.4/-7.1/-3.7) ($p < 0.05$). One-way ANOVA revealed no significant differences in ΔeGFR among the groups. Multiple regression analysis identified no significant impact of NSAID use on ΔeGFR at 5 years. [Conclusion] Our findings suggest that NSAIDs and SASP have comparable safety profiles for SpA treatment over a five-year period.

P2-291

A Case Suggesting Co-Existence of Rheumatoid Arthritis and Giant Cell Arteritis/Polymyalgia Rheumatica Detected by PET/CT Imaging

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Conflict of interest: None

[Case] A 86-year-old female with definite diagnosis of seronegative RA since 2014, had been managed with MTX. A continuous increase of CRP was observed after the first and second SARS-CoV-2 vaccinations in June and July 2021. Her CRP level exceeded 10 mg/dL even after treatment for pneumonia pointed out in December, followed by noticing of swelling temporal arteries (TA). Ultrasound and PET/CT revealed wall thickening and FDG uptake in TA, as well as uptake in vertebral, subclavian arteries and aorta, indicating the concurrent with GCA. Additional FDG uptake was seen in regions of PMR, such as ischial tuberosities. Administration of 20 mg of PSL led to rapid decrease in CRP and the dose was successfully tapered to below 5 mg. Due to worsening polyarthralgia and a CRP increase following the third and fourth vaccination, a follow-up PET/CT was performed to evaluate GCA activity. As FDG uptake in the arteries excluding synovitis resolved, abatacept was initiated. Subsequently, arthritis and CRP titer stabilized even after discontinuing PSL. [Discussion] This is a rare case of newly-onset GCA in a patient with pre-existing RA, triggered after vaccinations, was monitored through serial PET/CT examinations. We assess radiologically the progress of each disease.

P2-292

A case of Stevens-Johnson syndrome caused by salazosulfapyridine with intestinal involvement

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Conflict of interest: None

[Case Presentation] A 64-year-old woman with mixed connective tissue disease presented with fever, eye pain, and sore throat. While on PSL 5 mg maintenance, she started salazosulfapyridine (SASP) 500 mg for joint pain. Three days before admission, she developed a fever and sore throat, followed by eye pain and oral/lip ulcers. She was admitted for a suspected severe drug rash. SASP was discontinued, and steroid pulse therapy was initiated, followed by PSL 45 mg/day. On day 7, she developed hematuria, hematochezia, and abdominal pain. An acute abdomen emerged on day 17; a CT scan showed free gas. Emergency surgery revealed a 3 mm ileal perforation requiring ileostomy. PSL was reduced to 5 mg/day by day 30, and she was transferred to rehabilitation on day 94. [Discussion] SASP-positive drug-induced lymphocyte stimulation test and skin biopsy confirmed Stevens-Johnson syndrome (SJS). The intestinal injury differential included SJS and steroid-induced enteropathy. Intestinal damage related to SJS generally appears within two weeks of the onset of skin symptoms, and this was also the case in our patient. This rare complication presented a diagnostic challenge, as SJS requires increased PSL while steroid-induced injury needs rapid PSL reduction, creating a treatment dilemma.

P2-293

A case of methotrexate-associated lymphoproliferative disorder suspected to be caused by bisphosphonate-induced osteonecrosis of the jaw

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Conflict of interest: None

A 73-year-old woman was diagnosed with rheumatoid arthritis (RA) 19 years ago and was treated with methotrexate (MTX) 6 mg/week, salazosulfapyridine 500 mg/day, and iguratimod 50 mg/day. She had been treated with MTX for over 10 years, and had a history of bisphosphonate (BP) use and osteonecrosis of the jaw. She was referred to our dental and oral surgery department because of swelling in the right mandible that had begun 2 months earlier. A spontaneous tooth loss and bone exposure were noted in the same area. Initially, osteonecrosis of the jaw due to BP was suspected, but the pathological examination of the sequestrum revealed EBER-ISH positivity and a diagnosis of MALT lymphoma, so oral MTX was immediately discontinued. FDG-PET/CT showed increased accumulation in the right mandible, but no abnormal accumulation was noted in other areas. Blood tests showed elevated CRP and sIL-2R levels. Subsequent FDG-PET/CT showed that accumulation in the right mandible had weakened, with no accumulation in other areas. [Clinical Significance] When oral lesions occur in RA patients, methotrexate-associated lymphoproliferative disorder must always be kept in mind if they are receiving MTX, even if they have a history of using BP preparations or have been treated for osteonecrosis of the jaw.

P2-294

A case of Still's disease with pulmonary arterial hypertension (PAH)

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Conflict of interest: None

[Case Report] A 23-year-old woman with a past medical history of Still's disease at the age of 5, complained of dyspnea on exertion for the past two months. Her drug history was Prednisolone (PSL) 1 mg and Cyclosporine (CyA) 100 mg. Echocardiogram showed pulmonary artery pressure was estimated to be 79 mmHg. Taking diuretics and nitrous acid medicine were started, and her symptom improved slightly. Two weeks later, she had fever and skin rash. The blood tests showed White blood cell 9400/μL, C-reactive protein 5.79 mg/dL, Interleukin-6 63.1 pg/mL, Interleukin-18 ≧5000 pg/mL. PSL was increased to 20 mg. Several days later, using Swan-Ganz Catheterization, she was diagnosed with PAH. Steroid pulse therapy was given for 3 days (post PSL 40 mg) and the dose of CyA was increased to 150 mg/day. Macitentan and tadalafil started in sequence. Her symptom improved. [Discussion] This is a case of Still's disease transferred to an adult. Adult onset Still's disease is rarely associated with PAH, and an inflammatory mechanism has been postulated. There are reports that immunosuppressive therapy in addition to pulmonary vasodilator is effective for Still's disease with PAH. However, the choice of immunosuppressive drugs remains a matter for consideration.

P2-295

A case of cold agglutinin syndorome associated with low disease activity rheumatoid arthritis

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Conflict of interest: None

[Case] An 82-year-old woman with rheumatoid arthritis for 18 years was maintained with low disease activity on methotrexate 4 mg/week and golimumab 50 mg/4 weeks. When she came to our hospital in February 2023, HCT was markedly decreased to 9.6% and high titer of cold agglutinin was detected. Rheumatoid arthritis maintained low disease activity and there were no subjective symptoms. A simple CT scan of the chest and abdomen showed multiple lymphadenopathy throughout the body, and a bone marrow examination revealed CD20 (+) atypical cells, leading to the diagnosis of B-cell lymphoma. After chemotherapy, the lymphoma went into remission and cold agglutinin was no longer detected. Rheumatoid arthritis is also maintained at low disease activity with 500 mg/day of salazosulfapyridine. [Discussion] Cold agglutination syndrome involves erythrocyte aggregation and extravascular hemolysis induced by anti-erythrocyte IgM antibodies that react at temperatures below normal body temperature. It is known to occur secondary to infections, autoimmune diseases, and malignant lymphomas. It is important to take into account the possibility of lymphoma as a complication of cold agglutinopathy, which does not correlate with disease activity in rheumatoid arthritis.

P2-296

A case which liver injury persisted and developed to liver cirrhosis after discontinuing Methotrexate

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Conflict of interest: None

Liver injury induced by Methotrexate (MTX) is generally dose-dependent. In addition, it is said that liver damage is likely to worsen due to obesity, drinking and so on. If drug induced liver injury was suspicious, all drugs should be ceased. We experienced a case which liver injury persisted and developed to liver cirrhosis even after discontinuing MTX. A 61-year-old woman with rheumatoid arthritis (RA) was treated with MTX 6 mg/week solely. RA has been in remission. Both ALT level and AST level were abnormal. Abdominal ultrasonography showed fatty liver. Hepatitis B or C infection were negative. Anti-nuclear autoantibodies and anti-mitochondrial antibody were not detected. MTX induced liver injury was eventually diagnosed. After stopping of MTX, her liver function test had remained abnormal with thrombocytopenia. Diagnostic imaging showed cirrhosis. The cumulative dose of MTX was 820 mg. Her FIB-4 Index was 2.94. Drug withdrawal improve most liver injury caused by MTX. In this case, amount cumulative dose of MTX was small, there were no risk fac-

tors such as alcohol intake and obesity. But even after stopping taking MTX, liver injury persisted, progressed to liver cirrhosis. Although such case is rare, persistent liver injury after MTX withdrawal must be observed carefully.

P2-297

A case of thymic carcinoma in Sjögren's syndrome secondary to rheumatoid arthritis

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Conflict of interest: None

Case: 51-year-old female, Class 2, Stage IV. She was diagnosed with rheumatoid arthritis (RA) in X and MTX therapy was initiated. Low disease activity (LDA) was achieved with MTX 14 mg/week. In X+9, due to dry eye symptoms and positive for SS-A antibody, she was diagnosed as Sjögren's syndrome (SjS). After the diagnosis of SjS, LDA was maintained with MTX 14 mg/week + tacrolimus (TAC) 1 mg/day for RA. During follow-up with chest X-ray every year, a mass was noted in the right pulmonary hilar region. CT images showed a 36 mm-sized substantial mass in the anterior mediastinum. Robot-assisted thoracoscopic resection was performed for the diagnosis. The tumor was pathologically diagnosed as thymic carcinoma (pT1aN0M0 stage I). There was no additional treatment required in the staging and no recurrence. For RA, LDA was kept with the same medication. Clinical Significance: It is known that lung diseases such as interstitial pneumonia and lymphoproliferative diseases appear as extra-glandular symptoms in patients with SjS secondary to RA, and chest radiographs routinely every 6 months to 1 year is recommended. it is important to keep in mind not only lung disease but also the occurrence of thymic carcinoma, and to strive for early detection.

P2-298

A case of eosinophilic polyangiitis granulosa with impaired consciousness after administration of mepolizumab

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Conflict of interest: None

A 76-year-old man with eosinophilic polyangiitis granulosa was treated with high-dose steroid therapy and immunoglobulin therapy for bronchial asthma, polyangiitis of the extremities, and elevated eosinophils since October X. In February X+1, he began to fall more frequently, but there was no apparent worsening of his neurological symptoms. In early July, he was introduced to mepolizumab, and was admitted to our department about 3 weeks after administration because his level of consciousness gradually decreased and he had difficulty moving his body. Spinal fluid analysis and brain MRI showed no abnormality. On admission, the patient had muscle stiffness in the extremities and dopamine scintigraphy showed extensive hypoperfusion, leading to the diagnosis of Parkinson's syndrome, which was thought to be the cause of the patient's fall. On the other hand, EEG showed triphasic waves, which suggested the presence of some kind of metabolic encephalopathy, but the cause could not be identified. Since it was difficult to explain the disturbance of consciousness in Parkinson's syndrome, it was suggested that the metabolic encephalopathy was related to mepolizumab. We report here a rare case of encephalopathy after mepolizumab administration.

P2-299

Two cases of SARS-CoV-2 infection after rituximab therapy, with high viral load suggested by RT-PCR cycle threshold for a long time

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Conflict of interest: None

Background: COVID-19 is caused by SARS-CoV-2. In immunocompromised patients, especially those treated with anti-CD20 therapy, infections are often prolonged. We report two cases of prolonged viral shedding. Case 1: A 68-year-old male developed COVID-19 after rituximab (RTX) therapy for systemic sclerosis. Despite treatment with molnupiravir, the condition worsened. Although remdesivir (RDV) and dexamethasone (DEXA) provided temporary improvement, radiological findings worsened and oxygen demand increased. He was treated again with RDV and DEXA. RT-PCR cycle threshold (Ct) values remained low for over a month. Case 2: A 91-year-old female with ANCA-associated vasculitis developed COVID-19 after RTX therapy. She presented with cough. She was treated prophylactically with RDV due to RTX-related risks. She improved quickly, but RT-PCR Ct values stayed low for over 15 days. Discussion: In healthy individuals, RT-PCR typically becomes negative within 10 days. However, post-RTX patients can exhibit prolonged viral shedding due to RTX-induced suppression of antibody production.

P2-300

A case of mixed connective tissue disease with purpura fulminans after COVID-19 infetion

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Conflict of interest: None

[Case] A 46-year-old male. He came to our hospital because of Raynaud's symptoms since X-4 month. He was diagnosed as MCTD. He was rushed to the hospital for sudden vomiting one week after the onset of COVID-19, which temporarily improved. He was admitted to ICU with a diagnosis of septic shock and DIC. He remained in shock with the maximum dose of norepinephrine and vasopressin. Assuming bacterial infection, he was treated with antibiotics. Later, his general condition improved, but gangrene developed, and he was diagnosed as purpura fulminans. Blood culture was negative. Bilateral facial nerve palsy and left trigeminal neuropathy were also found. The patient was considered to have MCTD/SjS-related multiple cerebral neuropathy, and high-dose steroid therapy and cyclophosphamide pulse therapy were started. The patient was discharged from the hospital with no symptoms except facial paralysis. [Clinical Significance] Purpura fulminans is a rare condition that occurs after bacterial infection, and its occurrence after COVID-19 infection has also been reported, although rarely. In addition, this case is complicated by peripheral circulatory failure due to MCTD and subsequent multiple cerebral neuropathies, and we report the case including literature review.

P2-301

Development of cold agglutinin disease and Castleman disease after COVID-19 infection

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Conflict of interest: None

[Case] A 75-year-old man developed fever on April 5, 2024, and was diagnosed with COVID-19 by PCR. He was treated at home for mild illness, but was hospitalized on April 19 due to fever, loss of appetite, fatigue, and severe anemia. The patient was diagnosed with cold agglutinin disease based on a direct Coombs test and a high value of cold agglutinin. In addition, the patient had a high CRP level and multiple enlarged lymph nodes in the left supraclavicular fossa and mediastinum on CT. He was diagnosed with idiopathic multicentric Castleman disease (plasma cell type) based on a left supraclavicular lymph node biopsy. He was treated with prednisolone and showed a decrease in CRP levels and improvement in anemia. [Discussion] Although COVID-19 is known to cause cold agglutinin disease and multiple system inflammatory syndromes, there have been no reports of the simultaneous development of cold agglutinin disease and Castleman disease. We report this valuable case.

P2-302

A Case of Sudden Flare-Up of Systemic Lupus Erythematosus Following COVID-19 Infection During Long-Term Remission

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Conflict of interest: None

A 50-year-old woman was diagnosed with SLE and Sjögren's syndrome in 1997 at the age of 29. Her symptoms improved with steroid pulse therapy, maintenance PSL, and hydroxychloroquine, and she remained in remission for about 20 years. By October 2021, PSL was discontinued. In mid-January 2023, she contracted COVID-19. By February, her antinuclear antibody titer had risen to 1:5120, though she remained asymptomatic. In March, her Raynaud's phenomenon worsened, and by the end of the month, purpura developed. In early April, lab findings showed thrombocytopenia (platelet count 6,000/mm^3), anemia (RBC 3.12 million/mm^3, Hb 8.3 g/dL), elevated LD, increased reticulocytes, and positive direct and indirect Coombs tests. This led to diagnoses of autoimmune hemolytic anemia and thrombocytopenia. Anti-Sm antibodies became positive, and a significant decrease in complement levels confirmed an SLE flare-up. Treatment with platelet transfusions, steroid pulse therapy, and belimumab resulted in improvement of both symptoms and hematologic abnormalities. COVID-19 infection has been reported to trigger immune dysregulation, potentially leading to the onset or flare-up of autoimmune diseases. This case highlights a sudden flare-up of SLE following long-term remission, triggered by COVID-19 infection.

P2-303

Vaccine Associated Immune Thrombocytopenia Purpura caused by COVID-19 vaccine

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Conflict of interest: None

[Case Report] A 70-year-old woman had been diagnosed rheumatoid arthritis 18 years ago and taking 8 mg dose of methotrexate per week and 1.5 mg dose of tacrolimus per day. A few days after his sixth vaccination of SARS-CoV2, she had noticed purpura on his lower legs, and gingival bleeding. A blood test shows decrease of platelet (PLT) which was 6000/μL, indicating severe thrombocytopenia. Further investigation also showed a hyperconsumptive type of PLT depletion, and infection with Helicobacter pylori. The patient was finally diagnosed with immunogenic thrombocytopenia (ITP) and treated by 30 mg dose of prednisolone per day along with intravenous immunoglobulin therapy (IVIG) and platelet transfusion. [Discussion] Thrombocytopenia was reported in some cases. The median period of onset from the vaccination was about 12.5 days. Almost all cases were treated with regular treatment protocol with ITP such as corticosteroids, IVIG, and thrombopoietin receptor antagonists. [Conclusion] When thrombocytopenia occurs after SARS-CoV2 vaccination, the possibility of rare adverse events after vaccination such as thrombosis with thrombocytopenia (TTS/VITT), or vaccination-associated autoimmune thrombocytopenia (VA-ITP) should be considered.

P2-304

A case of EB virus-associated lymphoproliferative disease with multiple pulmonary nodules after COVID-19 infection requiring differentiation from MTX-associated lymphoproliferative disease

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Conflict of interest: None

[Case] 61 years old, female [Clinical history] The patient developed rheumatoid arthritis in 2012 and was introduced to treatment with oral DMARDs and a small dose of steroids. On June 28, 2024, she got a COVID-19. On July 1, she was aware of dyspnea. Chest CT scan showed multiple pulmonary nodules, enlarged hilar and mediastinal lymph nodes. Metastatic lung tumor was suspected, but no obvious primary tumor was noted on thoracoabdominal contrast-enhanced CT. Blood tests showed elevated soluble IL-2 receptor levels, and the patient was taking MTX for rheumatoid arthritis. CT-guided needle biopsy was performed for histological examination, which revealed the presence of EBV-positive B cells as the main component of lymphoproliferative disease, leading to the diagnosis of EBV-related lymphoproliferative disease. The patient's respiratory condition worsened after admission, and after treatment with steroid pulses and gradual reduction of PSL, his respiratory condition improved and the nodular shadow shrunk with time. [Conclusion] Reactivation of EB virus may occur after novel coronavirus infection. In suspected cases of lymphoproliferative disease following novel coronavirus infection, the involvement of EB virus as well as MTX should be suspected.

P2-305

Questionnaire Survey on Vaccines in Patients with autoimmune disease

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Conflict of interest: None

[Objectives] Patients with autoimmune disease, such as rheumatoid arthritis and systemic lupus erythematosus, frequently treated with immunosuppressive agents or biologics DMARDS. These treatments may result in serious complications of infection. For the patients with autoimmune disease, administering vaccine such as influenza, recombinant varicella-zoster virus, and pneumococcal is recommended. However, in clinical practice, many patients do not receive vaccinations. [Methods] In this study, we conducted a survey of a questionnaire with vaccination status and the reasons for not receiving the vaccine in our hospital. [Results] We received responses from 219 patients. The average age was 66.6±15.3 years, and the mean disease duration was 3.2±1.5 years. A hundred nighty seven patients were confirmed vaccinated with influenza vaccine, 191 patients with COVID19 vaccine, 65 patients with pneumococcal vaccine, and 43 patients with recombinant varicella-zoster virus vaccine. The most common reason for not receiving COVID19 vaccine was concern about adverse effects, and recombinant varicella-zoster virus vaccine was cost. [Conclusion] The reasons for not receiving vaccinations were different between each vaccine.

P2-306

A case of de novo hepatitis B in a patient with negative hepatitis B core and surface antibody treated with biologic agents for Rheumatoid arthritis

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Conflict of interest: None

We observed a 73 year-old. female case with negative HBs antigen, HBs antibody, and HBc antibody tests developed de novo hepatitis B after changing biological agents. She was diagnosed RA in 1995 (age 45). ETN and PSL had been administered at the previous hospital since 2014. In 2021 (age 71), she admitted to our hospital for asthma and RA treatment. High disease activity of RA persisted, and the drug was changed after confirming a negative infection screening test. A rapid increase in liver enzymes was observed during the change in SAR administration, and de novo hepatitis B was diagnosed based on the increase in HBVDNA antibody titers, and Tenofovir was started. A rapid decrease in ALT, AST, and non-detection of HBVDNA were obtained, avoiding fulminant symptoms. The trends in HBs antigen/HBs antibody/HBc antibody values before the drug change (2021/8) and after confirmation of HBVDNA 5.1 log IU/r (2022/11) were (-)/2.76/0.41→62.36/0.55/11.31 IU/ml, respectively. The trends in ALT/AST/Tbil values when liver damage worsened, and when it improved were 357/444/0.9→12/18/0.7. [Discussion] In this case, the HBs antibody titer was low, making it difficult to confirm a history of hepatitis B infection. In similar cases, HBVDNA testing are necessary when continuing or changing medication.

P2-307

Idiopathic Multicentric Castleman Disease (iMCD) with Unilateral Massive Pleural Effusion: A Case Report

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Conflict of interest: None

[Case] A 76-year-old man was incidentally found to have left pleural effusion and multiple lymphadenopathies on a CT scan 3 months before admission. He was asymptomatic and placed under observation. However, he later developed fatigue and dyspnea, leading to urgent hospitalization. A CT scan revealed a massive left pleural effusion with tracheal compression, and 3 liters of pleural fluid were drained. Despite an inguinal lymph node biopsy, no definitive diagnosis was reached, and he was transferred to our department for further examination. An FDG-PET/CT scan showed accumulation in the thickening pleura and multiple lymph nodes. A mediastinal lymph node biopsy demonstrated medullary and lymphoid follicular hyperplasia. No malignancies were found in the pleura, lymph nodes, or bone marrow. A diagnosis of iMCD was made. On day 27, treatment was initiated with tocilizumab at 8 mg/kg every 2 weeks, along with prednisolone at 30 mg/day, resulting in symptom improvement and a reduction in pleural effusion, and he was discharged on day 58. [Clinical Significance] Although unilateral pleural effusion has been reported in unicentric Castleman disease with primary involvement of the chest wall, there are few reports of that in iMCD. This case contributes valuable insight to the literature.

P2-308

A case of Erdheim-Chester disease presenting with bilateral orbital masses as the initial symptom, requiring differentiation from IgG4-related disease or GPA

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Conflict of interest: None

[Case] An 80-year-old female presented in November of year X-2 with orbital masses and was referred to the ophthalmology and hematology departments of our hospital. CT scans showed perirenal fat stranding without lymphadenopathy. PET scans indicated FDG uptake in the intraorbital masses, aorta, and bones. A biopsy of orbital mass showed no significant findings. In March of year X-1, she was referred to our department with suspected IgG4-related disease, ANCA-associated vasculitis, or giant cell arthritis. To prevent blindness, a high-dose steroid therapy was initiated, which was partially effective. However, due to recurrent fever and instability, tapering prednisolone (PSL) below 7 mg was not possible. In December of year X-1, a head MRI showed multiple bilateral subdural masses. Hypertrophic pachymeningitis was suspected, leading to increased PSL, but without improvement. Erdheim-Chester disease (ECD) was considered, prompting referral to a specialist. ECD was clinically diagnosed from typical findings, including sclerotic changes in the long bones, xanthelasma, hairy kidney sign, and coated aorta. Specific treatment was planned following a biopsy of the xanthelasma. [Conclusion] ECD is a rare disease that may mimic collagen diseases, necessitating careful differentiation.

P2-309

A case of mediastinal tumor associated with IgG4-related periaortitis

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Conflict of interest: None

We present a rare case of IgG4-related periaortitis involving the thoracic aorta in a 71-year-old woman who initially presented with scleritis. Blood tests indicated elevated inflammatory markers, and contrast-enhanced CT revealed a mass surrounding the aortic arch. Despite normal serum IgG4 levels (91 mg/dL), PET-CT showed abnormal FDG uptake in the aortic arch vessel wall adjacent to the mediastinal mass, suggesting periaortitis. Therefore, a thoracoscopic biopsy was performed. Histological examination revealed lymphocyte and plasma cell infiltration in the mediastinal adipose tissue, and immunostaining showed IgG4-positive plasma cells with an IgG4/IgG ratio > 40% and over 10 IgG4-positive cells per HPF. Malignancy and infection were ruled out, leading to a diagnosis of IgG4-related disease. The patient was treated with glucocorticoids (30 mg/day), resulting in significant improvement of symptoms and inflammatory markers. In this case, imaging alone could not definitively distinguish the mediastinal mass from malignancies such as thymic carcinoma and lymphoma, necessitating tissue biopsy. This case was classified as IgG4-related disease based on imaging and biopsy results. IgG4-related disease involving the mediastinal mass is rare.

P2-310

A case in which dialysis was initiated by MPO-ANCA and anti-GBM antibody double-seropositive (DPP) rapidly progressive glomerulonephritis after visiting the hospital with lower limb pain

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Conflict of interest: None

[Case] 72-year-old man [Recent medical history] Interstitial pneumonia diagnosed at X-13-month. X-2 months: haematuria noted and serum creatinine (Cr) 1.08 mg/dl. X-1 month: Visit to urology for nocturia and diagnosed benign prostatic hypertrophy. X month: He visited an orthopaedic surgeon because of numbing pain in both lower limbs, then blood test showed Cr 8.31 mg/dl and hyperkalemia (7.4 mmol/l). [Progression] Rapidly progressive glomerulonephritis due to vasculitis was suspected because of persistent low-grade fever and CRP 20.40 mg/dl. The patient was found to be positive for both P-ANCA 96.2 IU/ml and anti-GBM antibody >680 U/ml, and the lower limb pain was thought to be caused by mononeuritis of microscopic polyangiitis. The lower limb pain was gradually reduced by 20 mg/day of post-steroidal therapy while continuing haemodialysis, but during the course of the disease the patient became completely anuric. The patient's previous interstitial pneumonia did not worsen. [Discussion] We have experienced a case of DPP in which the patient presented with symptoms of mononeuritis preceded by interstitial pneumonia. This report includes a discussion of the clinical features of DPP.

P2-311

A case of lung adenocarcinoma complicated by immune-mediated necrotizing myopathy with macro-creatine kinase

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Conflict of interest: None

A 77-year-old male had a past history of hepatitis C and hepatocellular carcinoma. He also had several nodules of right lung, which were observed since X-4. In November X-1, he was admitted to the hospital because of weakness of limb muscles predominantly in the proximal muscles, dysphagia, and the elevation of CK. Laboratory tests demonstrated positive anti-HMGCR antibody and specific findings on muscle biopsy led to the diagnosis of IMNM. And he also had macro-CK. We performed induction therapy of prednisolone (PSL) 55 mg/day and IVIG, but that was not effective. Then we added methotrexate and tacrolimus, followed by 2nd IVIG. Since then, the disease activity decreased, PSL was reduced, and he was transferred to our department in February X. However, in late March X, his muscle symptoms flared up again, we increased PSL to 10 mg/day, and performed 3rd IVIG, which resulted in remission. Since late June X, laboratory tests showed the progressive elevation of CK with no muscle symptoms. Then imaging tests showed right pleural effusion, pleural fluid aspiration demonstrated the diagnosis of lung adenocarcinoma. Macro-CK can be a complication in malignant tumors and autoimmune diseases. We report the case with reviews of the literatures.

P2-312

A case of IgG4-related disease complicated with carcinomatous meningitis

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Conflict of interest: None

[Case] A 57-year-old woman. She was diagnosed with IgG4-related disease in 2014 and was followed up with prednisolone (PSL) 7 mg/day and azathioprine 100 mg/day. In August 2024, she was hospitalized due to headache, and loss of appetite. Her cerebral fluid culture did not show bacteials, tuberculosisand fungi. MRI findings did not revealed thickened dura. Contrast-enhanced fluid attenuated recovery MRI showed contrast enhancement leptomeningitis at parietal lobe. We suspected leptomeningitis associated with IgG4-related disease and started to treat with PSL 1 mg/kg/day. We performed upper gastrointestinal endoscopy to investigate the cause of loss of appetite. Its finding revealed type 4 gastric cancer, the histopathological diagnosis was adenocarcinoma. Despite steroid treatment, her headache did not improve. Therefore, we performed cerebrospinal fluid analysis again. Its histological diagnosis was adenocarcinoma and she was diagnosed as carinomatous meninditis. [Conclusion] It has been reported that IgG4-related disease is complicated with malignanncy. It is important to concider carinomatous meninditis as one of causease of headache inIgG4-related disease.

P2-313

Current Status and problems of Collaboration Between Hospitals, Clinics, and Pharmacies in Hokkaido: A Survey of Rheumatologists

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Conflict of interest: None

[Objectives] As rheumatoid arthritis (RA) treatment shifts to outpatient care, collaboration between hospitals and pharmacies is crucial. This study surveyed RA care physicians in Hokkaido to identify problems and needs in such collaboration. [Methods] A web-based survey targeting 168 RA care physicians in Hokkaido was conducted in July 2024. [Results] The response rate was 30.3%: 12 from clinics (Group A), 22 from general hospitals (Group B), and 17 from core hospitals (Group C). For collaboration necessity, 50% of Group A, 77.2% of Group B, and 70.6% of Group C answered it was “very necessary”. 33.3% of Group A, 11.8% of Group B, and 18.2% of Group C was Satisfied with the current collaboration. Key information needed included medication records from other institutions and adherence issues. [Conclusion] The need for collaboration is clear, but limited information sharing reduces satisfaction. Physicians seek details on remaining medication and prescriptions from other institutions. Efficient information-sharing methods are crucial to improve collaboration in RA care. The survey highlights the main problems and needs.

P2-314

Questionnaire Survey on the Onset and Relapse of Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] In clinical practice, we experience patients with rheumatoid arthritis (RA) who developed by excessive joint stress or physical/mental stress. In addition, it is not uncommon for patients with RA having flare-ups after remission triggered by various factors. Hence, we here investigated potential triggers that might be associated with the onset or relapse of RA. [Methods] A questionnaire survey by nurses was conducted (2020 - 2024) among 48 patients who developed (n = 38) or relapsed RA (n = 10) on factors that may have contributed to them. [Results] The mean age was 66 years. The affected joints in the onset included the wrist (n = 15), fingers (n = 14), shoulders (n = 7), knees (n = 5), and toes and whole body (each 4). Triggers were trauma in 10 patients (21%), joint overuse in 29 (60%), stress in 20 (42%), mental stress in 18, vaccination in 8 (30%), family history in 12 (25%), smoking in 18 (38%), dental problems in 11 (23%), sinusitis and hay fever in 20 (42%), lung involvement in 8 (17%), bowel symptom in 10 (21%), and skin disease in 5 (10%). [Conclusion] Avoidance of joint overuse and trauma, as well as that of potential environmental factors are necessary for the prevention of the development or the flare-ups of RA.

P2-315

What is expected of insurance pharmacists in rheumatology?-Including the current status of pharmacists in insurance pharmacy-

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Conflict of interest: None

[Objectives] The treatment for rheumatic diseases in outpatient, with many patients receiving medication at pharmacy. However, there are few the certified pharmacists by Japan Rheumatology Foundation (RA pharmacists) working in pharmacies. This study investigates the current status of pharmacists. [Methods] Case studies were conducted for two RA patients. Additionally, a survey was administered to 287 pharmacists. The survey covered topics such as access to medical information, awareness of the RA pharmacist system. [Results] One RA patient lacked sufficient understanding of the diagnosis and treatment plan, while another patient was unable to make an informed decision regarding the initiation of biologic therapy. The awareness rate of the RA pharmacist system was found to be 12%. Although 83% pharmacists had a history of guiding RA patients, about half reported that they were unable to provide adequate medication guidance, and 5% reported experiencing difficulty in doing so. [Conclusion] Pharmacists are required to provide all types of medication. Training sessions often focus on high-prevalence diseases, and there is an urgent need for a system that delivers essential information to pharmacists to enable specialized guidance in the RA field.

P2-316

Awareness survey on the daily lives of rheumatoid arthritis patients with

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Conflict of interest: None

objective: this study conducted a survey on the daily life of outpatients with rheumatoid arthritis to assess their current situation and the role of nursing clinics. **methods:** a survey was given to outpatients to understand their challenges. **results:** the study involved 65 individuals with an average age of 65.4 years and an average disease duration of 10 years. Many were treated with anti-rheumatic drugs and biologics. The most common daily activities were: 1) joint movement, 2) selecting footwear, 3) oral care, and 4) foot observation. About 49% reported difficulties, including 1) deformities in the hands and feet, and 2) calluses and corns. Additionally, 33% devised was to cope. **discussion:** rheumatoid arthritis is a chronic disease requiring lifelong care. Patients with foot deformities faced greater challenges and an increased risk of falls. These deformities also led to calluses and corns. therefore early nursing intervention is crucial, with a focus on foot care and footwear to pervert from developing skin ulcer. **conclusion:** foot issues are common among rheumatoid arthritis patients. Nursing clinics should provide guidance to help patients manage daily life with fewer difficulties.

P2-317

The Power of Ultrasound and Shared Decision-Making in RA Treatment: Enhancing Patient Satisfaction through Rheumatology Care Nurses

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Conflict of interest: None

Objective: To examine how rheumatoid arthritis care nurses can utilize joint ultrasound for patient communication and contribute to Shared Decision Making (SDM) through specific case examples. Additionally, to analyze why the previous Net Promoter Score (NPS) survey results were high and identify factors contributing to patient satisfaction. **Methods:** We presented specific cases where ultrasound was used, examining how it influenced patient understanding, acceptance, and communication with nurses. We analyzed the impact of ultrasound on reassurance and understanding of disease progression, with a focus on how empathy and trust-building with nurses contributed to satisfaction. **Results:** The use of ultrasound helped patients visually understand their condition, enhancing reassurance and acceptance of treatment. Through conversations with nurses, patients experienced reduced anxiety, and ultrasound aided treatment choice, contributing to the increased NPS. **Conclusion:** Ultrasound serves as a vital communication tool, reinforcing patient understanding and trust. By facilitating SDM, it fosters patient engagement in treatment. Further efforts will be made to enhance satisfaction through ultrasound-based care.

P2-318

Oral Care Status of Rheumatoid Arthritis Patients and the Relationship Between Self-Efficacy for Oral Health Behavior and Anxiety or Depression

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Conflict of interest: None

[Objectives] The purpose of this study was to investigate the oral care status in patients with RA and analyze the relationship between self-efficacy for oral health behavior and anxiety or depression. [Methods] We surveyed 102 patients with RA visiting rheumatology clinics to assess their oral care practices, oral care items, oral symptoms, and oral environment measured using a saliva test device. Self-efficacy for oral health behavior was evaluated using SEOH, whereas anxiety and depression were assessed using HADS. [Results] The analysis included 94 patients with RA without other collagen diseases, with a mean age of 66.9 ± 12.7 years and 79 (84.0%) being women. 65 (69.1%) used mouthwash and 32 (34.0%) used interdental brushes for oral care. 43 (45.7%) were concerned about bad breath, and 26 (27.7%) had difficulties with their oral environment or oral care. In SEOH and HADS, there was a weak negative correlation between "brushing behavior" and "oral occult blood". The SEOH and HADS analyses revealed that "anxiety" showed a negative correlation with "brushing behavior" and "psychological control". "Depression" showed a negative correlation with all items. [Conclusion] These findings indicate a need for targeted support regarding brushing behavior among patients with RA.

P2-319

A case of rheumatoid arthritis resulting in pregnancy and delivery after using etanercept biosimilar

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Conflict of interest: None

[Case] A 37-year-old woman presented with swelling and pain in the joints in X-2 years, and was diagnosed as RA 6 weeks after the onset. The patient was undergoing fertility treatment and expressed a desire to conceive. Disease control was poor, ETNBS 50 mg/week was initiated due to financial constraints. Symptoms improved 6 weeks after treatment commencement, around the same time, pregnancy was suspected. At 12 weeks of gestation, ETNBS was discontinued, but RA relapsed at 14 weeks of pregnancy. Following the resumption of ETNBS, remission was maintained, and the patient delivered a baby boy weighing 3322 g at term. Remission continued with ETNBS treatment even during lactation, and the child's development has been normal. [Discussion] It is important to maintain remission or low disease activity during pregnancy to ensure a favorable pregnancy outcome. ETN and CZP have low placental transfer and can be used in pregnant women under certain conditions. The JCR2024 guidelines recommend biosimilar to alleviate the financial burden on patients; however, there have been no prior reports of ETNBS use during the perinatal period. While close monitoring of the child is essential, this case suggests that ETNBS could be considered a viable treatment option during pregnancy in RA patients.

P2-320

A case of adult onset Still's disease (AOSD) complicated with hemophagocytic syndrome (HPS) during late pregnancy

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Conflict of interest: None

A 30-year-old woman at 34 weeks of pregnancy had been suffering from fever since mid-July of year X. Because of a persistent fever and elevated liver enzyme, she was hospitalized in mid-August. No viral infection was detected, and any culture tests were negative. Her symptoms improved without any medication. However she developed a fever again and a faint erythema over her body, and she was transferred to our hospital. Blood tests revealed elevated CRP and ferritin levels, anemia and leukopenia. We diagnosed with AOSD complicated with HPS. Treatment with steroid pulse therapy leaded to rapid decline of fever and improvement in laboratory findings, but fetal death was confirmed the day after the end of the pulse therapy. The following day, the fetus was delivered. Amniotic fluid turbidity suggested the possibility of intrauterine infection. After that she was treated with steroids, cyclosporine, and tocilizumab, resulting in a good maternal recovery and discharge. AOSD can rarely occur during pregnancy, and can be difficult to treat due to limited tests and immunosuppressive agents. It can also have a significant impact on pregnancy outcomes. We experienced a rare case which maternal treatment progressed well but the fetus died. We report the case with reviews of the literatures.

P2-321

A report of 4 cases of low bone mineral density in adulthood in women with childhood-onset SLE

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Conflict of interest: None

[Object] We report four cases of childhood onset SLE and childhood bone density loss in adolescents. [Methods] The subjects were four female patients with SLE who developed SLE before the age of 16 years. In each case, the patient's background, bone density, timing of measurement, and treatment details were extracted. [Result] In all cases, treatment with PSL was started at the time of onset. All patients had started taking active vitamin D medication within 1 year of initiation of PSL. There were no fractures. Case (1) She had no history of PSL pulse therapy. 16 years after the disease, 80% lumbar YAM and 78% hip. Bisphosphonates (BP) were started at the age of 8 years of illness. Case (2) She had PSL pulse history 3 times. 20 years after the disease, lumbar spine YAM value 98% and hip joint 76%. BP drugs were started at the age of 8 years of illness. Case (3) She had PSL pulse history 3 times. 25 years after the disease, lumbar spine YAM value 75% and 68% in the hip joint. BP drugs were started at the age of 13 years of illnes. Case (4) She had PSL pulse history twice. 21 years after the disease, lumbar spine YAM value 71% and hip joint 69%. BP drugs were started at the age of 13 years of illnes. [Conclusions] Bone density control from childhood is very important.

P2-322

A case of antiphospholipid syndrome (APS) in which the clinical course of three pregnancies was observed

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Conflict of interest: None

Two years ago, a 30-year-old woman was visit our hospital at 25 weeks pregnant due to hypertensive disorders of pregnancy (HDP) and intrauterine growth restriction. She delivered her first child weighing 226 g by emergency cesarean section, but her child died. Extensive infarction was observed in the placenta. She visited our hospital again because she became pregnant with her second child, and lupus anticoagulant was positive. She diagnosed with APS and low-dose aspirin (LDA) and unfractionated heparin (UFH) therapy were initiated. She developed HDP at 31 weeks pregnant, so an emergency cesarean section was performed and a boy weighing 1370 g was delivered. Two months later, the patient was diagnosed SLE. PSL20 mg and hydroxychloroquine (HCQ) were initiated. At the age of 32, the patient became pregnant with her third child. HDP developed and a cesarean section was performed at 36 weeks of pregnancy, delivering a boy weighing 2358 g. At the age of 34, the patient became pregnant with her fourth child. The patient's condition remained stable until 28 weeks of pregnancy. In this case, the combination of LDA and UFH therapy with steroid and HCQ led to an improvement in the pregnancy course. There have been few reports of multiple deliveries with APS, we think this is a valuable case.

P2-323

Cases of pregnancies complicated by immunological disorders treated at our clinic - Through experience with diseases outside of rheumatoid arthritis-

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Conflict of interest: None

[Objectives] Examining the effectiveness of approaches and their factors in cases of pregnancies complicated by immune disorders. [Methods] Pregnant patients treated from September 2022 to August 2024 was collected. [Results] (1) 34-year-old woman with Behcet's disease. She became pregnant. After consultation with obstetrician, she stopped taking colchicine. Stomatitis flared up and she had a threatened preterm labor. (2) 35-year-old woman with Sjögren's syndrome. She became pregnant and discontinued azathioprine at her own discretion. She subsequently miscarried. (3) 34-year-old woman with obstetric antiphospholipid antibody syndrome. She was referred to our clinic for treatment from the obstetrics department of a Hospital. She was started on low-dose heparin and aspirin. At 32 weeks' gestation, Hepatic dysfunction was observed, then she was hospitalized and delivered a baby. (4) 40-year-old woman with Hashimoto's disease. She was taking levothyroxine without knowing the reason for taking it. She had a history of threatened preterm labor. [Conclusion] It was considered necessary to consult with a rheumatologist to determine drug adjustments. Caution should also be made to ensure that the need for continuation of medications used for infertility is adequately explained.

P3-001

Definitions of fever of unknown origin (FUO) and final diagnoses in rheumatology practice

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Conflict of interest: None

[Objectives] Classic fever of unknown origin (FUO) is defined as a temperature >38.3˚C recorded on several occasions for >3 weeks. In recent rheumatology practice, we encounter cases where persistent fever is the main complaint but do not meet the definition of FUO. This study examined the impact of the definition of FUO on the final diagnosis. [Methods] Between January 2021 and December 2023, we identified cases admitted for a prolonged febrile illness of unknown etiology, where a fever of 37.5°C or higher persisted for at least 1 week. We compared the final diagnoses based on whether the temperature was 38.3°C or higher and whether the duration of fever was 3 weeks or longer using the chi-square test. [Results] The mean age of 90 patients was 60.5 years with 27 females. The majority of final diagnoses were rheumatic disorders (n=55) with MPA being the most common (n=14). 13 cases did not meet the maximum temperature criterion, and 29 cases did not meet the duration criterion. Comparisons of the two groups based on temperature and duration criterion did not show significant differences in the frequency of final diagnoses. [Conclusion] There is a certain proportion of febrile patients in rheumatology who do not fulfill the definition of classic FUO but have similar final diagnoses.

P3-002

Current Status and Prospects for PRICUREv2 (Pediatric Rheumatology International Collaboration Registry ver. 2)

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Conflict of interest: None

[Objective] PRICUREv2, a registry by the Japan Pediatric Rheumatology Society, aims to collect data on rare pediatric rheumatic diseases, serving as a foundation for secondary research. [Methods] The diseases include juvenile idiopathic arthritis, systemic lupus erythematosus, juvenile dermatomyositis, Sjögren's syndrome, mixed connective tissue disease, scleroderma, Behçet's disease, antiphospholipid syndrome, vasculitis, and autoinflammatory diseases. The registry system, built with FileMaker Server, enables secure data entry via web browsers. Centralized ethical approval was obtained from Nippon Medical School Hospital, allowing data collection at member facilities, focusing on information for Pediatric Chronic Specific Disease and Designated Intractable Disease applications. [Results] PRICURE began in April 2016 and was updated to PRICUREv2 in March 2019. As of October 2024, it includes 58 facilities and 1,006 cases. Secondary data use in approved studies has also started. [Conclusion] PRICUREv2 serves as a valuable nationwide registry for rare pediatric rheumatic diseases, supporting further understanding and treatment development. Collaboration across multiple institutions is expected to strengthen support for pediatric rheumatic patients.

P3-003

Clinical characteristics of non-renal SLE patients who achieved glucocorticoid-free status

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Conflict of interest: None

[Objective] Although the latest EULAR recommendation recommends achieving glucocorticoid (GC)-free status in non-renal SLE patients who achieved remission, the data on GC-free status is limited. This study examines the traits of patients in non-renal SLE who achieved it. [Methods] We studied 113 SLE patients with GC use history, excluding 46 with biopsy proved lupus nephritis, and compared between two groups: a group achieved GC-free status and a group received prednisolone (PSL) 5 mg/day or more. We also described the features of the GC-free group.

[Results] Twenty-three patients achieved GC-free status, while 48 were on more than 5 mg/day of PSL. No significant differences were seen in patients' backgrounds, initial symptoms and disease activity, or proportion of concomitant use of disease-modifying medications. The GC-free group had shorter illness duration and earlier hydroxychloroquine (HCQ) initiation, lower biological agent use, and lower GC-related SDI scores. The median time from PSL 5 mg to GC-free status was 29 months in GC-free group. The relapse rate after achieving GC-free status was 8.7% but they improved with intensified treatment. [Conclusion] In non-renal SLE, initial symptoms and disease activity didn't relate to GC-free status. Early HCQ use may help achieve it.

P3-004

Characteristics of Poor Treatment Response in Patients with Polymyalgia Rheumatica

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Conflict of interest: None

[Objectives] Polymyalgia rheumatica (PMR) causes pain and stiffness in proximal extremities and is managed by internists and orthopedic surgeons. This study aimed to examine characteristics of PMR cases, focusing on those unresponsive to treatment. [Methods] We retrospectively analyzed 71 PMR patients (29 males, 42 females) diagnosed at our hospital between May 2011 and February 2022. The average age was 77 years (range: 61-99), with mean CRP of 6.8 mg/dl, erythrocyte sedimentation rate of 75 mm/h, and rheumatoid factor positivity in 10% (7 patients). [Results] The initial prednisolone (PSL) dose for PMR was 7.9 mg (range: 5-15 mg), and PSL could be discontinued in 66% of patients (47 cases) after 16 months (range: 3-60 months). Among 24 patients unable to discontinue PSL, 9 (37.5%) had malignancies, and 7 (29.2%) developed rheumatoid arthritis (RA). Two of the 7 RA cases were anti-CCP positive, with a mean time to RA diagnosis of 24 months (range: 4-49 months). [Conclusion] PMR generally has a good prognosis with mineralocorticoid treatment, as 66% of cases responded. However, in patients unable to discontinue PSL, around 60% had malignancies or progression to RA. Poor PSL response should prompt consideration of malignancy or diagnostic reevaluation.

P3-005

Glucocorticoid-free achievement rates in polymyalgia rheumatica

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Conflict of interest: None

[Objectives] To analyze the glucocorticoid (GC)-free achievement rates and their predictive factors in polymyalgia rheumatica (PMR) in our hospital. [Methods] We retrospectively identified patients who received a final diagnosis of PMR after October 2016 and did not have giant cell arteritis. We calculated GC-free achievement rates using a Kaplan-Meier method and identified the predictive factors using a Cox proportional hazard model. [Results] 81 patients were included; mean age was 77 year-old and 49 were women. 1-year and 2-year GC-free achievement rates were 11.3% and 18.6%, respectively. In univariate analyses, combination therapy (GCs+immunosuppressants/biologics) was the only significant predictive factor for GC-free achievement (hazard ratio [HR] 5.33, p=0.008). In a multivariate model incorporating combination therapy and age, combination therapy was again only significant predictive factor for GC-free achievement (HR 4.84, p=0.012). GC-free achievement rates for GC alone and combination therapy were 1-year 2.4%/33.3% and 2-year 10.6%/38.9%, respectively. Drugs used in patients who achieved GC-free were IL-6 inhibitors (n=3), TNF inhibitors (n=2), and methotrexate (n=2). [Conclusion] GC-free achievement in PMR with GC alone is rare and combination therapy may contribute to it.

P3-006

Examination of polymyalgia rheumatica at our hospital-To what extent can steroids actually be discontinued-

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Conflict of interest: None

[Objectives] We examined the following groups of 71 patients with PMR who had visited our hospital and who had received steroids as of October 2024. One is complete remission patient group and the other is patients in non-remission patient group were compared. In addition, among the latter, patients who were treated with steroid drugs again after steroid withdrawal for more than half a year (temporary remission group). [Methods] After extracting PMR cases and confirming the contents and course of medical records, we selected and analyzed cases with an onset date of October 2019. [Results] 28 males, 43 females. The average onset is at 74.9 years old. The average length of hospital visit is 7.98 years, the longest hospital visit is 21.86 years, and the shortest is 0.34 years. 14 were in complete remission, 57 were unremitting, and 5 were in temporary remission. [Conclusion] Almost 20% of patients with PMR were able to wean themselves off steroids. 19 patients in remission, including those who were able to wean themselves off steroids temporarily, were 19, 27%. On the other hand, out of all 19 patients in remission, 5, 26.3%, patients were in temporary remission. Even if they were able to withdraw from steroids temporarily, about 1/4 of them needed to be administered steroids again.

P3-007

Factors Associated with Exacerbation of Lung Lesions in Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To identify factors contributing to the worsening of lung lesions in rheumatoid arthritis (RA) patients, as such exacerbations significantly affect prognosis and lack clear indicators. [Methods] We retrospectively analyzed 93 RA patients with lung lesions treated at our hospital, examining clinical symptoms, blood tests, respiratory function tests, and chest CT findings. Thirty-six patients with complete data (median age 73.5 years) were included. Over a median follow-up of 60 months, patients were classified into an exacerbation group (20 cases) and a non-exacerbation group (16 cases) based on imaging deterioration, treatment for exacerbation, or hospitalization. [Results] The exacerbation group had a significantly lower initial percent vital capacity (%VC) compared to the non-exacerbation group (85.7% vs 102.4%; p=0.014). No significant differences were found in age, sex, or CT. However, bird-specific IgG antibody positivity was higher in the exacerbation group (55% vs 31.3%; p= 0.19). [Conclusion] A decreased VC at initial may indicate a higher risk of exacerbation of lung lesions in RA, necessitating early therapeutic intervention. Positivity for bird-specific IgG antibodies may also be associated with exacerbations.

P3-008

Clinical Characteristic of Organizing Pneumonia (OP) Associated with Rheumatoid Arthritis (RA)

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Conflict of interest: None

Objective: To clarify the clinical features of OP associated with RA (RA/OP). **Subjects and Methods:** Patients hospitalized between 2013 and 2023 were included. RA was classified by the the 1987 ACR or 2010 ACR/EULAR classification criteria. OP was defined by the followings: (1) typical findings confirmed by a radiologist (2) good response to glucocorticoid (3) refractory to antibiotics. Clinical information was collected from the records retrospectively. **Results:** Seventeen were included, who were all Anti-CCP-positive at onset and received various DMARDs. RA disease activity was distributed from remission to high, 14 presented OP after RA, 1 developed OP before RA, and 2 developed OP simultaneously. Six cases had OP recurrence. Interestingly, the recurrence were occurred in all patients with preceding and simultaneous cases, who were treated with MTX alone as the maintenance. Of 6 recurrents, 4 had only once and 3 were treated with tocilizumab for the maintenance. Also, 2 with multiple recurrence were in remission after introduction of IL-6 blockade. **Conclusion:** Our results suggest that we need to be cautious for the recurrence especially in cases with preceding or simultaneous OP onset. Also, sufficient treatment including IL-6 inhibitors may be necessary to maintain remission.

P3-009

Two cases of organized pneumonia following JAK inhibitor cessation or dose reduction because of an acute bacterial infection

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Conflict of interest: None

[Case 1] An 82-year-old woman. She diagnosed with rheumatoid arthritis (RA) and had been well-controlled on peficitinib (PEF) at a dose of 150 mg. She was admitted to the hospital with a left empyema. She was treated with chest drainage, antibiotics, and a reduction in PEF dose to 50 mg. The left empyema improved, but a new infiltrative shadow appeared in the right lung, and respiratory failure worsened. A relapse of organizing pneumonia was suspected, and treatment with glucocorticoids (GC) led to rapid improvement. [Case 2] A 33-year-old man. He diagnosed with RA had been well-controlled on filgotinib (FIL) 200 mg and methotrexate 6 mg. He was admitted to the hospital with a right cheek cellulitis and bacterial pneumonia. He was treated with antibiotics and discontinuation of FIL, but the inflammatory response persisted, and a new infiltrative shadow appeared in the right lung. A diagnosis of organizing pneumonia was made, and treatment with GC led to rapid improvement. [Clinical Significance] Generally, the administration of JAK inhibitors is contraindicated in patients with severe infections. In patients with conditions such as rheumatoid arthritis, careful attention must be paid to the potential onset of organizing pneumonia following the discontinuation of treatment.

P3-010

Helicobacter pylori seroprevalence in rheumatoid arthritis patients with interstitial lung disease

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) is complicated with interstitial lung disease (ILD). Gastroesophageal reflux disease is prevented by Helicobacter pylori infection and is a predisposing factor for idiopathic pulmonary fibrosis. However, the prevalence of H. pylori infection in RA patients with ILD has not been sufficiently investigated. In this study, we analyzed anti-H. pylori antibodies in RA patients with ILD. [Methods] Anti-H. pylori antibodies were analyzed in the sera of RA patients using a commercially available enzyme-linked immunosorbent assay kit. [Results] The positivity of anti-H. pylori antibodies in RA with ILD (n=30 [18.0%], P=0.0227), and airway disease (n=30 [18.0%], P=0.0227) was significantly lower than that of RA without chronic lung disease (n=78 [27.5%]). The positivity of anti-H. pylori antibodies was also lower in RA with chronic lung disease (n=68 [18.2%], P=0.0059). [Conclusion] The seroprevalence of H. pylori was lower in RA with ILD. H. pylori infection prevented ILD in patients with RA by protecting them from gastroesophageal reflux disease.

P3-011

Comparison of non-TNF inhibitors and JAK2 inhibitors for rheumatoid arthritis associated interstitial lung disease (RA-ILD) in clinical practice

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Conflict of interest: None

[Objectives] To investigate effectiveness and safety of non-TNF inhibitors, which have been used in rheumatoid arthritis (RA) with interstitial lung disease (ILD), and JAK2 inhibitor, which are assumed to be protective for ILD based on their mechanism of action, in daily practice. [Methods] Using daily medical records, we are comparing the effects of non-TNF inhibitors and JAK2 inhibitor on radiological findings and pulmonary functions in the RA patients with ILD. Imaging tests are performed using HRCT, and functional tests are performed at 0, 6, and 12 months after the start of treatment. [Results] Six patients were included between June 2023 and May 2024. There are four male and two female patients, with an average age of 74.7 years, a median of RA duration of 3.6 years. Three patients were treated with abatacept and the other three patients with baricitinib. The average DAS28-ESR and CDAI at the start of treatment were 5.0 and 17.5, respectively. The drug continuation rate was 100% at 6 months, and there was no exacerbation of ILD within 6 months. No patient showed a change of more than 5% in FVC or DLCO. [Conclusion] We will increase the number of cases and examine whether there are differences between drugs in changes in images and pulmonary function tests over one year.

P3-012

Investigation of the Inhibitory Effect of Ozoralizumab on Joint Destruction in RA Patients at High Risk of Joint Destruction

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Conflict of interest: None

[Objectives] This study examined the effect of ozoralizumab on the inhibition of joint destruction in cases with a high risk of joint damage. [Methods] We evaluated disease activity at 1, 3, and 6 months after ozoralizumab administration in 32 cases, as well as its inhibitory effect on joint destruction in the hands, feet, and medium-to-large joints after one year. [Results] Of the 32 patients, there was 1 male and 31 females, with a mean age of 77.5 years. Sixteen patients had been previously treated with either biologics (BIO) or JAK inhibitors, and 17 had been treated with MTX. Imaging results showed that 20 patients exhibited bone marrow edema in the hands, feet, or medium-to-large joints. Ozoralizumab was effective in patients with MTX, untreated with BIO or JAK inhibitors, RF or ACPA

positive. No differences were observed based on the presence of MRI-detected bone marrow edema or the affected region. Among 18 cases followed for one-year, radiographic progression of joint destruction was not observed in most cases. [Conclusion] Ozoralizumab demonstrated an inhibitory effect on joint destruction in rheumatoid arthritis patients at high risk of progression.

P3-013

The comparison of 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

[Objectives] To compare the clinical efficacy of Sarilumab (SAR) and Tocilizumab (TCZ) in patients with rheumatoid arthritis (RA). [Methods] We evaluated inflammatory marker and disease activities in RA patients for 52 weeks (w) after administrations of SAR (N=55) and TCZ (N=182). [Results] The mean CRP/DAS28-CRP of SAR and TCZ groups were 1.94/4.39 and 2.28 (NS)/4.51 (NS) (vs SAR) at baseline (BL), 0.09/2.93 and 0.64 (**P=0.04**)/3.09 (NS) at 52W, respectively. CRP was significantly lower at 52W in SAR group than TCZ group. When looking at the clinical courses in both groups in only using as second line, the mean CRP/DAS28-CRP of SAR (N=16) and TCZ (N=56) groups were 2.29/4.27 and 1.79 (NS)/4.24 (NS) at BL, 0.03/2.87 and 0.51 (**P=0.01**)/3.63 (NS) at 4W, 0.02/2.62 and 0.52 (NS)/3.44 (**P=0.03**) at 12W, 0.02/2.39 and 0.29 (NS)/3.16 (**P=0.03**) at 52W, respectively. CRP at 4W and DAS28-CRP at 12, 52W in SAR group were significantly lower than TCZ group. [Conclusion] SAR has higher occupancy rate of IL-6 receptor than TCZ in normal dosage, and SAR significantly decreased CRP compared to TCZ, although both of SAR and TCZ had good clinical efficacy. Especially, SAR had better clinical efficacy than TCZ in second line using.

P3-014

A Novel TNF Inhibitor Ozoralizumab is Unaffected by Rheumatoid Factor in the Recycling Mechanism via Neonatal Fc Receptor

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Conflict of interest: Yes

[Objectives] It is known that the efficacy of TNF inhibitors with Fc portion is reduced in cases with high rheumatoid factor (RF). Ozoralizumab (OZR) is a novel TNF inhibitor that lacks an Fc portion and has the ability of binding to serum albumin. OZR is effective even in cases with high RF, but the mechanism is unclear. This study investigates whether the structural characteristics of OZR contribute to the efficacy in the presence of RF. [Methods] The binding affinity of OZR and IgG-type TNF inhibitors (IgG-TNFi) to human plasma-derived IgM-RF was evaluated by ELISA. Furthermore, the effect of IgM-RF on the binding of OZR and IgG-TNFi to the neonatal Fc receptor (FcRn) was also evaluated by ELISA. [Results] IgM-RF showed high binding affinity to IgG-TNFi, but low binding affinity to OZR. IgM-RF dose-dependently inhibited the binding of IgG-TNFi to FcRn. But, IgM-RF did not inhibit on the binding of OZR to FcRn even at high RF. [Conclusion] Unlike IgG-TNFi, OZR has a structural feature that lacks an Fc portion, make it less likely for RF binding. By utilizing the recycling mechanism of FcRn via serum albumin, OZR might maintain blood drug levels without being affected by RF. These results suggest that OZR is a promising candidate for the treatment of RA patients with high RF levels.

P3-015

Structural design of next generation anti-TNF alpha NANOBODY compound, ozoralizumab, to support its potent and sustained clinical efficacy

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Conflict of interest: Yes

[Objectives] Ozoralizumab (OZR) is a next-generation TNFα inhibitor for treating rheumatoid arthritis (RA), composed of two identical humanized anti-TNFα NANOBODY molecules (TNF30) linked via a single humanized anti-serum albumin (HSA) NANOBODY molecule (ALB8) and two peptide linkers. This study verified the importance of TNF30 bivalency for potent TNFα-neutralizing activity and ALB8 for long serum half-life. [Methods] Recombinant proteins of OZR and its partial constructs were prepared, and their TNFα-neutralizing activity and mouse serum half-life were evaluated. In addition, in silico structural modeling of TNFα-OZR-HSA complex was conducted to reveal binding mode of OZR, TNFα and HSA. [Results] The importance of TNF30 bivalency for potent TNFα-neutralizing activity and ALB8 for long serum half-life of OZR were verified by in vitro TNFα-neutralizing assays and mouse PK studies of recombinant OZR and its partial constructs. *In silico* structural modeling based on co-crystal structure analyses suggested OZR binds to TNFα trimer via TNF30s and to HSA via ALB8. This was confirmed by OZR maintaining its TNFα-neutralizing activity even with excess HSA. [Conclusion] These results corroborate the potent and sustainable clinical efficacy of OZR observed in RA patients.

P3-016

Similar clinical effectiveness and differential pharmacodynamic changes of immune subsets after treatment with Abatacept or Adalimumab in patients with dual seropositive RA patients in the Phase3 AMPLIFIED trial

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Conflict of interest: Yes

[Objectives] High titers of ACPA and RF and presence of the shared epitope (SE) HLA risk allele were reported to be predictive of an enhanced response of abatacept (ABA) compared with adalimumab (ADA). To determine if the clinical profile of dual seropositivity and SE+ in early RA patients can predict a superior response and better control of immune homeostasis to ABA compared with ADA. [Methods] AMPLIFIED (NCT 00929864) is a phase 3 study of ABA vs ADA in adults with early, ACPA and RF positive, MTX-IR RA patients. The primary endpoint was ACR50 at week 24. Flow cytometry analysis was conducted to investigate the change of immune subsets in peripheral blood. [Results] The ACR50 rate in the SE+ subset at week 24 was 59% with ABA and 60% with ADA. From baseline to week 24, ABA resulted in a greater increase in naive T cells and B cells and Th2 cells whereas ADA resulted in increased levels of Th1 and Th17 cells. [Conclusion] In this study, patients responded well to both ABA and ADA. Despite similar efficacy outcomes, a distinct difference in immune system modulation between ABA and ADA was revealed.

Further investigation is warranted to understand the clinical significance of these findings.

P3-017

A multicenter retrospective study of the efficacy and safety of sarilumab

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Conflict of interest: None

[Objectives] To assess sarilumab (SAR) efficacy and safety in rheumatoid arthritis (RA) patients. [Subjects] SAR has been introduced until September 2023 for the treatment of 118 RA patients at our hospital and affiliated facilities. [Methods] We investigated CDAI, continuation rates and adverse events at weeks 0, 12, 24, and 52 [Results] Average age was 66.1 years, disease duration 11.6 years, and continuation rate 82.0%. SAR was discontinued in 8 cases due to adverse events (e.g., rash, liver dysfunction, tuberculosis) and in 10 cases due to inefficacy. CDAI dropped significantly from 17.6 at baseline to 7.07 at 12 weeks and 6.94 at 52 weeks ($p < 0.05$). MTX was administered to 39 patients (33.0%) at a dose of 7.5 mg/week on average, with no significant differences in CDAI, adverse events, and continuation rates with or without MTX. Among 90 patients (76.3%) who switched from biologics or JAK inhibitors, CDAI improved in both groups (15.43/24.35 baseline to 8.05/3.54 at 52 weeks), with greater improvement in the naive group ($p < 0.05$). RF status did not affect efficacy. In 44 glucocorticoid users (37.3%), prednisolone dose fell from 4.7 mg/day to 2.1 mg/day ($p < 0.05$). [Conclusion] SAR reduced disease activity, lowered GC use, and was effective without MTX.

P3-018

Poor prognostic factors in rheumatoid arthritis patients under treatment with SAR

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Conflict of interest: Yes

[Objectives] Patient background of sarilumab (SAR)-treated rheumatoid arthritis (RA) patients at the time of SAR induction was compared. [Methods] Patients who received SAR of whom 45 were eligible for analysis, were classified into three groups: good progress group: 32 patients, poor progress group: 7 patients, and adverse event group: 6 patients. Patient background (age, gender, duration of RA, rheumatoid factor (RF) positivity rate and RF level, anti-CCP antibody (ACPA) positivity rate and ACPA level, use of bDMARD before SAR, use of concomitant methotrexate (MTX) or not, and dose of MTX, concomitant use of prednisolone (PSL), and dose of PSL were evaluated. [Results] The poor progress group had a higher rate of concomitant PSL (85.7% vs. 34.4%, $p=0.03$) and a higher SDAI value at the start of SAR administration (25.2 vs. 14.8, $p=0.02$) than the good progress group. No significant differences were observed in other parameters. Of the 6 patients in the adverse event group, 3 had injection site reactions, 1 had severe infection, 1 had skin rash, and 1 had interstitial pneumonia. [Conclusion] Concomitant PSL or high SDAI at the start of SAR may be a poor predictor at 12 months. Patients with a history of allergy prior to SAR should be alert for adverse events.

P3-019

Changes in Prescribing and Disease Activity After Sarilumab Supply Stops and Resumes

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Conflict of interest: Yes

[Objectives] To investigate the judgment and prescribing behavior of physicians in cases where patients using sarilumab were forced to change their medication due to a supply shortage, and whether measures were taken to prevent worsening of disease activity, and to examine changes in disease activity after the change. [Methods] Patients with rheumatoid arthritis who visited the Department of Rheumatology, Daido Hospital, between February and May 2024 and were prescribed sarilumab were selected, and the type of drug, concomitant medications, history of IL-6 inhibitor administration, measures in case of re-administration, and disease activity before and after the change in administration were examined. [Results] Thirty-nine patients received sarilumab during the same period. All patients underwent a drug change, with 31 changing to tocilizumab, 5 to a JAK inhibitor, and 3 to a drug withdrawal. 20 of the 39 patients resumed sarilumab after resumption of supply, and the reasons for resumption included worsening disease activity and ease of use of the device. [Conclusion] After sarilumab supply was stopped, patients often switched to another IL-6 inhibitor, Tocilizumab, and about half of them resumed sarilumab again because of worsening disease activity after supply.

P3-020

Analysis of cases of ozoralizumab administered to patients with rheumatoid arthritis at our institution

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Conflict of interest: None

[Objectives] We evaluated the efficacy of ozoralizumab in cases in which it was administered to treat rheumatoid arthritis at our hospital. [Methods] We examined 12 cases in which ozoralizumab was injected in the Rheumatology Department of our hospital between December 1, 2022 and September 30, 2024. Statistical analysis was performed using Microsoft Excel. [Results] Eleven of the 12 cases (92%) were women. The median values for each patient were age 64 years (range 53-81), 15.5 years with RA (1-40), anti-CCP antibody (ACPA) titer 81.65 U/mL (0.5-1040), DAS28-ESR 4.43 (0.49-7.39), DAS28-CRP 4.075 (0.97-6.3), SDAI 15.68 (0.02-28.88), and CDAI 12.4 (0-47). Methotrexate (MTX) was used in 67% of patients, with a median dose of 9 mg/w (4-12 mg). Prednisolone (PSL) was used in 33% of patients, with a median dose of 2.5 mg/day (1-4 mg/day). The rate of ozoralizumab continuation during the observation period was 67%. Ozoralizumab was discontinued in 4 of the 12 cases, with the reasons being ineffectiveness in 2 cases, side effects in 1 case, and economic reasons in 1 case. Side effects that led to discontinuation of administration included diarrhea and skin rash. [Conclusion] Ozoralizumab may be effective in cases of long-term, treatment-resistant rheumatoid arthritis.

P3-021

The efficacy of upadacitinib in three patients with difficult to treat rheumatoid arthritis

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Conflict of interest: Yes

Objectives We report three cases of rheumatoid arthritis (RA) patients who had been refractory to multiple biologic agents and who were successfully treated by switching to Upadacitinib (Upa). Case 1: A 67-year-old man with stage IV, class2 disease for 18.5 years. He was treated with etanercept (ETN), tocilizumab (TCZ) and sarilumab, but switched to Upa after secondary failure. He was treated with upa 15 mg/day in combination with anti-rheumatic drugs (DMARD) and steroids (PSL), and is doing well. Case 2: A 67-year-old woman with stage IV, class2 disease for 37 years. She was treated with infliximab, TCZ, ETN, and ETN-BS, but switched to UpA due to worsening disease activity and is doing well. Case 3: A 73-year-old woman with stage III, class2 disease for 15 years. ETN and TCZ were secondarily ineffective, and peficitinib and baricitinib were discontinued due to side effects. He was treated with Upa 7.5 mg/day un-

der DMARD and PSL combination and is doing well Conclusion Although the efficacy of treatment with Upa in patients with inadequate response to bioeffectiveness has been reported, a good long-term therapeutic effect was obtained even in patients with multiple drug ineffectiveness.

P3-022

Efficacy and safety of switch therapy from b/tsDMARDs to ozoralizumab for rheumatoid arthritis patients in real clinical practice

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Conflict of interest: None

[Objectives] Ozoralizumab (OZR), a new structure as a next-generation antibody for TNF inhibitors. In this study, we report the usefulness and safety of 27 patients who switched from b/tsDMARDs to OZR. [Methods] 27 patients who visited our clinic from December 2022 to September 2024 and switched from b/tsDMARDs to OZR were included. The efficacy was evaluated by DAS28-CRP, SDAI, and CDAI, and the safety was evaluated by the incidence of adverse events. [Results] The mean age was 70.1 years, and the number of patients using OZR in our hospital was 36 (including 9 bionaive patients), 27 of whom switched from b/tsDMARDs to OZR. The continuation rate of patients switched from b/tsDMARDs to OZR was 74.1% (20/27). The number of patients who switched to b/tsDMARDs was 12 for one agent, 5 for two agents, and 10 for three or more agents. Six patients had a history of using tsDMARDs. Safety: 5 patients discontinued due to inadequate efficacy, 2/36 (5.5%) of OZR users and 2/27 (7.4%) of switchers experienced adverse events (skin rash, 1). In safety, 2/27 (7.4%) of OZR users experienced adverse events (skin rash in 1, psoriasis in 1), and treatment was discontinued. [Conclusion] The results suggest that the switch from b/tsDMARDs to OZR is effective.

P3-023

Report on Four Cases of Reduced Disease Activity Following a Successful Switch to a Subsequent Etanercept Biosimilar from the Prior Etanercept for the Treatment of Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of etanercept biosimilar (ETN-BS) 50 mg/w after switching from etanercept (ETN-RP) 25 mg/w or less to ETN-BS 50 mg/w in real-world clinical practice. [Methods] This was a single-center, single-arm, prospective, interventional study conducted in RA patients. The primary endpoint was ΔDAS28-ESR at 24 w. Secondary endpoints included functional efficacy and structural efficacy. Safety was also evaluated. [Results] Four patients were able to switch to a higher dose of ETN-BS. The mean ΔDAS28-ESR at 24 w was -1.78 ± 0.51, and disease activity decreased in all patients. HAQ decreased and EQ-5D achieved and maintained functional remission. There were no anti-drug antibodies. Total Sharp Score and PD method score increased. In the safety evaluation, there were no serious adverse events that required discontinuation of the drug. ETN-BS 50 mg/w was shown to be able to reduce disease activity while providing an economic benefit to patients. [Conclusion] The clinical and functional benefit of ETN-BS 50 mg/w was suggested when the dose was increased from ETN-RP 25 mg/w to ETN-BS 50 mg/w and continued for 52 w, and we believe that increasing the dose of ETN-BS is a treatment proposal that is also economically beneficial.

P3-024

Examination of the continuation rate of b/tsDMARDs in rheumatoid arthritis with interstitial lung disease: Analysis using the Kansai multicenter ANSWER cohort

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Conflict of interest: None

Objective: Reports on the continuation rates of b/tsDMARDs in rheumatoid arthritis (RA) with interstitial lung disease (ILD) are limited. This study examined the continuation rates of b/tsDMARDs in RA patients with ILD in the ANSWER cohort. Methods: The subjects included 1823 b/tsDMARDs-naïve RA. Drug continuation rates and the hazard ratio (HR) for discontinuation were evaluated. The evaluation periods were 6 months post-initiation (primary inefficacy) and 6 months to 5 years (secondary inefficacy). Results: Ratios and median values: 20.5% male, age 52 years, disease duration 48 months, CDAI 14.5, ILD+ group 10.6%. The ILD+ group was older, with longer disease duration and higher seropositivity, and KL-6 levels. There was no difference in the overall drug continuation rate between patients with and without ILD, but the difference for anti-IL-6 drugs for first 6 months and anti-TNF drugs from 6 months to 5 years was significant respectively (p=0.0022*, p=0.0040*). In the ILD+ group, the discontinuation HR for above anti-IL-6 drugs and anti-TNF drugs discontinuation was 3.81 (p=0.0020*), and 2.03 (p=0.0144*) respectively. Conclusion: RA patients with ILD had higher drug discontinuation rates due to primary inefficacy with IL-6 inhibitors and secondary inefficacy with TNF inhibitors.

P3-025

15-year retention rate and prognosis of etanercept in rheumatoid arthritis

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Conflict of interest: None

[Objectives] Biologics are effective in the treatment of rheumatoid arthritis (RA), but there are cases where it is difficult to continue in the long term. We investigated the long-term retention rate and prognosis of etanercept (ETN) in patients with RA. [Methods] We included 166 patients with RA who started ETN at our hospital between 2005 and March 2024. We also evaluated the continuation rate divided into three groups by the year of initiaton. We also examined the prognosis of 55 patients who had been on the drug for more than 15 years. [Results] The overall 15-year continuation rate was 37%, and 19 of the patients who started treatment by 2009 actually continued ETN at our hospital. Patients who continued at 15 years with ETNs were significantly younger at initiation than those who discontinued (mean age 48.6±13.3 vs. 58.3±13.1, p=0.01), but there was no difference in other patient backgrounds. The mean age at death was 72.0 years, and the causes of death were 6 infectious diseases, 5 malignant tumors, 2 respiratory diseases, and 1 renal failure. [Conclusion] The 15-year ETN retention rate was relatively good at 37%. After 15 years, 41% of patients continued to visit the hospital, which was a relatively large number of cases, including those that stopped ETN.

P3-026

Efficacy and corticosteroid dose reduction effect of sarilumab in patients with 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 sarilumab (SAR) in patients with rheumatoid arthritis (RA) in clinical practice. [Methods] This retrospective observational study enrolled RA patients who received SAR from January 2019 to March 2023. The clinical efficacy of SAR was examined up to 52w in MTX-IR group, Bio-IR group, SAR with MTX group, SAR without MTX group. The rate and dose of corticosteroid were also evaluated respectively. [Result] This study was comprised consecutive 44 patients with RA (20 in MTX-IR, 24 in Bio-IR, 20 in SAR with MTX, and 24 in SAR without MTX). CDAI remission rate at 52w was 30% in MTX-IR, 33% in Bio-IR, 30% in SAR with MTX group, and 33% in SAR without MTX group, respectively. The rate and dose of corticosteroid were lower at 52w compared with at the baseline (85% vs 40%, 10.2 vs 3.8 mg/day in MTX-IR, 75% vs 35%, 6.0 vs 3.8 mg/day in Bio-IR, 65% vs 33.3%, 7.4 vs 2.9 mg/day in SAR with MTX, 91.7% vs 42.9%, 8.4 vs 4.7 mg/day in SAR without MTX). The 34.3% (12/35) of patients treated with corticosteroid could suspend corticosteroid at 52w. [Conclusion] SAR was effective in the RA patients of MTX-IR, Bio-IR, with or without MTX. It is possible to treat more safely by reducing the dose of corticosteroid using SAR.

P3-027

Reactivation of Epstein-Barr virus (EBV) with persistent elevation of VCA-IgM antibodies and EBV-DNA during methotrexate (MTX) and golimumab (GLM) combination therapy in rheumatoid arthritis (RA): A case report of successful biologic reintroduction

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Conflict of interest: None

Reactivation of EBV during RA therapy can present with fever and lymphadenopathy, necessitating differentiation from lymphoproliferative disorders (LPD). This case involves a man in his 60s with anti-CCP-positive early RA who achieved remission with MTX and GLM. However, 1.4 years post-treatment, he developed persistent fever, night sweats, and polyarthralgia. Lab findings showed leukocytosis (19,100/μL) with atypical CD8-predominant lymphocytosis, confirming EBV reactivation (EBV-DNA 4.9, VCA-IgM 1.3, VCA-IgG 1:160, EBNA). CT revealed axillary and abdominal lymphadenopathy, suggesting possible LPD. MTX and GLM discontinuation resolved the lymphadenopathy and atypical lymphocytes in 2 months, although VCA-IgM positivity and elevated EBV-DNA persisted. Two months post-cessation, RA symptoms relapsed; treatment with prednisolone, bucillamine, and sulfasalazine was insufficient. With EBV-DNA at 2.5 and VCA-IgM 0.6, GLM was reintroduced, achieving RA remission without signs of EBV reactivation. This case highlights the feasibility of biologic therapy reintroduction under persistent VCA-IgM and EBV-DNA positivity.

P3-028

A study of cases of prolonged sarilumab dosing interval in our hospital

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Conflict of interest: None

[Objective] To examine the treatment efficacy and background of cases with rheumatoid arthritis who extended the interval of sarilumab (SAR) at our hospital. [Methods] Subjects are 29 cases with extended interval in 86 cases who began SAR from June 2018 to May 2024. Disease activity after the start of extended interval was surveyed in 27 cases who could keep the interval for at least 2 months. They were divided into 2 groups: 16 cases (Group A) who could keep the extended interval and 11 cases (Group B) who returned the interval to the normal. Comparison of disease activity and background was surveyed at baseline and 3 months. [Results] The overall DAS28-CRP/CDAI (median) was 1.17/1.5 at baseline and 1.19/1.8 at 3 months (p=0.44/0.61). In the 2-group comparison, DAS28-CRP/CDAI was as follows; group A vs B: baseline 1.12/1.05 vs 1.59/2.9, 3 months 1.13/1.1 vs 2.67/5.9. The physician VAS and DAS28-CRP were significantly worse in group B at 3 months (p=0.03/0.03). The interval was extended due to SAR shipment stoppage in more cases of group B (p=0.04) and group A had lower WBC/neutrophil counts at baseline (p<0.02/0.01). [Conclusion] It was suggested that the interval could be extended in cases with feature of IL-6 inhibition, but this was a small scale study and more cases will be needed.

P3-029

Treatment Outcomes of Ozoralizumab for Rheumatoid Arthritis at Our Hospital -Including Effects on Foot Symptoms-

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Conflict of interest: None

[Objectives] Ozoralizumab (OZR), is expected to have favorable migration to sites of inflammation due to its nanobody structure. We evaluated the treatment outcomes of OZR in patients with rheumatoid arthritis (RA) at our hospital, including its effects on foot symptoms. [Methods] We retrospectively investigated the medical records of 20 RA patients who started OZR treatment between January 2023 and April 2024, focusing on patient backgrounds, changes in disease activity, OZR continuation rate, reasons for discontinuation, and evaluation of foot symptoms using the SAFE-Q. [Results] The average age was 62.6 years, with 90% of the patients being female, and the RA duration was 145 months. The dosage and administration rates of methotrexate (MTX) and prednisolone (PSL) were 8.4 mg/week (80%) for MTX, and 4.83 mg/day (45%) for PSL at initiation. The average DAS28-ESR improved from 5.1 at initiation to 3.2 after 6 months. Similarly, the average SDAI improved from 17.1 at initiation to 3.5 after 6 months. Fourteen patients (70%) continued OZR treatment for more than 6 months, of whom 11 (79%) reported foot symptoms, with improvements the SAFE-Q scores. [Conclusion] OZR is not only effective for the treatment of RA but may also be beneficial in improving foot symptoms.

P3-030

Rheumatoid arthritis treatment at our hospital with an aging patient population

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Conflict of interest: None

[Objectives] To investigate rheumatoid arthritis (RA) treatment patterns in our aging patient population. [Methods] We analyzed patient demographics and prescription data for MTX and b/tsDMARDs initiated from January 2011 to March 2024. [Results] Mean patient age was 70.7 years, with 72.1% aged >65 years. As of January 2024, MTX and b/ts DMARDs utilization rates were 48.4% and 41.4%, respectively. MTX usage decreased in patients over 70, while b/tsDMARDs maintained high utilization in elderly patients. In total, 769 b/tsDMARDs were prescribed to 421 patients, with patient population showing an aging trend. TNF-alpha inhibitors showed the highest MTX combination rate (57.2%). As first-line therapy, TNF-alpha inhibitors were selected in >60% of cases with MTX combination, while non-TNF-alpha inhibitors or JAK inhibitors were chosen in >60% of MTX-naive cases. Drug retention rates were similar across all agents. [Conclusion] Despite low MTX utilization, prescriptions for non-TNF-alpha inhibitors and JAK inhibitors are increasing, with retention rates comparable to TNF-alpha inhibitors. The aging of patients using b/tsDMARDs raises concerns about infection risks and other complications.

P3-031

A report of rheumatoid arthritis patients using ozoralizumab without methotrexate at our hospital

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Conflict of interest: None

[Objectives] A phase III clinical trial (NATSUZORA Trial) has shown that ozoralizumab is effective in the treatment of rheumatoid arthritis without methotrexate (MTX). We report on seven patients treated with ozoralizumab without MTX at our hospital. [Methods] Seven patients with rheumatoid arthritis treated at our hospital were reviewed. There were 3 males and 4 females, mean age 76.6 (66-81) years, and mean time to ozolalizumab administration was 21.2 (4.8-43.0) years. [Results] Steroids were used in 3 patients, and the mean dose of prednisolone was 6.7 mg (5-10) mg. One patient was naïve, one patient was on the second drug, and five patients were on the third drug. The naïve patient was refractory to anti-rheumatic drugs and requested subcutaneous injection every 4 weeks. The reasons for switching were reduced efficacy for pain and hyperCRPemia. No significant side effects were observed. [Conclusion] We report and discuss our experience with ozoralizumab, including background, efficacy, etc., in patients treated with ozoralizumab at our institution.

P3-032

Background and clinical course of rheumatoid arthritis patients introduced ozoralizumab in our department

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Conflict of interest: None

[Objectives] Ozoralizumab (OZR) is an anti-TNFα agent approved for the novel treatment of rheumatoid arthritis. We report our experience with OZR in our laboratory. [Methods] We evaluated the backgrounds of 14 patients who received OZR after February 2023, and the changes in each disease activity index before and 12 weeks after the introduction of OZR. [Results] The background of the 14 patients was 9 females, age 67.5 (60.75-71.75) years [median (IQR)], disease duration 50 (6.25-150.75) months, 9 positive for RF, 9 positive for anti-CCP antibody, methotrexate 10 (6.6-11.5) mg/week, and concomitant medication salazosulfapyridine in 5 cases, iguratimod in 5 cases, and glucorticoids in 1 case. There were 3 cases of switch from biologics and JAK inhibitors. The continuation rate at 12 weeks of OZR induction was 78.5%, with 2 patients discontinuing due to primary ineffectiveness and 1 patient discontinuing due to skin rash. The change in disease activity indices before induction and at 12 weeks were CDAI: 22.1±6.8 to 13.4±10.5 (p=0.022), DAS-CRP: 4.41±0.95 to 3.17±1.53 (p=0.022), mHAQ: 1.193±0.752 to 0.920±0.797 (p=0.057). The CDAI and DAS-CRP showed a significant decrease. [Conclusion] In our experience, we observed improvement in disease activity in many cases in which OZR was introduced.

P3-033

Short-term Outcome of Ozoralizumab in Rheumatoid Arthritis at Our Clinic

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Conflict of interest: None

Introduction: We present short-term treatment outcomes of Ozoralizumab (OZR) in rheumatoid arthritis (RA) patients treated at our clinic. **Subjects:** Seven patients administered OZR 30 mg from April 2023 onward were included. One male case, 7 female cases. The mean age was 80 years (75-93 years), with the mean treatment duration of 11.8 months (4 months-1 year and 6 months). Among these, two patients received OZR with methotrexate (MTX), one with MTX and mizoribine, while four patients were on OZR monotherapy. All had previously been treated by other biologic agents: five patients switched from a state of remission, one due to an allergic reaction, and one due to symptom worsening. **Results:** At the last follow-up, the DAS28 (ESR) score averaged 2.04 (0.97-2.84). Complications observed, all of which were manageable, allowing continuation of treatment. Four patients sustained remission with extended dosing intervals due to sustained symptom remission. **Conclusion:** All patients switching from other biologic agents achieved remission, indicating the potential efficacy of OZR monotherapy. Furthermore, remission was maintained in some patients with prolonged OZR dosing intervals, highlighting OZR's possible role in sustained RA management with extended dosing flexibility.

P3-034

Experience with ozoralizumab in patients aged 70 years or older with rheumatoid arthritis

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Conflict of interest: None

[Objectives] We report 9 cases of RA patients aged 70 years or older who were treated with ozoralizumab (OZR). [Methods] Retrospective survey was conducted to investigate patient background, disease activity at the start of treatment, 4 weeks after treatment, and 12 weeks after treatment, continuaction rate, and safety. [Cases] 9 female patients. Mean age 79.3 years, mean disease duration 25 years, mean weight 51.7 kg, all seropositive. MTX was not used in any cases. 2 cases used PSL, All had history of use biological therapy. Mean DAS28-ESR 4.4, mean CRP 1.65 mg/dl, mean ESR 41.3 mm/h, mean MMP-3 276.6 ng/ml. [Results] Mean treatment period 13.6 months. 1 cases of ineffective, 3 cases were in remission and 5 cases had low disease activity 4 weeks after, 7 cases were in remission and 1 case had low disease activity 12 weeks after. Continuation rate up to 12 weeks after was 88.8%, No side effects at 12 weeks after. Weakening of efficacy was not observed in 7 patients who used more than 40 weeks. 2 patients who were using PSL were able to discontinue. [Conclusion] OZR was effective regardless of previous treatment. Efficacy was rapid and continuation was high. Secondary Invalid was not observed, but further follow-up observation is considered necessary.

P3-035

Investigation of the Relationship between Bone Density, Lifestyle and Calcium Intake in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] This study aims to evaluate and compare the relationship between bone mineral density (BMD), lifestyle, and calcium intake in RA patients. [Methods] The study included female outpatients aged 70 and older who underwent BMD testing and completed questionnaires at our hospital, consisting of 68 RA patients (RA group) and 109 non-RA patients (non-RA group). The questionnaire assessed fracture risk factors, lifestyle, dietary preferences, and calcium intake. [Results] Compared to the non-RA group, the RA group showed a significant decrease in femoral BMD, a higher rate of oral GC, less frequent back pain, and fewer instances of regular exercise. In the osteoporosis subgroup, body mass index (BMI) was significantly lower, and there was a higher prevalence of cancer history compared to the non-osteoporosis subgroup, but no significant difference was found in calcium intake. [Conclusions] RA patients showed lower BMD, more GC medications, and less back pain, alongside reduced regular exercise, potentially due to joint pain and deformities. No clear relationship with calcium intake or other lifestyle habits was observed, but should be investigated in further case series.

P3-036

The Relationship Between Sleep Disorders and Fall Risk in Patients with Primary Osteoporosis

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Conflict of interest: None

Objective: To investigate the association between sleep patterns and fall risk in patients with primary osteoporosis (OP). Methods: Forty-four OP patients (mean age 71.8±11.0 years, 3 males/41 females) were included. Fall history within the past year was assessed using a questionnaire. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). Additionally, the Falls Score questionnaire developed by the Japan Geriatrics Society was administered. Results: 36.3% (16 patients) reported a history of falls. The incidence of falls exhibited a U-shaped curve relative to sleep duration, with the lowest rate of 7.7% (1/13 patients) in the 6-hour sleep group, followed by 37.5% (3/8) in the ≦5-hour group, 28.6% (2/7) in the 7-hour group, and 62.5% (10/16) in the ≧8-hour group. Multivariate analysis, including age, sex, BMI, eGFR, fall score, and PSQI subscale C7 (daytime dysfunction) as independent variables, revealed that only C7 was significantly associated with fall risk. The majority of falls (75%, 12/16) occurred during daytime hours. Conclusion: Both short and long sleepers are presumed to have some form of sleep disorder. Decreased alertness due to daytime sleepiness may contribute to an increased risk of falls in these patients with primary OP.

P3-037

Deepening Remission Prevents Vertebral Fractures by Preserving Bone Quality

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Conflict of interest: None

[Objective] Serum pentosidine levels, a marker of bone quality, increase over time even after remission in patients with rheumatoid arthritis, but this rise is suppressed by b/tsDMARDs usage. It is unclear whether these changes relate to fragility fractures. We investigated the correlation between b/tsDMARDs use and the incidence of fragility fractures. [Methods] Patients in remission based on DAS28-CRP scores were used to evaluate bone turnover and matrix markers and underwent thoracolumbar spine radiography. They were classified into non-b/tsDMARDs and b/tsDMARDs groups. Various parameters and the prevalence of vertebral fractures were compared between the groups. [Results] Serum pentosidine levels were significantly lower in the b/tsDMARDs group. Fewer patients in this group exhibited aortic calcification affecting two or more vertebrae on radiographs. The prevalence of vertebral fractures was significantly lower in the b/tsDMARDs group. [Conclusions] Even in patients who achieved remission, elevated serum pentosidine levels were associated with impaired bone quality and an increased risk of fragility fractures. The use of b/tsDMARDs may exert a bone-protective effect by preventing the rise in serum pentosidine levels.

P3-038

A case of rheumatoid arthritis with multiple fragility fractures due to vitamin D deficiency after gastrectomy for gastric cancer and osteoporosis due to androgen deprivation therapy for prostate cancer

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Conflict of interest: None

A 74-year-old man who had undergone gastrectomy for gastric cancer had been treated with androgen deprivation therapy (ADT) for prostate cancer for 10 years and methotrexate and iguratimod for rheumatoid arthritis (RA) for 4 years. He complained of perianal pain combined with alkaline phosphatase elevation and next both ankle joint pains. A contrast MRI of the left ankle revealed fractures of the distal tibia, fibula, and calcaneus. Subsequently, fragility fractures also appeared in the right knee and right ankle. The serum 25 (OH) vitamin D (VitD) was significantly decrease. It has been reported that the serum 25 (OH) VitD is decreased in patients with gastrectomy for gastric cancer (Gastric Cancer 2007), and the fracture rate is elevated in patients with prostate cancer who received ADT compared to those who did not receive the treatment (19.4% vs 12.6%) (NEJM 2005). In this case, we thought that the multiple fragility fractures were due to VitD deficiency after gastrectomy for gastric cancer and osteoporosis due to ADT for prostate cancer. After treatment with natural VitD, calcium, and denosumab successfully prevented the new fractures. RA patients with bone metabolic disorders may develop fragility fractures, so it is important to carefully management for osteoporosis.

P3-039

Increasing Fracture Incidence in Japanese Patients with Rheumatoid Arthritis: A Longitudinal Study of the IORRA Cohort (2011-2023)

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Conflict of interest: None

[Objectives] This study examined fracture incidence in rheumatoid arthritis (RA) patients over 13 years, from 2011 to 2023. [Methods] 10,257 RA patients from the IORRA cohort were included, and self-reported fracture data were collected every 6 months. The fracture incidence was standardized by sex, age, and DAS28, and analyzed every 2 years. [Results] From 2011 to 2023, DAS28 remission rate increased from 41.1% to 64.5%, bDMARD use from 14.8% to 41.2%, osteoporosis medication use from 31.3% to 38.6%, and glucocorticoid use decreased from 37.8% to 22.2%. The incidence of all and non-vertebral fractures increased from 44.7 and 34.5 per 1,000 person-years in 2011 to 50.8 and 42.4 in 2023. Using 2023 as the reference, the standardized incidence ratios (SIRs) for all and non-vertebral fractures were: 2011-2012, 0.80 (95% CI 0.73-0.88) and 0.73 (95% CI 0.66-0.80); 2013-2014, 0.83 (95% CI 0.75-0.90) and 0.76 (95% CI 0.69-0.84); 2015-2016, 0.86 (95% CI 0.79-0.94) and 0.79 (95% CI 0.71-0.87); 2017-2018, 0.90 (95% CI 0.82-0.99) and 0.86 (95% CI 0.77-0.95); 2019-2020, 0.92 (95% CI 0.82-1.04) and 0.89 (95% CI 0.77-1.01); 2021-2022, 1.00 (95% CI 0.88-1.13) and 0.98 (95% CI 0.86-1.12). [Conclusion] Despite advancements in RA management over 13 years, the fracture incidence may have increased.

P3-040

Non-adherence to the 2023 Glucocorticoid-Induced Osteoporosis Guidelines in Japanese Patients with Rheumatoid Arthritis: A Cross-Sectional Study Using the IORRA Cohort

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Conflict of interest: None

[Objectives] This study applies the 2023 guidelines for managing glucocorticoid-induced osteoporosis to rheumatoid arthritis (RA) patients, examining the proportion of non-adherence and associated factors. [Methods] We conducted a cross-sectional analysis of 2,047 RA patients from the 47th IORRA cohort study in 2023. Adherence to the guidelines was evaluated without considering bone mineral density (BMD). Factors related to non-adherence were analyzed by multivariate analysis. [Results] Among the RA patients, 454 (22.2%) used glucocorticoids (GC). Of these, 343 (75.6%) scored ≧ 3, classifying them as the treatment group. In this group, 125 patients (36.4%) did not follow the recommended medications following the guidelines. Comparisons between adherence and non-adherence groups showed the non-adherence group had significantly more males ($P = 0.0085$), higher BMI ($P = 0.018$), and lower J-HAQ scores ($P = 0.035$). Multivariate analysis indicated that male sex was significantly

associated with non-adherence (OR 2.1, 95% CI 1.03-4.23, P = 0.04). [Conclusions] While 75.6% of RA patients using GC were in the treatment group according to the guidelines without BMD, 36.4% of the patients were not using the recommended medications. Males may be associated with non-adherence to the guidelines.

P3-041

A Case of Lupus Nephritis with TMA Achieving Remission by Plasma Exchange

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Conflict of interest: None

[Case] A man in his 20s developed fever, dyspnea, and edema, and visited A hospital. He was later transferred to our hospital and diagnosed with SLE, based on renal dysfunction, urinary abnormalities, pancytopenia, positive anti-dsDNA antibody and hypocomplementemia. Findings of schistocyte and hemolytic anemia suggested secondary TMA or acquired TTP due to SLE. Hemodialysis and plasma exchange (PE) were initiated. Additional treatment including mPSL pulse therapy, PSL, HCQ and MMF were started. The patient was negative for APS-related autoantibodies and ADAMTS13 inhibition, suggesting secondary TMA as the main etiology. By day 16, anti-dsDNA antibody levels normalized, yet renal dysfunction and anemia persisted. Further treatment with RTX and BLM were initiated. Renal function improved and hemodialysis was discontinued on day 40. However, nephrotic syndrome became apparent as urine output increased. Despite additional mPSL pulse therapy, severe proteinuria persisted. Additional PE sessions were performed. Proteinuria, schistocyte, and anemia gradually improved, allowing discharge on day 87. [Discussion] The combination of immunosuppressive drugs with PE may have eliminated residual autoantibodies which led to remission of secondary TMA.

P3-042

A study of the treatment course and electroencephalogram (EEG) evaluation of cases of elderly onset neuropsychiatric systemic lupus erythematosus (EONPSLE) with drug therapy and rehabilitation

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Conflict of interest: None

[Background] The treatment for NPSLE is potent immunosuppressive therapy. There are various difficulties in the treatment of elderly patients because their activity of daily living has already declined, and rehabilitation is required. We report three cases in which drug therapy was continued in EONPSLE, rehabilitation was strengthened, and consciousness disorder was evaluated using EEG. [cases] 56-year-old women with lupus nephritis and cerebral infarction developed tonic-chronic convulsive seizure, 67-year-old women with SLE and left caudate hemorrhage developed fever and impaired consciousness, and 72-year-old women with cognitive decline and difficulty walking developed convulsions and impaired consciousness. They diagnosed NPSLE due to elevated cerebrospinal fluid IL-6 levels, high activities of SLE and no abnormalities in head MRI. [Result] In the 1st one the level of consciousness and EEG findings improved after rituximab therapy. In the 2nd one, the level of consciousness did not change but EEG findings slightly worsened. And in the last one the level of consciousness improved and the EEG findings slightly improved. [Conclusion] For EONPSLE, drug therapy combined with rehabilitation is effective, and EEG is useful for monitoring the progress of impaired consciousness.

P3-043

Retrospective Analysis of Relapse and Treatment Status Associated with Glucocorticoid Tapering in Patients with SLE Attending Our Hospital

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Conflict of interest: None

[Objectives] This study retrospectively analyzed the feasibility of GC tapering, the disease activity, relapses, and treatment status in SLE patients treated at our hospital. [Methods] The subjects were: 1) SLE patients who visited our hospital after October 2023, b) those with a history of GC administration for more than three months within the past five years, and 3) those who achieved LLDAS5 and opted for GC tapering. The clinical and serological indicators of GC tapering and clinical outcomes over the past five years were retrospectively evaluated. [Results] The study included 75 patients. The mean GC doses were 1.3 mg/day in PSL equivalents and the GC discontinuation rate was 52%. The median annual dose reduction was 0.9 mg/day in PSL equivalents. The most recent LLDAS5 and 2021DORIS achievement rates were 96% and 73%, respectively. During the period, 24 patients (32%) required intensification of therapy, and 4 of them were hospitalized. [Discussion] Our analysis and a literature review suggested that risk factors for relapse include the lack of concomitant use of HCQ, the lack of concomitant use of IS or bio, a PSL dose of less than 3 mg/day, failure to achieve 2021DORIS, and worsening serological findings. Particular attention is needed when multiple risk factors are present.

P3-044

Investigations of the Certified Pharmacist by Japan Rheumatism Foundation Intervention with Hydroxychloroquine (HCQ) for SLE - Discontinuation Cases

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Conflict of interest: None

[Objectives] HCQ improves disease activity and mortality, but retinal damage by accumulation and risk of recurrence by discontinuation is problematic. Here we investigated the characteristics of the discontinuation cases, which were observed in our report of 65th JCR Meeting, of patients with high-dose HCQ or renal dysfunction. [Methods] We retrospectively investigated the reason for discontinuation of HCQ, daily/cumulative doses, concomitant drugs of patients whose HCQ was discontinued as of December 2023. [Results] HCQ was discontinued in 27 cases, due to adverse events (2 cases), remission (5 cases), transfer to another hospital (14 cases). The median duration of HCQ prescription was 1650 days, the cumulative dose was 330 g, and SLEDAI scores improved at 12 months after discontinuation. [Conclusion] Although there were no HCQ discontinuation due to allergiy, it is important to consider desensitization therapy for patients with allergic symptoms and to propose not to avoid discontinuation. It is also important to provide safe treatment without overlooking the overdosage. In addition, I would like to actively participate in treatment planning through follow-up of discontinued cases and contribute to the improvement of outcomes as the Certified Pharmacist by Japan Rheumatism Foundation.

P3-045

Three Cases of Initial-Onset SLE Managed Solely with Hydroxychloroquine

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Conflict of interest: None

[Background] Hydroxychloroquine (HCQ) was approved in Japan in 2015 and is now recommended as a baseline treatment for SLE. Here, we report three cases of SLE successfully managed with HCQ monotherapy,

maintaining stable disease without glucocorticoid use. [Case 1] A 34-year-old female, referred in April 2022, was diagnosed with SLE (ANA 640, anti-dsDNA, low complement, leukopenia, thrombocytopenia, joint pain), Sjögren's syndrome, and antiphospholipid antibodies. HCQ was introduced in June 2022. Her pregnancy after embryo transfer in April 2023 was stable, and her disease has remained stable for 2 years and 6 months. [Case 2] A 49-year-old female presented with fever and erythema nodosum in March 2023 and was diagnosed with SLE (ANA 5120, anti-Sm, anti-RNP, low complement, leukopenia, thrombocytopenia, joint pain, alopecia) and Sjögren's syndrome. HCQ was initiated in July 2023, maintaining stability for 1 year and 3 months. [Case 3] A 38-year-old male with joint pain and positive ANA was diagnosed with SLE in August 2023. Due to a worsening rash, HCQ was started in April 2024, with stable disease for 6 months. [Clinical Significance] Early HCQ in mild SLE without severe systemic symptoms or organ involvement may prevent disease progression and reduce glucocorticoid use.

P3-046

Changes of treatment for systemic lupus erythematosus over time in our hospital

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Conflict of interest: None

Objectives: To compare the time course changes of SLE treatment and outcome in our hospital. Methods: We analyzed 36 patients with SLE receiving first remission induction therapy between 2008 and 2012 (group1; male9, 40.8±17.4 years old) and 44 patients receiving first remission induction therapy between 2018 and 2022 (group2; male8, 44.5±17.7 years old). We compared clinical characteristics at the time of remission induction therapy and maintenance therapy. Maintenance therapy was analyzed at 2014 for group1 and at 2024 for group2. Results: Disease activity measured by SLEDAI was significantly higher in group2 at the time of diagnosis. The initial dose of PSL was comparable between the groups, but the concomitant use of immunosuppressive agents was more frequently observed in group2 (38.9% vs. 65.9%, p=0.045). In maintenance therapy, the dose of PSL was significantly lower in group2 (11.7±3.4 vs. 5.7±2.9, p<0.001). SLICC/ACR damage index was lower in group2 (0.69±0.8 vs. 0.35±0.6, p=0.04). The rate of disease flare was comparable between the groups (13.9% vs 4.5%, p=0.071) Conclusion: In recent SLE cases, with a high rate of immunosuppressive agents, the amount of PSL use in the maintenance therapy was reduced, resulting in less accumulation of organ damage.

P3-047

A case of thrombotic microangiopathy (TMA) due to SLE successfully treated with plasma exchange therapy and rituximab (RTX)

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Conflict of interest: Yes

[Present Illness] A 69-year-old woman with SLE and ITP, diagnosed X-14 years ago, was treated with PSL and CyA, though adherence was poor. From the 17th of month Y in year X, she experienced worsening fatigue, leading to impaired mobility on the 22nd and emergency transport. Diagnosed with dehydration, she was advised to see her physician but didn't. On the 24th, she was transported again due to impaired consciousness and hospitalized. Suspecting adrenal insufficiency and SLE exacerbation, steroid pulse therapy began on the 25th. Temporary improvement was followed by severe coagulopathy on the 27th (unmeasurable PT/APTT, low fibrinogen, thrombocytopenia), and TTP was suspected, prompting her transfer for plasma exchange on the 30th. [Course After Admission] Plasma exchange was done thrice, with steroid pulse and 60 mg oral PSL. Consciousness improved rapidly post-therapy. ADAMTS13 activity was 73% with negative antibodies, confirming SLE-related TMA. RTX was initiated due to deterioration under PSL and CyA. Platelets improved, PSL was tapered, and discharge followed. [Discussion] Plasma exchange for SLE-related TMA may help remove cytokines and activated complement, though efficacy is unclear. Severe coagulopathy warranted combined plasma exchange and RTX therapy.

P3-048

Change of therapeutic agents for patients with SLE in a single-center cohort from 2018 to 2024

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Conflict of interest: None

[Objective] We aim to investigate the change of therapeutic agents for patients with SLE and the achievement of GC-free in our hospital. [Methods] The treatment of SLE patients attending our department between 2018 and 2024 was examined retrospectively. [Results] During the 7 years, the number of patients receiving GC decreased from 83% to 36%, and the median prednisolone dose decreased from 5 (2-8) mg/day to 0 (0-2) mg/day. Hydroxychloroquine use increased from 24% to 72%, immunosuppressant use increased from 38% (11/29) to 72% (36/50), and biologic agents use increased from 0% to 22% respectively. GC was discontinued in 29 cases, but not a single relapse was observed (mean observation period 21 months after discontinuation). Two patients received induction therapy without GC use. [Conclusions] During a 7-year period from 2018 to 2024, the number of patients receiving GC and the GC dose have decreased substantially, while those using hydroxychloroquine, immunosuppressants, and biologics have increased. GC is no longer a cornerstone in the treatment of SLE.

P3-049

Eltrombopag treatment was effective for a patient with immune thrombocytopenia secondary to SLE

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Conflict of interest: None

[Background] It had been reported that 10 to 15% of patients with SLE were complicated by immune thrombocytopenia (ITP). Eltrombopag (ETP) is a thrombopoietin receptor agonist which has been used for the treatment of idiopathic thrombocytopenic purpura. We report a case of SLE associated with ITP successfully treated with ETP. [Case] A 29-year-old woman was managed with 10 mg/day of PSL. She showed subcutaneous hemorrhage when her platelet (PLT) count decreased to $0.7x10^4/\mu l$. Since her PLT count did not increase after 30 mg/day of PSL, she admitted to the university hospital. She was diagnosed as ITP secondary to SLE (ITP-SLE) and treated with 50 mg/day of PSL and IVIG, but its effectiveness was transient. She was added 12.5 mg/day of ETP and her PLT count increased to $20x10^4/\mu l$ in two weeks. Her PLT count had been normal range after tapering down of PSL dosage to 40 mg/day, and she had transferred to our hospital. She had achieved response when PSL was tapered to 20 mg/day, then she discharged our hospital. She discontinued ETP seven months later. She had took 13 mg/day of PSL and her PLT count had been kept to $12x10^4/\mu l$. [Clinical Significance] ETP was effective to ITP-SLE. ETP is a viable option for treating severe ITP-SLE.

P3-050

A case of Takayasu's arteritis with ANCA-negative pauci-immune crescentic glomerulonephritis

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Conflict of interest: None

A 44-year-old Japanese man presented to our hospital with chest pain, fever, headache, and cough, which had persisted for seven days. He was initially diagnosed with pleurisy and treated with antimicrobials. However, his fever remained unresponsive until the fourth day, prompting further examination. Blood tests revealed a significantly elevated serum CRP level of 42.8 mg/dL, along with increased fatty tissue density around the aortic arch and left subclavian artery on cervicopelvic contrast-enhanced CT. Additionally, worsening hematuria and proteinuria were noted, leading to a renal biopsy. Pathological findings indicated pauci-immune crescentic glomerulonephritis. The patient was then treated with prednisolone, after which his fever quickly resolved, serum CRP levels normalized, and both proteinuria and hematuria disappeared. Our case is that Takayasu's arteritis complicated by glomerulonephritis. Although Takayasu's arteritis primarily affects the aorta, glomerulonephritis rarely has been reported as an associated complication. It is crucial to consider that Takayasu's arteritis accompanied by abnormal urinalysis findings may be associated with various types of glomerulonephritis.

P3-051

A case of Takayasu arteritis complicated by cranial hypertrophic pachymeningitis

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Conflict of interest: None

70-year-old woman visited the ophthalmologist because of decreased vision in the left eye and double vision. The results of examination showed left optic nerve and abducens nerve disorders. She had been suffering from intermittent left temporal pain and dizziness for the past six months. The brain MRI scan detected thickened dura mater in the left frontal lobe, enlargement of the left optic nerve and thickened extraocular muscle. Based on the findings, she was diagnosed with hypertrophic pachymeningitis (HP). Laboratory findings showed elevated C-reactive protein and erythrocyte sedimentation rate, and human leukocyte antigen B52 positivity. Contrast-enhanced CT revealed thickening of the vessel wall of the ascending aorta, brachiocephalic artery, left common carotid artery, subclavian artery, and descending aorta. She had valve replacement surgery due to severe aortic regurgitation seven years ago and was eventually diagnosed with Takayasu arteritis (TAK). Methylprednisolone pulse therapy was administered, followed by prednisolone 1 mg/kg/day, and eyesight and MRI findings improved. TAK mainly causes inflammation in large vessels, but it has also reported to affect the smaller vessels, such as retina and skin. This case, although rare, shows the relationship between HP and TAK.

P3-052

A case of takayasu arteritis presenting pericardial effusion as initial manifestation

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Conflict of interest: None

[Case Presentation] A 57-year-old woman saw the cardiologist due to pericardial effusion (PE) found by medical check-up eight months ago. A cardiac ultrasound showed moderate volume of PE over the entire circumference, and serum CRP was 0.50 mg/dL. The effusion volume decreased slightly without further intervention. One month before admission, she began to suffer from the recurrent chest pain. A coronary angiography revealed 99% stenosis at the left coronary main trunk (LMT), and catheter intervention was performed. High accumulation at the wall of the ascending aorta, aortic arch and LMT was observed on FDG-PET/CT. She was diagnosed with Takayasu arteritis (TA) and treated with prednisolone of 40 mg (0.6 mg/kg) and tocilizumab of 162 mg per week. The thickening of blood vessel wall improved and the PE disappeared one month later. [Discussion] Unstable angina pectoris developed during follow-up of PE and she was diagnosed with TA. FDG-PET demonstrated inflammation at ascending aorta and LMT, anatomically connected to pericardium. The fluid disappearance after treatment suggested that TA caused PE. In cases of persistent PE and elevated serum CRP, TA should be considered as a differential diagnosis.

P3-053

A case of an elderly woman who developed giant cell arteritis (GCA) while taking tacrolimus (Tac) for rheumatoid arthritis (RA)

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Conflict of interest: None

A 73-year-old woman had a history of treatment for Harada's disease with prednisolone (PSL) and cyclosporine between 202X-10 and 202X-5. And she was diagnosed with seronegative rheumatoid arthritis (RA) in 202X-3 and treated with only tacrolimus (Tac). In June 202X, she presented with a new fever, headache, jaw claudication, and dizziness. The inflammatory response in her blood test was elevated, and her right temporal artery was swollen and tender. Ultrasound and MRI showed thickening of the bilateral temporal artery walls. FDG-PET showed FDG uptake in the temporal artery, the blood vessel walls from the thoracic aorta to the femoral artery, the vertebral spinous processes and the left ischial tuberosity. There was no ischemia in the fundus. She was diagnosed with GCA and treated with PSL 1 mg/kg/day and tocilizumab 162 mg/week. The symptoms improved quickly. The biopsy result of her left temporal artery was also consistent with GCA. This is a very rare case of a patient with RA who was in remission with only Tac, and then developed GCA, so it is important to consider GCA when a new headache develops. And the FDG uptake in the spinous processes and ischial tuberosity on PET-CT was thought to suggest the possibility of polymyalgia rheumatica.

P3-054

A case of ANCA-associated vasculitis with jaw claudication

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Conflict of interest: None

The patient was a man in his 80s with a history of hypertension, diabetes, and prostatic hyperplasia. After farm work in early October of year X, he experienced fatigue, joint pain, morning stiffness, difficulty in opening his mouth despite being able to eat, and jaw claudication, and visited a local hospital on October 11. Palpation showed no abnormalities in the temporal artery. On October 21, he was admitted to our department for further examination and treatment. WBC 15,600/μl, CRP 11.53 mg/dl, and ultrasound examination showed no edema of the superficial temporal artery or dark halo sign. After admission, PET scan performed on the third day of admission showed no abnormal accumulation in the superficial temporal artery or aorta. On the fourth day of admission, urine occult blood level was 2+, and red blood cell casts were present. A blood test revealed MPO-ANCA 1835. Treatment with PSL 30 mg was started on the sixth day of admission, and fever and jaw claudication disappeared. this case, no findings were observed on ultrasound, but the positive MPO-ANCA result may have been due to inflammation in the small artery wall.

P3-056

A case of Takayasu arteritis with coronary artery lesions that experienced reocclusion following percutaneous coronary intervention

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Conflict of interest: None

Case: A 30-something female presented with elevated inflammatory markers in June X-4. A CT scan revealed shadows around the right subclavian artery, leading to observation. In January X-2, she suffered a myocardial infarction and cardiac arrest during coronary angiography, but circulation was restored. Angiography showed intimal thickening in the left

main coronary artery and right coronary artery origin, prompting percutaneous coronary intervention (PCI). The diagnosis of Takayasu arteritis (TA) was made based on the findings, her age, persistent inflammation, and the results of contrast-enhanced CT and PET-CT. Treatment began with prednisolone (PSL) at 55 mg/day and tocilizumab at 162 mg/week, reducing PSL to 5 mg/day by March X-1. However, in April X, coronary CT indicated reocclusion of the left main coronary artery, requiring another PCI and an increase in PSL to 25 mg/day, along with methotrexate 6 mg/week. **Discussion:** Coronary lesions occur in 5-20% of TA cases, with type 1 commonly affecting proximal segments. Reports indicate that half of cases with drug-eluting stents may experience restenosis within two years. In this case, coronary disease recurred despite PET-CT improvements. Future management will involve regular assessments and potential TNF inhibitor therapy.

P3-057

A case of Takayasu arteritis during adalimumab treatment for Crohn's disease

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Conflict of interest: None

[Case Report] The patient is a 21-year-old male. He developed Crohn's disease of the small and large intestine type in February X-1 year. He started treatment with 50 mg of prednisolone (PSL) and 3000 mg of mesalazine, and 160 mg of ADA was introduced in March and his disease had settled down. In February of X year, elevated serum C-reactive protein (CRP) level appeared. Although no abdominal symptoms were observed, the ADA dose was increased to 80 mg/2w, but the CRP remained in the 8 range. Contrast-enhanced CT scan showed thickening of the arterial wall from the ascending aorta to the aortic arch, which was diagnosed as a complication of Takayasu's arteritis. HLA was A 24, A 31, and B 51. ADA was discontinued, PSL was increased, and tocilizumab (TCZ) was administered, and Takayasu's arteritis improved. [Clinical Significance] Large vessel vasculitis is a known extraintestinal lesion in Crohn's disease, and TNF inhibitors can induce large vessel vasculitis. In this present case, the intestinal lesions were stable, suggesting that ADA may have induced Takayasu arteritis. It is important to note that patients with inflammatory bowel disease can develop large vessel vasculitis even when using TNF inhibitors.

P3-058

A Case of Large-Vessel Giant Cell Arteritis Presenting with Lower Limb Weakness Diagnosed by FDG-PET

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Conflict of interest: None

[Case] An 83-year-old woman presented with sudden weakness in both lower limbs upon awakening in February, which resolved spontaneously. She also experienced progressively worsening pain in her shoulders, knees, and lower back, accompanied by a low-grade fever (37°C) and fatigue. Laboratory tests revealed elevated CRP levels (8.87 mg/dL), leading to a referral for suspected Polymyalgia Rheumatica (PMR). Due to atypical symptoms, a chest and abdominal contrast CT scan was performed, showing thickening of the aortic artery and its branches, raising suspicion for giant cell arteritis (GCA). Despite the absence of classic GCA symptoms and normal temporal artery ultrasound findings, FDG-PET revealed inflammation in the bursae and major arteries, confirming PMR with large-vessel-type GCA (LV-GCA). The initial weakness was attributed to transient ischemia from femoral artery inflammation. Treatment with prednisolone (20 mg/day) and tocilizumab (162 mg/week) resulted in significant improvement, allowing for gradual tapering of prednisolone. [Clinical Significance] This case highlights the need to consider GCA in atypical PMR presentations, even without head and neck symptoms, and emphasizes the utility of FDG-PET for diagnosis.

P3-059

A Case Presenting Imaging Findings Similar to Aortitis and Retroperitoneal Fibrosis After a Marathon

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Conflict of interest: None

[Case] A patient, 54-year-old male was transported to our hospital due to abdominal pain on the day following a full marathon in November of Year X-1. A contrast CT indicated an increase in fat density around the aorta, leading to hospitalization with a suspicion of aortitis. After treatment with intravenous fluids, proton pump inhibitors, and antibiotics, both symptoms and imaging findings improved, allowing for discharge on the sixth day of hospitalization. He participated in more full marathons and experienced abdominal pain, which was addressed as acute enteritis. In July of Year X, after jogging, he experienced abdominal pain again. A contrast CT revealed an increase fat density around the abdominal aorta and inferior vena cava, prompting hospitalization. Imaging findings raised suspicion of retroperitoneal fibrosis. With rest and antibiotic treatment, both symptoms and imaging findings improved, allowing for discharge on the sixth day. [Discussion] Increased fat density around the aorta on CT can indicate aortitis or retroperitoneal fibrosis. To our knowledge, there have been no reported cases like this one that present transient inflammatory findings induced by exercise. This case is valuable for its necessity to differentiate aortitis and retroperitoneal fibrosis.

P3-060

A case of giant cell arteritis diagnosed following a pontine infarction

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Conflict of interest: None

[Case] 71-year-old man [Chief complaint] Fever, temporal headache [History] Palmoplantar pustulosis [Clinical Course] On 15 June 202X, the patient presented with weakness of the left upper and lower limbs and dysarthria. An MRI of the head revealed a pontine infarction. He had fever since the first visit and a CRP level of 1.78 mg/dL, however, contrast-enhanced CT and blood cultures showed no abnormalities. A temporal artery ultrasound revealed compression sign which represented an oedematous Intima-Media Complex. At the time of referral, the patient's PR3-ANCA, MPO-ANCA and antinuclear antibodies were negative. Contrast-enhanced MRI of the head showed thickening of the vessel walls of the bilateral vertebral arteries and internal carotid arteries and contrast in the right temporal artery. A temporal artery biopsy showed multinucleated giant cells and a diagnosis of giant cell arteritis was made. Treatment with prednisolone 55 mg/day and tocilizumab 162 mg/week was started. By the end of July, CRP level had improved to 0.01 mg/dL. [Discussion] If the stroke is associated with fever and elevated C-reactive protein levels, the possibility of an autoimmune disease such as vasculitis should be considered as a cause of the stroke.

P3-061

A case of arteritis that was diagnosed with the onset of pneumonia and spontaneously resolved with its improvement

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Conflict of interest: None

A 74-year-old male presented to our hospital with a few days history of fever and productive cough. Blood tests revealed elevated levels of white blood cell count (WBC) and C-reactive protein (CRP). Chest X-ray showed pulmonary opacity in his lift lower lung field and computed tomography exhibited pulmonary consolidation in the dorsal area of left lower lung. He was diagnosed as aspiration pneumonia and admitted to our facility due to respiratory failure. Sulbactam/ampicillin was initiated and his symptoms and elevated levels of WBC and CRP were being alle-

viated while CRP level started to increase again on day 8. Sulbactam/ampicillin was switched to tazobactam/ piperacillin. Contrast-enhanced CT on day 11 showed improvement of lung consolidation and thickening of vessel wall in subclavian and brachiocephalic artery and aortic arch. Following a three-week course of antibiotic therapy, an FDG-PET scan was conducted, yet the notable accumulation in the vessel wall was not discerned. On day 47, the CRP continued to decline, and the contrast-enhanced CT revealed a reduction in the wall thickening of the affected vessels. We report a case of arteritis that developed concurrently with pneumonia and abate with the improvement of the pneumonia.

P3-062

Examination of the efficacy of biologics and JAK inhibitors in elderly patients with rheumatoid arthritis at our hospital

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Conflict of interest: None

[Objective] We investigate the differences in the efficacy and safety of biologics (Bio) and Janus kinase inhibitors (JAK-i) between younger-onset rheumatoid arthritis (RA) and elderly-onset RA (EORA). [Methods] Among RA patients at our hospital in 2022, patients aged 60 years or older who were being treated with Bio or JAK-i were selected. They were divided into two groups: elderly RA with onset before 60 (group A; 36 cases) and EORA (group B; 73 cases), and the patient background, concomitant medications, and disease activity were compared between the two groups. [Results] In group A, more patients had advanced stages of disease and a history of Bio or JAK-i therapy. In group B, more patients had interstitial pneumonia and impaired renal function. After therapy, disease activity scores such as DAS28ESR and CDAI significantly decreased in both groups. There was little improvement in mHAQ in both groups. Group B needed higher dose of PSL at initiation, but the dose was significantly reduced at the final evaluation. The retention rate was 80% in group A and 69% in group B, with no significant difference. [Conclusions] Appropriate use of Bio and JAK-i in elderly patients with RA, regardless of age at onset, is considered to be useful for controlling disease activity.

P3-063

Proposal of Rheumatoid Arthritis Classification Criteria to Classify Elderly-Onset Rheumatoid Arthritis Without Leakage

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Conflict of interest: None

[Objective] The 2010 ACR/EULAR classification criteria (CC2010) may have reduced sensitivity for elderly-onset RA (EORA), as it emphasizes small joint involvement and RF. We propose a simplified modified version of CC2010 (SmCC2010) to better classify EORA and compare its diagnostic performance to CC2010. [Methods] We included new patients from our clinic since 2020. RA was diagnosed clinically. EORA was defined as onset at 65 years or older, while younger-onset RA (YORA) referred to those under 65. Non-RA diseases included OA, Gout, PMR, PsA. SmCC2010 modifications were: (1) combining small and large joints into a single category, thus eliminating separate criteria for small joints, (2) reinstating symmetrical arthritis from the CC1987, scoring 1 point if present. [Results] ROC analysis determined a 6-point cut-off for SmCC2010. In EORA, the number of patients scoring>= 6 /5> points was 19/7 in CC2010 and 25/1 in SmCC2010, while in YORA, it was 24/8 in CC2010 and 26/6 in SmCC2010. SmCC2010 improved sensitivity, particularly for EORA. In non-RA cases, 0/19 in CC2010, 2/17 in SmCC2010, showing a slight decrease in specificity. [Conclusion] SmCC2010 increases sensitivity for EORA compared to CC2010, with a minor decrease in specificity for non-RA diseases.

P3-064

Administration Status of Methotrexate and its Impact on Disease Activity and Drug Costs for Rheumatoid Arthritis Treatment

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Conflict of interest: None

Objective: To clarify methotrexate (MTX) administration in rheumatoid arthritis (RA) patients, reasons for non-administration, and its impact on disease activity and treatment costs. **Methods:** We surveyed 1591 RA patients treated from April 1990 to March 2023 regarding MTX status and reasons for non-administration via physician questionnaires. Patients were categorized into three groups: “MTX administered”, “MTX discontinued”, and “MTX not administered”. Disease activity and RA treatment costs were compared, based on drug prices over three months. **Results:** Among 1591 patients, 273 did not receive MTX and 129 discontinued treatment. Common reasons for non-administration included pulmonary infiltrates (126 patients, 46.2%) and chronic kidney disease (34 patients, 12.5%). Major discontinuation reasons were hematological disorders (40 patients, 31%) and interstitial pneumonia (18 patients, 14%). No significant differences in disease activity indices (CDAI, SDAI, DAS28-CRP, DAS28-ESR) were found. However, in low disease activity or remission, the MTX group had significantly lower treatment costs. **Conclusion:** MTX may reduce RA treatment costs. While potential side effects should be considered, its use as an anchor drug in RA treatment is recommended.

P3-065

The difference of medication for rheumatoid arthritis on the database of theumatia patients between hospitals and clinics by Koto Medical Association

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Conflict of interest: None

[Objectives] To recognise the difference of medication for rheumatoid arthritis between hospitals and clinics in database by Koto Medical Association. [Methods] The Association sent the questionnaire to the institutions where RA patients in Koto-ku visit. The questionnaire in two A4 papers was consist of age, sex, body height, body weight, pain VAS, patient global VAS, doctor VAS, the counts of swollen joints and tender joints (28 joints), the value of ACPA, RF, CRP, serum creatine, and the kind of drugs. [Results] The Association received the data of 370 cases from 7 institutions. The rate of steroid usage was 18.6% in total, 12.4% in clinics, and 20.6% in hospitals, respectively. The rate of MTX usage was 61.1% in total, 74.2% in clinics, and 56.9% in hospitals. The rate of biological agents was 23.8% in total, 5.7% in clinics, and 29.5% in hospitals. The rate of JAK inhibitors usage was 4.3% in total, none in clinics, and 5.7% in hospitals. The rate of MTX mono-therapy was 67.3% in total, 76.4% in clinics, and 64.4% in hospitals. MTX over 8 mg per week was used 5.6% in clinics and 12.8% in hospitals. Remission rate in RAPID3 was 28.1% in total, 27% in clinics, and 28.5% in hospitals. [Conclusion] MTX mono-therapy was preferable, but high dose of MTX usage was rare in clinics.

P3-066

Prediction of Continuation Rates of Subcutaneous Methotrexate in Rheumatoid Arthritis

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Conflict of interest: None

Objective: Methotrexate (MTX), an anchor drug for rheumatoid arthritis (RA), is now available as a subcutaneous form (sc) in addition to the oral form (po). MTX-sc may cause fewer gastrointestinal side effects, making it easier to continue. This study examined the continuation rates and efficacy of MTX-sc. Methods: We analyzed 25 RA patients who started MTX-sc, investigating reasons for initiation, continuation rates, efficacy, and safety. Results: The mean age at MTX-sc initiation was 58.1 years, with a mean disease duration of 18.7 years. A total of 68.0% switched from MTX-po, and 68.0% used biologics or JAK inhibitors. MTX-sc was started due to gastrointestinal symptoms from MTX-po (G group, 24.0%) or for treatment intensification (S group, 76.0%). Ten patients discontinued within 13 weeks, with the G group showing a lower continuation rate. Multivariate analysis showed that treatment intensification was a significant predictor of MTX-sc continuation (OR=17.4, p=0.03). Among those switching from MTX-po, no significant changes were seen after 13 weeks, while those without prior MTX use showed improvements in disease activity. Conclusion: Treatment intensification was an independent predictor of MTX-sc continuation. Disease activity improved in patients without prior MTX use.

P3-067

Two cases of rheumatoid arthritis treated with biologic agents showed widening of the joint space and functional recovery of the knee joint

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Conflict of interest: None

[Objectives] We report two cases in which biologics was administered to patients with progressive knee joint deformity associated with rheumatoid arthritis (RA) and resulted in joint repair and functional recovery. [Cases] Case 1: A 58-year-old woman with RA who had Larsen grade 4 in her left knee was treated with adalimumab. Two years after treatment, she lost about 10 kg of body weight due to weight loss to maintain her physical condition, and Rosenberg images of both knees showed an enlarged medial joint space and thickening of the cartilage layer on MRI. The left knee showed pain reduction and improvement in walking distance. Case 2 was a 60-year-old woman who had been receiving tocilizumab for RA for 1.5 years. She had bilateral knee deformities (right knee valgus, left knee varus). She underwent artificial knee arthroplasty for her painful left knee. Two years after surgery, standing radiographs of both knees showed an enlarged lateral joint space with improve of valgus alignment. The left knee showed improvement in pain resolution, range of motion, and walking distance. [Conclusion] Joint repair may be possible for load-bearing joints with advanced joint deformity associated with RA by administration of a biologic agent and improvement of joint load balance.

P3-068

Evaluation of serum albumin levels as an interleukin-6 signature

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Conflict of interest: None

[Objectives] Interleukin-6 (IL-6) is the most important key cytokine in the pathology of rheumatoid arthritis (RA). Serum albumin levels (ALB) reflect IL-6 activity. Therefore, ALB is decreased by IL-6 hyperactivity. ALB was evaluated as an IL signature. [Methods] Outpatients with RA were picked up. The associations between ALB and 28-joints disease activity index (DAS28) at methotrexate (MTX) administration and every three months in Phase 1 and at biological or targeted synthetic disease-modifying anti-rheumatic drugs (btsDMARDs) administration and the same interval as MTX were evaluated statistically. [Results] ALB correlated reversely with the DAS28 score at every time point until one year after MTX administration in Phase 1. ALB at the administration of MTX, IL-6 inhibitor, and Janus Kinase inhibitors correlated significantly with the change after administration in Phase 2. ALB correlated significantly with the DAS28 score after administering tumor necrotizing factor inhibitor with MTX concomitant. [Conclusion] ALB is suggested to be an available prognosis prediction indicator as an IL-6 signature.

P3-069

Survey on User Experience of Cases Switching from Methotrexate Syringe to Pen

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Conflict of interest: None

[Objectives] followed by the introduction of the pen-type device. Even with less expensive treatment options, relief from arthritis symptoms has been observed. Therefore, we conducted a survey to assess the user experience of cases that switched to the pen-type device. [Methods] the61 cases that transitioned from the Metject syringe to the Methotrexate pen. The questionnaire included questions related to “device usability”, “difficulty”, “pain”, “injection stress”, and “cost”. [Results] device usability”, all35 respondents (100%) rated the stability and force application during injection as “good”. For ease of holding the device, 31 respondents (86%) rated it as “good”, and34 respondents (94%) rated the injection speed as “good”. Regarding “difficulty”, 32 respondents (89%) described the process as “easy”. Concerning “pain”, 30 cases (83%) reported “no pain”, while for “injection stress”, 28 respondents (78%) indicated that stress was “eliminated”. On the topic of “cost”, 29 respondents (81%) reported “no issues”. Many patients expressed that the administration method was simple. [Conclusion] the device is rated highly in terms of ease of use, minimizing pain, and reducing injection stress, with manageable costs. However, some patients may still feel stressed about self-injection with pen-type.

P3-070

Utility of Methotrexate in Cases Not Previously Treated with MTX

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Conflict of interest: None

[Objectives] Metject (MJT), however, its effectiveness remains unclear. Thus, we administered MJT to cases not previously treated with MTX to evaluate its usefulness and adverse events in untreated RA pts. [Methods] 8 cases (total of10 cases) not treated with MTX, with an avg age of56.2 yr and an avg disease duration of9.7 yr. The positive rate for anti-CCP was87.5%, with average PSL dosage of2.18 mg/day and avg weight of48.7 kg. 2 cases (25%) had a family history of RA, and 3 cases (37.5%) had a smoking. Cases taking B/TsDMARDs were excluded. We evaluated CRP and DAS28CRP at baseline, 1 mo, 3 mos, and 6 mos post-treatment. we examined the proportion of patients achieving remission at each endpoint and presented improved joint ultrasound images. Adverse events experienced by these cases within 6 months. [Results] CRP was1.39 mg/dL, improving to1.82 mg/dL at 1 mos, 0.80 mg/dL at 3 mos, and1.41 mg/dL at 6 mos. The DAS28CRP scores2.23 before treatment, 2.45 at 1 mo, 1.76 at 3 mos, and1.53 at 6 mos. Notably, the rate of patients achieving remission was high, with62.5% at 1 mo, 87.5% at 3 mos, and87.5% at 6 mos. Only 2 case xperiencing fatigue. [Conclusion] MJT effectively suppresses disease activity early in RA treatment. Therefore, MJT has the potential to serve as an anchor drug.

P3-071

A Case of Methotrexate-Associated Lymphoproliferative Disorder After Long-Term Methotrexate Therapy

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Conflict of interest: None

[Case Report] A 78-year-old woman had been receiving methotrexate (MTX) at 12 mg per week for rheumatoid arthritis since Year X-19. In Year X, a 4.5 cm × 6 cm mass appeared on her left buttock, along with a 2 cm × 2.5 cm ulcer on her forehead. A skin biopsy revealed numerous atypical lymphocytes, suggesting Epstein-Barr virus (EBV) infection. Based on histopathological findings and clinical course, she was diagnosed with methotrexate-associated lymphoproliferative disorder (MTX-LPD). After discontinuing MTX, the ulcer gradually shrank and was nearly epithelized by September 2023, indicating healing. There has been no recurrence of arthritis or worsening of inflammatory markers since stopping MTX, and remission has been maintained. [Clinical Significance] MTX-LPD is a lymphoproliferative disorder associated with MTX-induced immunosuppression, potentially presenting with lymphadenopathy, skin masses, or ulcers. Many cases improve upon discontinuation of MTX, but some may progress to malignancy, warranting careful attention in rheumatoid arthritis management. In this case, despite long-term remission, MTX dosing had not been adjusted, which may have contributed to disease onset. It is essential to continuously assess whether MTX dosage is appropriate and not excessive.

P3-072

Usefulness of subcutaneous injection formulation of methotrexate for rheumatoid arthritis

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Conflict of interest: None

[Objective] The purpose of this study was to investigate whether subcutaneous methotrexate can improve the side effects of oral methotrexate and whether it is useful in patients who have had inadequate response to oral methotrexate. [Methods] The medical records of 44 patients who used subcutaneous methotrexate from October 1, 2022 to October 16, 2024 at our hospital and Aoki Medical Clinic were examined retrospectively for patient background, clinical symptoms, course of treatment, and side effects. [Results] Subcutaneous injection was introduced in 44 patients, 27 of whom were switched to subcutaneous injection due to adverse reactions to oral administration, and 16 of whom had resolved adverse reactions after subcutaneous injection. 17 cases were introduced due to inadequate efficacy or other reasons, and in 14 cases, the efficacy of the treatment could be evaluated. [Conclusion] When gastrointestinal symptoms occur with oral medications, switching to subcutaneous formulations can improve symptoms in some cases. In addition, subcutaneous injection may be effective for patients with inadequate response to oral medication.

P3-073

Adverse Events and Therapeutic Efficacy of Switching from Oral to Subcutaneous Methotrexate in Rheumatoid Arthritis

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Conflict of interest: None

Objective: Methotrexate (MTX) is the anchor drug for rheumatoid arthritis (RA), but some patients cannot tolerate adequate doses due to gastrointestinal side effects. Subcutaneous MTX is reported to cause fewer symptoms, but the effects of switching from oral to subcutaneous MTX are unclear. **Methods:** We prospectively studied RA patients who had nausea or fatigue while taking oral MTX for 12 weeks with folic acid. Patients who switched to subcutaneous MTX formed the injection group, while those continuing oral MTX were controls. Primary outcomes were changes in nausea (Δ nausea VAS) and fatigue (Δ fatigue VAS) on the Visual Analogue Scale (VAS) over 13 weeks. MTX doses were adjusted to subcutaneous equivalents, and MTX and folic acid doses were stable. **Results:** We analyzed 42 patients (21 per group). Baseline characteristics were similar, except for higher baseline nausea VAS in the injection group (47.2 vs 30.2, p=0.024). After 13 weeks, the injection group showed greater improvements in Δ nausea VAS (-39.3 vs 1.6, p<0.001) and Δ fatigue VAS (-12.2 vs 13.1, p=0.004). Disease activity (Δ CDAI, Δ DAS28-CRP) also improved more in the injection group. **Conclusion:** Switching to subcutaneous MTX significantly improved nausea, fatigue, and disease activity in RA patients.

P3-074

The usefulness of small daily doses of folic acid in rheumatoid arthritis patients on methotrexate

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Conflict of interest: None

[Objectives] We investigated whether daily folic acid administration is effective in reducing side effects in rheumatoid arthritis patients using methotrexate (MTX), and whether it reduces RA disease activity in patients with no change in RA treatment. [Methods] Of 81 patients who received 1 mg folic acid daily during treatment with MTX, we analyzed 66 patients, excluding 15 whose progress cannot be assessed. Next, 11 patients who had no change in treatment other than the change from 5 mg folic acid once a week to 1 mg folic acid every day were followed for 6 months, and DAS-28, ESR, SDAI, ESR, CRP, AST, ALT, WBC, PLT, and other side effects. [Results] The analysis of 66 patients showed that gastrointestinal symptoms improved with a significant difference. Analysis of 11 patients who did not change their treatment showed no significant difference in DAS-28 (ESR), SDAI, ESR, CRP, AST, ALT, WBC, and PLT. AST showed significant improvement. Other side effects showed a trend toward improvement in gastrointestinal symptoms. [Conclusion] In an analysis of 66 patients, daily administration of folic acid reduced adverse effects. Although this is a small number of cases, the analysis of 11 patients showed that daily folic acid administration may have no effect on disease activity.

P3-075

Experience with the Use of Subcutaneous Methotrexate in Established Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] Subcutaneous methotrexate (MTX S.C.) became available in Japan in 2022 for rheumatoid arthritis (RA). Studies have shown MTX S.C. to be more effective and cause fewer gastrointestinal side effects than oral MTX. This report summarizes our experience with MTX S.C. in RA patients. [Methods] We evaluated 19 RA patients treated with MTX S.C. (mean age 56.2 years; 8 males, 11 females; mean disease duration 14.3 years). Of these, 15 had previously used oral MTX, with an average dose of 9.2 mg/week. Four patients were also taking steroids (PSL), with an average dose of 2.9 mg/day. We assessed disease activity, PSL dosage, and tolerability. [Results] The Simplified Disease Activity Index (SDAI) decreased from 7.29 to 5.95. PSL dosage was reduced from 2.9

mg/day to 1.6 mg/day. Liver function improved in 1 patient, and no gastrointestinal symptoms were observed. Four patients discontinued treatment due to adverse effects. The initial MTX S.C. dose averaged 8.4 mg/week, increasing to 9.3 mg/week. [Conclusion] MTX S.C. improved disease activity without causing gastrointestinal symptoms and allowed steroid reduction. It is a viable option for patients intolerant to oral MTX or those requiring dose escalation.

P3-076

A study of cases of MTX subcutaneous injection formulation use in our hospital

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of MTX subcutaneous injection (sc) in cases who were introduced to MTXsc at our hospital. [Methods] Subjects were 13 rheumatoid arthritis cases who started MTX-sc from March 2023 to October 2024. They were evaluated by LOCF method using DAS28-CRP and CDAI at the start of sc, 1, 2, 3, 6M and 1Y. Adverse events (AE) during the first year of therapy were also surveyed. [Results] They were divided into 3 groups: 1) MTXsc from the beginning (4 cases), 2) Insufficient effect of oral MTX/Cases wanted to (2 cases), and 3) Difficulty in increasing the oral MTX dose due to AE (7 cases). The overall disease activity showed a significant decrease and statistically difference ($p<0.01/p<0.05$) in DAS28-CRP/CDAI (median); 0w: 3.27/6.5, 3M: 1.83/3.1, 6M: 1.93/2.1,1Y: 1.61/1.8 respectively. In 7 cases with AE to the oral MTX, one had similar AE after switching to sc and was re-changed to oral, but other 6 cases could have improvement of AE after switch to sc and continue the sc therapy. AE was mostly minor (24 events/12 cases), but one case was hospitalized due to bacterial pneumonia. Two cases received additional intensified therapy while the study. [Conclusion] MTXsc was considered safe and effective as a means of switching from oral method or intensifying therapy.

P3-077

A study of hepatotoxicity in rheumatoid arthritis patients treated with methotrexate

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Conflict of interest: None

[Objective] MTX has been associated with fatty liver and steatohepatitis, necessitating the evaluation of hepatotoxicity alongside therapeutic efficacy. This study investigates the progression of liver injury in RA who initiated MTX treatment at our department. [Methods] We retrospectively evaluated 4 RA patients, diagnosed between Jan 2018 and Dec 2022, who presented with fatty liver at the start of MTX therapy. We assessed RA disease activity, theatment, and liver injury. Liver damage was evaluated using Fib4. [Results] The average age was 66 years (1 male). All patients commenced MTX at doses of 6 or 8 mg/week, with GC. The mean BMI was 27, three patients reporting occasional alcohol consumption. All patients had HTN and HPL, leading to a diagnosis of MASLD. Three patients achieved remission, they continued MTX at an average dose of 11 mg/week. The mean Fib4 value was 1.32 at 6 months, 1.42 at month 12 and 1.95 at month 24. No patient exhibited significant liver enzyme elevation, suggesting that the increase in Fib4 may be attributed to age and a declines in PLT. [Conclusion] Long-term MTX administration can lead to MASLD, even when transaminase levels remain nearly within normal limits. It is desirable to provide certain indicators of liver damage during MTX treatment.

P3-078

Gastrointestinal Symptoms of Subcutaneous Methotrexate

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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, 6 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 4.8±2.4 to 2.8±1.9. No significant improvement was observed in the other parameters. patients were able to continue MTXsc for more than 52 weeks. [Conclusion]: All 4 patients who were treated with MTX and then MTXsc continued for at least 12 weeks. “Nausea” improved the most.

P3-079

Efficacy and liver damage of methotrexate subcutaneous injection in our clinic

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Conflict of interest: Yes

[Objectives] Methotrexate (MTX) is an anchor drug in the treatment of rheumatoid arthritis (RA). However, there are many cases in which it is difficult to continue or increase the dose due to side effects of oral administration. Subcutaneous injections of MTX (MTX s. c) are increasingly reported to attenuate or disappear side effects of gastrointestinal symptoms due to changes. However, there are fewer reports about efficacy and hepatic dysfunction after changes in MTX s. c compared before and after changes. [Methods] We included 400 patients with MTX s. c changes who were able to continue to be followed for at least 6 months. Efficacy and hepatic impairment were compared with 1 month, 3 months, and 6 months at the time of change in MTX s.c. as baseline. [Results] As for efficacy, there was a tendency to improve disease activity regardless of the duration of disease. In addition, improvement was observed in the group with hepatic impairment during oral MTX administration. [Conclusion] It was suggested that changing to MTX s. c could be expected to improve efficacy and side effects in patients who had inadequate control of disease activity but could not use MTX orally due to side effects or who could not increase the dose.

P3-080

Comparison of efficacy and safety of JAK inhibitor upadacitinib and IL-6 inhibitor sarilumab using propensity score matching in each phase of the RA treatment algorithm

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Conflict of interest: None

[Objectives] We compared the efficacy and safety of JAK inhibitors and IL-6 inhibitors using propensity scores in the treatment RA. [Methods] We studied two groups (413 cases in total) of patients who met the ACR/EULAR RA classification criteria: 143 cases treated with JAK inhibitor upadacitinib and 270 cases treated with IL-6 inhibitor sarilumab. In raw data and propensity score matching data, treatment continuation rates and treatment responses were compared using CDAI. [Results] In a comparison of 112 patients after propensity score matching, the treatment continuation rate at 48 weeks was 79.4% for upadacitinib and 76.0% for sarilumab, which was not significantly different (Log-rank, p=0.0.7412). The

CDAI LDA/REM achievement rate at 12 weeks was 87.4% for the upadactinib group and 83.0% for the sarilumab group. The CDAI improvement rate at 4 weeks after the start of treatment contributed to the LDA/REM achievement rate in both groups (p=0.0077, p=0.0194). Herpes zoster was observed in 16 patients only in the upadacitinib group (p <0.0001), and malignant tumors was observed in upadacitinib group (5 patients) and the sarilumab group (4 patients) (p=0.0286). [Conclusion] These results suggested that treatment selection should take into account risk factors for adverse events.

P3-081

Analysis of Clinical Features Based on Upadacitinib Dosage in Rheumatoid Arthritis

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Conflict of interest: None

Objective: Upadacitinib (UPA) is approved in two doses (7.5 mg and 15 mg) for rheumatoid arthritis (RA). This study examines clinical outcomes based on UPA dosage. **Methods:** We retrospectively analyzed RA patients treated with UPA for over 12 months. Patients were divided into two groups: those treated with 7.5 mg or less (7.5 mg group) and those treated with 15 mg (15 mg group). We compared patient backgrounds, disease activity and adverse events. **Results:** A total of 97 patients were included (7.5 mg group: 51, 15 mg group: 46). The 7.5 mg group was older (75 vs. 69 years), had higher RF positivity (94% vs. 78%), lower body weight (52 kg vs. 57 kg), and fewer had previously used b/tsDMARDs (65% vs. 87%) compared to the 15 mg group. Both groups started with moderate disease activity, and after 12 months, there were no significant differences in disease activity or remission rates. The treatment continuation rate after 12 months was similar between the groups (80% vs. 79%). Among adverse events, herpes zoster occurred more frequently in the 15 mg group (10 vs. 17/100 person-years). **Conclusion:** Starting UPA at 7.5 mg may be a viable option for elderly patients at risk of herpes zoster or those who are DMARD-naïve, especially for RA patients with moderate disease activity.

P3-082

Impact of Upadacitinib in the Treatment of RA Patients

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Conflict of interest: Yes

[Objective] We investigated the impact of Upadacitinib (UPA) on RA patients. [Methods] We examined changes in disease activity and blood test data from the start to the final observation in patients who could continue UPA for more than one year at our hospital. [Results] 14 patients were included in this study. Mean age was 64.1 years, mean disease duration was 11.1 years, and mean duration of UPA use was 2.6 years. 69% had RF-positive, 71% had ACPA-positive, and 93% had a history of using two or more b/tsDMARDs. Mean DAS28CRP/ESR/SDAI/CDAI was 3.45/3.77/18.8/18.4 before UPA treatment. Disease activity improved in 11 patients, unchanged in 2, and worsened in 1. In 13 patients, except for one worsened patient, the swollen joint counts significantly decreased. Blood test showed a decrease in CRP/ESR, and no significant changes were observed in liver or kidney function. CK and LDH significantly increased and RBC and Hb decreased in all patients. [Conclusions] UPA is also effective for D2TRA, mainly inhibiting JAK1 to reduce inflammation, but may affect JAK2, which causes anemia. Increased CK suggests that it may be involved in muscle mass increase rather than drug side effects. It is unclear whether LDH increase is derived from muscle or blood, so isoenzymes need to be examined.

P3-083

The efficacy of Peficitinib (PEF) in Niigata Rheumatic Center

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Conflict of interest: None

[Objectives] To analyze the efficacy of PEF in clinical practice. [Methods] We retrospectively analyzed 28 cases (mean age 67.8 years old, female 71.4%, ACPA positive 75%) in which PEF was used for the first time in our hospital. [Results] The retention rate with PEF for 6 months was 64.3% (18 cases), which was almost same as 62.2% in the post-marketing surveillance. We evaluated efficacy using DAS28-ESR and SDAI, and both have improved at 4 and 24 weeks ($p<0.05$). In cases of renal impairment with an eGFR<60 ml/min/1.73 m^2 without MTX, the retention rate was 66.7%, which was no significant difference from all cases. The most common reason for discontinuation was lack of efficacy (6 cases). Discontinuation occurred within 9 weeks in all cases. [Conclusion] In our hospital, the retention rate with renal impairment was the same for other patients, and efficacy was observed without MTX. PEF has the lowest renal excretion rate among all JAK inhibitors, and there are reports of its use in dialysis patients, so we believe it is the useful option for monotherapy in renal impairment cases. Also, the rate of achieving ACR20 has plateaued after about 20 weeks in previous reports. Therefore, it is possible that some cases may have shown a good effectiveness with continued use.

P3-084

The safety and efficacy of upadacitinib in Fukui Ishikawa Toyama Database of Rheumatoid Arthritis (FIT-RA), 12 months observation

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Conflict of interest: None

[Objective] We aimed to clarify the safety and efficacy of upadacitinib in daily clinical practice. [Methods] Patients with rheumatoid arthritis who were enrolled in the FIT-RA by May 2023 and who received upadacitinib were included in the study. The drug retention rate, DAS28-CRP, and adverse events for 12 months observation period were investigated. [Results] Sixty-six patients were included. Median age was 66.9 years, and fifty-eight (87.9%) patients were female. The continuation rate at 12 months was 70%; DAS28-CRP remission was 16% at baseline and 49% at 12 months. Adverse events included two cases of herpes zoster (incidence rate 1.10/100 patient-years), two malignancies, and one cardiovascular disease. No infections leading to drug discontinuation were observed. [Conclusion] Upadacitinib demonstrated a rapid onset of efficacy and acceptable safety, even in the FIT-RA patient group, which included many patients with highly active disease resistant to multiple b/tsDMARDs and for whom MTX co-administration was challenging.

P3-085

Examination of the efficacy of IL-6 inhibitors and JAK inhibitors based on baseline CRP levels: -Analysis of the Kansai multi-institutional collaborative study ANSWER Cohort-

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Conflict of interest: Yes

[Objective] In the treatment of rheumatoid arthritis (RA), differences in effectiveness between JAK inhibitors and IL-6 inhibitors in patients with elevated baseline CRP levels have not been thoroughly investigated. This study aims to compare the efficacy of JAK inhibitors and IL-6 inhibitors. [Method] Patients treated with either JAK inhibitors or IL-6 inhibitors were analyzed, with effectiveness differences based on baseline CRP levels assessed using linear regression analysis. Patients were also categorized into multiple CRP ranges, and treatment effects were compared using changes in CDAI scores as an indicator. [Result] In patients with low to moderate CRP levels, no significant difference in efficacy was observed between JAK inhibitors and IL-6 inhibitors. However, in patients with CRP levels of 1.8-3.0 mg/dl, IL-6 inhibitors tended to show superior therapeutic effects compared to JAK inhibitors. Linear regression analysis indicated that the interaction term between CRP level and treatment group was statistically significant, suggesting that as CRP levels increased, IL-6 inhibitors were potentially more effective than JAK inhibitors. [Conclusion] This analysis suggests that for RA patients with high CRP levels, IL-6 inhibitors may be more effective than JAK inhibitors.

P3-086

The prevalence of malignancy in patients with rheumatoid arthritis after the administration of Janus kinase inhibitors

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Conflict of interest: None

[Objectives] To elucidate the association between Janus kinase inhibitors (JAKi) and the incidence of malignancy with rheumatoid arthritis (RA) patients. [Methods] RA patients (n=204) were analyzed the background and the incidence of malignancy after treatment of JAKi under the pre-treatment malignancy screening at our facility between April 2015 and March 2024. [Results] In the baseline characteristics, mean age is 66.6 years and mean disease duration is 125.9 months. 5.4% of patients (n=11) were diagnosed in malignancy during the treatment of JAKi (the incidence rate of 1.33 per 100 person-years). Lymphoma was the most frequent (27.3%, n=3), followed by lung cancer (18.2%, n=2) and other malignancies. The patients with malignancy were older and had a higher rate of drinking and smoking than those of without malignancy. The mean RA disease duration was much longer ($p=0.154$) and a higher rate of anti-CCP antibody positivity ($p=0.343$) in malignancy group. However, there was no statistical significance. [Conclusion] Malignancy could be developed after JAKi administration, even in patients undergone pre-treatment screening. No remarkable risk factors related to the onset of malignancy though, periodical screening for malignancy is mandatory during the treatment of JAKi.

P3-087

Study on patients who relapsed after a 1-year remission based on CDAI and SDAI following Janus Kinase inhibitors therapy initiation

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Conflict of interest: None

Objectives: we analyzed patients who relapsed after maintaining remission for at least 1 year, as measured by CDAI) and SDAI, following the initiation of Janus kinase inhibitors (JAKi). **Methods:** As of September 2024, JAKi therapy was initiated in 188 patients at our hospital, and 61 maintained remission based on CDAI and SDAI for at least 1 year. Among these, 21 patients relapsed. We analyzed the patient characteristics at the time of JAKi therapy initiation and the status of dose reductions in JAKi and concomitant csDMARDs during treatments in these patients. Moreover, RF, MMP-3, IgG, and IgM, at the time of relapse were compared with the corresponding values obtained monthly during the treatment up to 12 months before relapse. **Results:** Among the patients studied, JAKi doses were reduced in 13 patients, and csDMARD doses were reduced in 8 patients. Compared to the levels at the time of relapse, RF, MMP-3, and IgG levels were higher in 12 patients, 7 patients, and seven patients, respectively, 2 to 7 months earlier. **Conclusions:** The current study suggests that careful follow-up is required after reducing JAKi or csDMARDs doses in patients achieving CDAI and SDAI remission. Additionally, RF, MMP-3, and IgG levels are useful indicators for predicting relapse in these patients.

P3-088

The Fate of Unresurfaced Patellae with Lateral Patellar Facetectomy in Total Knee Arthroplasty in Patients with Rheumatoid Arthritis: Midterm Results

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Conflict of interest: None

[Objectives] At our center, total knee arthroplasty (TKA) without patellar resurfacing has been standard for rheumatoid arthritis (RA) cases without patellofemoral symptoms. Lateral facetectomy has been routinely performed since 2014. [Methods] We reviewed 7 RA patients (9 knees; 1 male, 6 female) who underwent TKA without patellar resurfacing from October 2014 to March 2020. Mean age at surgery was 62.4 years (range: 38-72), with an average follow-up of 6 years and 5 months. All cases used the Persona (Zimmer Biomet) implant (8 CR, 1 PS). Evaluations included revision rates, Knee Society Knee Score (KSS), range of motion, patella gliding test, anterior knee pain (AKP), and radiographic findings. [Results] No revisions occurred. The KSS improved from 58.2 preoperatively to 93.3. Extension improved from -12° to 0.6°, and flexion from 123.9° to 128.3°. No positive patella gliding tests or AKP were reported. Radiographs showed lateral wear and osteophytes in the PS knee, while 2 CR knees exhibited sclerosis, along with 1 medial cyst and 1 lateral osteophyte in the other CR knees. [Conclusion] Midterm outcomes of TKA without patellar resurfacing in RA patients were favorable, with a 100% survival rate. Radiographic changes indicate the need for careful long-term follow-up.

P3-089

Alteration and clinical results of Total hip arthroplasty for Rheumatoid arthritis

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Conflict of interest: None

[Objectives] This report was the details of the patient who performed the THA in our hospital. [Methods] The patient who performed THA for RA patient from 1994 through 2022 was 37 people (38 joints for 32 wom-

en, 6 joints for five men). At operation, the age were 66.5±9.4 years old, the height were 151.9±8.7 cm, and the weight were 54.4±13.2 kg. The postoperative follow-up period was 10.7±6.1 years (range, 2.3-23.8 years). The THAs were performed using posterolateral approach without separating greater trochanter by all cases and depending on the degree of the acetabular bone defect, used bone graft together. [Results] The Japanese orthopedics society hip joint criteria (one hundred perfect score) were improved after the operation from 34.3±12.1 in preoperation to 86.5±10.6 points of last follow-up ($p < 0.05$, t-test with the correspondence). The total hip arthroplasty was revised for 3 joints of two patients. [Conclusion] Acetabular Protrusion is characteristic, and, as a hip joint lesion of the RA patient. Not only that, the number of cases itself of the THA decreases, too. These are regarded as a great usefulness and achievement of the biological preparation medicine.

P3-090

"Investigation of the CPAK Classification and Short-term Clinical Outcomes Before and After TKA for Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] This study investigates the CPAK classification in rheumatoid knees, focusing on its relationship with clinical outcomes before and after TKAs. [Methods] We analyzed 67 patients (79 knees) undergoing primary TKA for RA. The average patient age was 75 years, and BMI was 23.5 kg/m^2. We measured LDFA and MPTA, classified by Arithmetic HKA and JLO, and evaluated range of motion, JOA score, pain NRS, and TUG at preoperative and discharge stages. [Results] Preoperatively, the CPAK classification showed: I: 42 knees, II: 5, III: 16, IV: 10, V: 3, VI: 2, VII: 1, VIII: 0, IX: 0. Postoperatively, it changed to: I: 1 knee, II: 9, III: 0, IV: 6, V: 61, VI: 1, VII: 0, VIII: 0, IX: 1. Knee extension improved from -12° to -2° and flexion from 110° to 114°, with the JOA score increasing from 39.4 to 71.7. There were no significant differences in clinical outcomes between mechanical alignment (MA) and non-MA knees, nor between kinematic alignment (KA) and non-KA knees. Among 15 knees with reduced motion, 10 belonged to MA (+) group, and changes in JLO observed in 13 knees. [Conclusion] The preoperative phenotype revealed a higher proportion of III group compared to OA reports. Short-term outcomes indicated no advantage of MA or KA, but suggested that JLO may influence the range of motion.

P3-091

Treatment Outcomes of Total Knee Arthroplasty in Patients with Rheumatoid Arthritis with Knee Joint Disorders and Those with Concomitant Osteoarthritis

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Conflict of interest: None

[Objectives] Valgus knee deformities are common in rheumatoid arthritis (RA) patients. With improved treatments, elderly RA patients with controlled disease now present with varus deformities caused by osteoarthritis (OA), leading to total knee arthroplasty (TKA). This study compared postoperative TKA outcomes in patients with RA alone and those with RA and OA (RAOA). [Methods] A total of 44 knees from RA patients (average age 74±7.7 years) who underwent TKA between 2016 and 2023 were studied. The patients were divided into RA (26 knees) and RAOA (18 knees) groups. The same surgical approach and prosthesis were used for all cases. Data included age, gender, femorotibial angle (FTA), KL and Larsen classifications. Postoperative assessments at 3, 6, and 12 months included range of motion (ROM), JOA knee score, Forgotten Joint Score (FJS), and complications. Statistical analysis was done using the Mann-Whitney U test. [Results] A significant difference was found in FTA ($P = 0.000013$), but no differences in other factors or outcomes (ROM, JOA, FJS). The only complication was wound dehiscence in one RA patient due to a fall, with no infections or loosening. [Conclusion] Postoperative outcomes of TKA were similar between RA and RAOA patients, suggesting similar effectiveness in both groups.

P3-092

Impact of the limb muscle mass on QOL after Total knee Arthroplasty -Comparison of Osteoarthritis and Rheumatoid arthritis -

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Conflict of interest: None

[Objectives] To compare the influence of limb muscle mass on QOL after total knee arthroplasty (TKA) between knee osteoarthritis (OA) and rheumatoid arthritis (RA). [Methods] The subjects were 82 knees after TKA. All were female. 53 knees had OA and 29 had RA. The lean muscle mass of the limbs measured by DEXA were divided by the square of the height to determine the skeletal muscle index (SMI). The SMI of all cases was classified sarco group and normal group. The JKOM score was evaluated pre- and post surgery. In the normal and sarco group of the OA and RA groups, the JKOM scores were compared. The grip strength and walking speed were measured. [Results] The JKOM scores of OA were lower than RA for pre- and post- surgery. The scores OA normal group were higher than RA for pre- and post-surgery. In the normal group, the JKOM scores of OA were lower than those of the RA for both pre- and post-surgery. The grip strength of the both OA and RA normal groups were greater than the Sarco groups. The OA grip strength was greater than the RA in both normal and Sarco groups. There was no significant difference in SMI between OA and RA in both the normal and Sarco groups. [Conclusion] The QOL of OA was higher than that of RA, but the influence of muscle strength was greater than limb muscle mass.

P3-093

Postoperative clinical results of RA knee TKA complicated by severe obesity at our hospital

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Conflict of interest: None

[Background] There are few reports of TKA for RA with severe obesity. [Purpose] The purpose was to compare the postoperative clinical outcomes of TKA on RA deformed knees in severely obesity with the outcomes of RA deformed knees in normal. [Subjects and Methods] The subjects were 67 knees that underwent primary TKA for RA performed between February 2010 and December 2020, and were able to be followed up for more than 2 years after surgery, and whose postoperative ROM, KOOS, KSS, and FJS-12 were confirmed. We retrospectively observed and compared the postoperative clinical outcomes and complications at the final observation of 6 knees in the severely obesity with a BMI: 35 or more and 26 knees in the normal weight group with a BMI: 18.5 to 25. [Results] The pain of the KOOS was significantly lower in the severely obesity. The operation time was longer and the surgical infection was higher in the severely obesity group. [Discussion] At the past research, TKA for OA with severe obesity has been reported to have no difference in clinical outcomes compared to the normal weight, but the operation time is longer and there are more postoperative complications. [Conclusion] TKA for RA knee deformities combined with severe obesity was considered to be an effective treatment method.

P3-094

Essential Anatomy of the Popliteal Artery in Total Knee Arthroplasty -A Cadaveric Study-

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Conflict of interest: None

[Objectives] The aim of this study was to clarify the anatomical characteristics of the popliteal artery during total knee arthroplasty (TKA) using cadavers. [Methods] 51 formalin-fixed cadavers with 102 knees were included in the study. After identification of the popliteal artery and posterior cruciate ligament (PCL), the shortest distance between the posterior wall of the tibia and the popliteal artery was measured. Measurements were taken at three levels: lateral articular surface, 1 cm distal from the lateral articular surface, and 1.5 cm distal from the lateral articular surface. [Results] The shortest distance from the posterior wall of the tibia to the popliteal artery was 10.1 ± 2.3 mm at the level of the lateral articular surface, 6.1 ± 1.5 mm at 1 cm distal from the lateral articular surface, and 4.9 ± 1.1 mm at 1.5 cm distal from the lateral articular surface. [Conclusion] The popliteal artery was located approximately 6 mm from the posterior wall of the tibia in an osteotomy 1 cm from the lateral articular surface, which is a common level for TKA. The osteotomy 1.5 cm from the lateral articular surface was even closer, suggesting that more attention should be paid when adding osteotomies distally.

P3-095

two case report of TKA with preventive peroneal nerve release for severe valgus deformity

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Conflict of interest: None

[Objective] TKA for severe valgus knees increases the risk of common peroneal nerve palsy. We report two cases of TKA with preventive peroneal nerve release for severe valgus deformity. [Case Presentation] Case 1: A 64-year-old female with a preoperative left knee range of motion of 90° flexion and 0° extension. Radiographs showed Krackow type II deformity with an FTA of 154°. Case 2: A 59-year-old female with a preoperative right knee range of motion of 90° flexion and -20° extension. Radiographs showed Krackow type II with an FTA of 149°. In both cases, before TKA, preventive peroneal nerve release was performed via a 4 cm incision distal to the fibular head, incising the peroneus longus fascia, and dissecting the common peroneal nerve. Implants were then placed, confirming no visible nerve traction. Nerve stimulator assessments showed no muscle contraction loss before and after implant placement. Postoperative FTAs were 172° and 168°, with no nerve palsy observed. [Discussion] Common peroneal nerve palsy in TKA for severe valgus knees is often due to nerve traction. Here, TKA was performed after confirming no peroneal nerve traction via inspection and electrophysiology, preventing palsy. Thus, preventive peroneal nerve release may be valuable in TKA for severe valgus knees.

P3-096

A case of high tibial osteotomy in a patient with psoriatic arthritis

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Conflict of interest: None

Traditionally, patients with rheumatic diseases, such as rheumatoid arthritis, were considered contraindication for joint-preserving surgery. In the present study, we report a bilateral high tibial osteotomy for osteoarthritis in a patient with psoriatic arthritis, with good, short-term, results. The patient was a 62-year-old woman who was treated for psoriatic arthritis with a biologic (adalimumab). The Disease Activity in Psoriatic Arthritis (DAPSA) index was 7.24, indicating low disease activity. At the initial visit, tenderness in the medial joint line of both knees was observed. Simple X-rays showed medial type osteoarthritis (Kellgren-Lawrence classification grade IV) in both knees. First, interlocking CWHTO (closed wedge high tibial osteotomy) was performed on the right knee. 1 year later CWHTO was performed on the left knee. One year later, KOOS (Knee Injury and Osteoarthritis Outcome Score) total improved from 26.0 to 59.4 points for the right knee and from 48.6 to 70.5 points for the left knee. Considering the patient's background, it was thought that high tibial osteotomy could be considered if the disease activity was controlled. However, if the disease control worsens in the future, joint destruction may occur, so careful follow-up is necessary.

P3-097

Bimekizumab (BKZ) treatment was efficacious to 2 years (yrs) regardless of duration of axial spondyloarthritis (axSpA) symptoms (DoS): Results from two phase 3 studies (encore)

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Conflict of interest: Yes

Objective Compare DoS impact on BKZ efficacy to 2yrs in axSpA. Methods BE MOBILE 1/2 (non-radiographic/radiographic axSpA; NCT03928704/NCT03928743): randomised to BKZ, placebo (PBO); Weeks (Wks) 16-52: BKZ; Wk52: open-label extension (NCT04436640). ASAS40, ASDAS<2.1, BASDAI change from baseline (CfB) reported for DoS≦5/>5 (both trials), DoS≦2/>2 (BE MOBILE 1). SIJ SPARCC reported for MRI substudy DoS≦5/>5 (BE MOBILE 1). Wk16 relative odds ratio (ASAS40, ASDAS<2.1)/relative difference (BASDAI CfB, MRI SIJ SPARCC) calculated. Results Better Wk16 outcomes with BKZ vs PBO for all DoS, sustained/improved to Wk104. % BKZ-treated with ASAS40/ASDAS<2.1 at Wk16 & Wk104 larger for DoS≦5 vs >5 & ≦2 vs >2; no significant difference at Wk16. Wk16 mean BASDAI CfB relative difference not significant for DoS≦5 vs >5 & ≦2 vs >2 (BE MOBILE 1), improvement larger for DoS≦5 vs >5 (BE MOBILE 2); Wk104 improvement larger for DoS≦5 vs >5 & ≦2 vs >2. Baseline MRI SIJ SPARCC (more inflammation for DoS≦5 vs >5) reduced with BKZ to Wk16, vs PBO no significant difference found between DoS≦5/>5 (BE MOBILE 1); scores remained low (inflammation resolution) to Wk104 for all DoS: ≦5 n=40: 2.03/>5 n=55: 2.83. Conclusion BKZ efficacious to 2yrs for all DoS; no difference found in Wk16 BKZ vs PBO between shorter/longer DoS.

P3-098

CT evaluation of the sacroiliac joint in patients with arthritis attending our rheumatology outpatient clinic

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Conflict of interest: Yes

[Objective] To evaluate by CT scan whether erosion or ankylosis has occurred in the sacroiliac joint in patients diagnosed with RA (rheumatoid arthritis) or PMR (polymyalgia rheumatica). [Subjects] Patients with RA or PMR who visited and were treated at our hospital's rheumatology outpatient clinic between July 2020 and September 2024 and underwent abdominal CT scans. However, patients with inflammatory bowel disease, psoriasis, or palmoplantar pustulosis were excluded. [Method] The rate of

patients with sacroiliac joint changes in abdominal CT axial positions was calculated. A logistic analysis was performed to determine risk factors for sacroiliac joint changes. [Results] The study included 126 RA and PMR patients (RA; 97, 47 males). The mean age at onset was 62.7 years, and 66 patients (52.3%) were both RF and ACPA positive, while 39 patients (31.0%) were both negative. Of these, 13 patients (10.3%) had sacroiliac joint changes. As a result of the logistic analysis, both RF and ACPA negativity were significant risk factors, with the odds ratio 6.27 ($p<0.01$). [Conclusion] The results of this study showed that when both RF and ACPA were negative, many patients had sacroiliac joint findings and suggested that SpA may occur not only in young people but also in relatively elderly people.

P3-099

Long -Term Experience with Biologics for Ankylosing Spondylitis

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Conflict of interest: None

Purpose: We report two patients with ankylosing spondylitis (AS) who experienced no improvement in symptoms despite various therapies. In case 1, the patient was a 38-year-old male, with disease onset in 2012. He was diagnosed with AS as seronegative and started on methotrexate (MTX) treatment; however, the effect was insufficient. In case 2, the patient was a 38-year-old female, with disease onset in 2011. She presented with arthralgia, lumbosacral pain, and adhesiolysis, and was diagnosed with AS with seronegative symptoms. After more than 1 year, while the Bath Ankylosing Spondylitis Metrology Index (BASMI) did not improve in case 1, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) decreased, and Bath Ankylosing Spondylitis Functional Index (BASFI) improved and was maintained. In other words, the disease activity was suppressed, and functional capacity improved. Conversely, in case 2, BASMI, BASDAI, and BASFI remained unchanged. Both cases had no progression of joint destruction observed on the radiographic examination. **Conclusion:** Infliximab and adalimumab were found effective and their efficacy was maintained when administered early in the treatment of AS for patients with inadequate response to MTX and prednisone and with high disease activity.

P3-100

A case of ankylosing spondylitis (AS) complicated with various gastrointestinal lesions

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Conflict of interest: None

[Case] Male in his 50s, X-15, was started with IFX at AS, moved for work and was transferred to a new hospital, where he was further switched to ADA and IXE; moved to Kansai in March, X-2, at this hospital again. 1/28, referred to Hospital A for enterocolitis, 2/15: Suspected IXE-related IBD, IXE was withdrawn, but CRP persisted, and the patient was switched to CZP. On July 3, He was rushed to Hospital B because of abdominal pain and diarrhea after eating raw senmai, and was transferred to our hospital. GIF showed multiple ulcers, AGML image, CS showed, ring and longitudinal ulcer. Both CMV-DNA positive with additional treatment; Bio Tx was changed to UPA on 7/21. On 9/6, patient was rushed to the emergency department of Hospital A at night due to lower abdominal pain, was admitted for surgery as he needed urgent decompression. At his request, he was transferred from Hospital A to our hospital, and his condition became mild with control of ileus tube and bowel movement. The patient symptoms have been stable since then. [Conception and Conclusion] This is a case of AS complicated with various gastrointestinal lesions. Analysis of the various factors that could be attributed to drug (IXE, NSAIDs), viral, and dietary factors was important for the differential diagnosis.

P3-101

A case of ankylosing spondylitis complicated with renal dysfunction due to retroperitoneal fibrosis and cervical myelopathy, which was difficult to pathological diagnose and treat

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Conflict of interest: None

[Case] A 73-year-old man was diagnosed with cervical and lumbar spondylosis in our orthopedics 11 years ago. He underwent surgery for lumbar vertebral osteomyelitis 6 years ago. Thereafter, he had persistent back pain that did not improve with rest and was treated with loxoprofen. Gradually, CRP value elevated, and his range of motion in the back was limited. X-rays showed cervicothoracic fusion and sacroiliitis. He was diagnosed with ankylosing spondylitis (AS) 1 year ago. Suddenly, fever, weakness of the legs, and dysuria appeared. He underwent surgery for a suspected lumbar epidural abscess, but no abscess was found. Antibacterial drugs did not improve his condition. Gradually, renal dysfunction developed and loxoprofen was discontinued. He was referred to our department after a CT scan showed retroperitoneal lesions and hydronephrosis, and an MRI scan showed cervical spondylitis and spinal cord lesions. We diagnosed with retroperitoneal fibrosis (RPF) and cervical spondylitis due to AS. Prednisolone 35 mg/day improved RPF, but chronic renal failure was complete. Secukinumab improved AS, but cervical myelopathy remained. [Conclusion] In patients with RPF-induced renal dysfunction and AS, aggressive administration of biologics with steroid therapy may improve the disease state.

P3-102

A Case of a Woman with Ankylosing Spondylitis that Improved with Certolizumab Pegol 400 mg Every Other Week and Experienced Pregnancy and Delivery

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Conflict of interest: None

[Case] Twenty-six woman [Current history] At the age of nine, she developed multiple joint pains. At age of twenty-three, she was diagnosed with spondyloarthritis and was treated with salazosulfapyridine plus methotrexate (MTX), which mildly improved but later worsened. [Clinical Course] At age 25, she was diagnosed with ankylosing spondylitis (AS). Iguratimod was added but was ineffective, and bDMARD was scheduled to be started. Considering future fertility, The MR vaccine was given while only MTX was continued, and then adalimumab (ADA) 40 mg bi-weekly was started but remain ineffective, and the ADA dose was increased to 80 mg. Her symptoms slightly lessened. Considering the need to discontinue ADA in the middle of pregnancy and the possibility of worsening due to discontinuation of ADA, she was switched to certolizumab pegol (CZP) 400 mg bi-weekly. Her arthralgia improved markedly and she became pregnant ten months later. Her symptom slightly worsened and she gave birth at 37 weeks' gestation without any pregnancy complications. [Clinical Significance] She was able to experience pregnancy and delivery with the introduction of CZP. CZP 400 mg bi-weekly may be considered one option in AS patients who wished to have a child, when disease activity was high.

P3-103

Prediction equation for appendicular lean mass using anthropometric measurements in patients with SLE

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Conflict of interest: None

[Objectives] This study aims to calculate a prediction equation for appendicular lean mass (ALM) using anthropometric measurements in pa-

tients with SLE. [Methods] We conducted a cross-sectional survey of SLE patients. The ALM was assessed by DXA. The prediction equation for ALM was a multiple regression equation using six factors: age, sex, height, weight, grip strength, and calf circumference. The LOOCV was used for validation of the prediction equation. The agreement between the measured and the estimated ALM was verified by the Concordance Correlation Coefficient (CCC). In addition, the accuracy and agreement for determining skeletal muscle mass loss were evaluated. [Results] A total of 110 SLE patients (mean age 48 years, 84% female) were included in the analysis. The accuracy of the ALM prediction equation was good (R^2 = 0.91, SEE = 1.28), and the validation results were consistent (R^2 = 0.88, RMSE = 1.38, MAE = 1.08). The agreement between measured and estimated ALM was moderate (CCC = 0.90). The accuracy of determining skeletal muscle mass loss was sensitivity: 100%, specificity: 63.5%, PPV: 44.6%, NPV: 100%, and kappa coefficient: 0.44. [Conclusion] It might be possible to estimate ALM in SLE patients with a certain degree of accuracy using anthropometric measurements.

P3-104

Investigation of Serum Parameters Associated with Abdominal CT Findings in Lupus Enteritis

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Conflict of interest: None

[Background] Lupus enteritis (LE), a rare manifestation of systemic lupus erythematosus, is typically diagnosed through abdominal CT. This study explored correlations between serum parameters and CT findings in LE patients. [Methods] This single-center cross-sectional study examined LE cases diagnosed at our department from January 2009 to September 2024. We analyzed correlations between CT findings and serum parameters (anti-dsDNA antibody, complement levels, calprotectin, anti-gAChR antibody) using Spearman's correlation. [Results] The study included 15 patients (19 events), median age 44, with 14 females. Abdominal CT showed median values [IQR]: maximum external intestinal diameter 22.0 mm [19.0-31.0], internal diameter 18.0 mm [14.0-25.0], and wall thickness 8.3 mm [4.8-10.6]. Maximum external diameter correlated positively with C3 (p=0.001, r=0.69), C4 (p=0.002, r=0.71), and CH50 (p=0.003, r=0.65). Maximum internal diameter also correlated with C3 (p<0.001, r=0.83), C4 (p=0.001, r=0.75), and CH50 (p=0.002, r=0.68). Other parameters showed no significant correlations. [Conclusion] In LE, greater intestinal dilation correlates with increased complement levels, while calprotectin and anti-gAChR antibody levels show no association with CT findings.

P3-105

Rheumatic Diseases Associated with Antiphospholipid Syndrome: A Single-Center Retrospective Study

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Conflict of interest: Yes

Background: APS can occur as an isolated (primary APS), or secondary to rheumatic disease. In a large European study, 40% of APS is associated with systemic lupus erythematosus (SLE) and 5% with other rheumatic diseases. **Objective:** To investigate the clinical and serological characteristics of patients with secondary APS (sAPS) in our hospital. **Methods:** We retrospectively reviewed medical records of patients with positive antiphospholipid antibody (APLA) at our hospital from March 1, 2013, to September 30, 2024. APS diagnosis was based on the Revised Sapporo Classification Criteria. **Results:** Of the 57 patients with APS, 17 (29.8%) had rheumatic diseases. Thirteen (76.4%) of the patients had SLE, 3 (17.6%) had primary Sjogren's syndrome, and 1 (5.6%) had rheumatoid arthritis. Among 20 patients with positive APLA who did not meet the criteria for APS, 16 (80%) of the patients had SLE and 4 (20%) were positive for anti-Ro antibody. **Conclusion:** Sjogren syndrome may be more common in patients with sAPS.

P3-106

Comparative study on new and previous classification criteria for antiphospholipid antibody syndrome

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Conflict of interest: None

[Objectives] Comparative study between 2023 ACR/EULAR classification criteria for antiphospholipid antibody syndrome (APS) (APS2023) and 2006 Sapporo Criteria Sydney Modification (APS2006) was performed. [Methods] Sixty-three APS cases diagnosed by APS2006 from 2013 to 2024 were reassessed by APS2023 (mean age: 55±18 years-old, eight males, fifty-five females). There were 29 cases of primary APS and seven cases were obstetric APS. [Results] All cases fulfilled three or greater points in the clinical domain of APS2023. On the other hand, eight cases could not be classified as APS because the antiphospholipid antibody titer measured by chemiluminescence immunoassay (CLIA) did not meet the ACR2023 laboratory criteria. [Conclusion] The clinical domains of APS2023 were considered to be comparable to ACR2006. On the other hand, some cases might not be diagnosed as APS based on the laboratory domain of ACR2023.

P3-107

Cases of elderly patients with serologically positive anti-dsDNA antibody

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Conflict of interest: None

[Objective] Anti-dsDNA antibody is a specific antibody for systemic lupus erythematosus (SLE), more likely to occur in young women. We discuss the clinical significance of positive anti-dsDNA antibodies in elderly patients. [Method] We investigated 11 elderly patients (7 women and 4 men) with positive anti-dsDNA antibodies who were referred to our department from May 2022 to August 2024. [Result] The mean age of women was 71.8 years and men 72.3 years, with no differences between the sexes. Anti-nuclear antibody was positive in all patients. The median anti-dsDNA antibody titer was 84 for all patients, 158.5 for women and 21 for men. The chief complaint of each of the 4 male patients was fever in 2, lymphadenopathy in 1, and pleural effusion in 1. The All patients fulfilled the EULAR/ACR2019 classification criteria. The diagnosis of 6 in 7 female patients and 1 in 4 male patient was SLE. In male patients, glucocorticoid therapy was administered in 1 case with SLE. In other 3, anti-dsDNA antibody titers declined without glucocorticoid therapy. [Conclusion] Anti-dsDNA antibodies have high sensitivity and specificity in the diagnosis of SLE. But, epidemiologically atypical cases require multifaceted evaluation, and initiation of glucocorticoid therapy should be carefully considered.

P3-108

Osteonecrosis and Thrombosis in Systemic Lupus Erythematosus: A 143-patient Retrospective Cohort Study on the Impact of Glucocorticoid Pulse Therapy

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Conflict of interest: None

[Objectives] Osteonecrosis of the femoral head (ONFH) and thrombo-

sis are serious complications in patients with systemic lupus erythematosus (SLE), but the impact of glucocorticoid pulse therapy (IVMP) remains controversial. This study investigated risk factors for both complications. [Methods] We conducted a retrospective cohort study of 143 SLE patients treated at Osaka University Hospital from 2010 to 2024. ONFH was diagnosed by MRI or requirement for surgical intervention. Antiphospholipid syndrome (APS), disease duration, age at SLE onset, relapse, lupus nephritis, IVMP, and biological agents (Bio) were analyzed using univariate and multivariate logistic regression. [Results] 25 patients developed ONFH at a mean age of 37.6 years. Univariate analysis identified longer disease duration (p=0.042) and younger age at SLE onset (p=0.012). Thrombosis occurred in 40 patients, with 31 having APS. APS was an independent risk factor for thrombosis (p<0.001). 72 patients received IVMP and 43 received Bio. Multivariate analysis showed no significant association between IVMP and either complication. [Conclusion] Younger age at onset and longer disease duration were associated with ONFH, while APS was associated with thrombosis. No association was found between IVMP and either complication.

P3-109

Hydroxychloroquine initiation timing is associated with the osteonecrosis of the femoral head in SLE patients

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus (SLE) is a risk factor for osteonecrosis of the femoral head (ONFH), and glucocorticoids (GC) are implicated in its pathogenesis. The 2023 EULAR recommendations advocate GC reduction or discontinuation and the use of hydroxychloroquine (HCQ). This study aims to investigate the incidence of ONFH in SLE patients and to explore the association between ONFH development and HCQ administration. [Methods] We conducted a cross-sectional study of 155 patients (137 females and 18 males) at the Department of Collagen Diseases. The mean age at SLE onset was 34.6 years, and the disease duration was 15.5 years. GC pulses were administered in 41.9%, with a mean maximum GC dose of 49.7 mg. The mean maintenance GC dose was 3.1 mg. 65% patients were continuing HCQ at the time of suurvey. We evaluated factors associated with ONFH, comparing the ONFH and non-ONFH groups. [Results] Maximum GC dosage (ONFH group: mean 49.7 mg, non-ONFH group: 35.6 mg, p=0.002) and HCQ initiation time (ONFH group: mean 13.8 years, non-ONFH group: 8.8 years, p=0.003) were significant factors associated with ONFH. [Conclusion] HCQ also plays a role in preventing flares. The prevention of flares by HCQ is expected to decrease in the use of GCs and to reduce the risk of ONFH development.

P3-110

Patient background and clinical course of a case of anifrolumab introduced for systemic lupus erythematosus

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Conflict of interest: None

[Objectives] We aimed to evaluate the clinical features and efficacy of anifrolumab (ANI) in patients with systemic lupus erythematosus (SLE). [Methods] 11 patients included initiated ANI at our department from 2022 onwards and had follow-up for 12 months by October 2024. We assessed disease activity indices, laboratory findings, glucocorticoid (GC) dosage, the achievement rate of LLDAS, the Lupus Impact Tracker (LIT), before and after treatment. [Results] All 11 patients were female, with a mean age of 42.27±13.23 years and a mean disease duration of 95.45±59.07 months. Main symptoms included joint pain (6), skin rashes (5), fever (1), fatigue (1). Concomitant medications included hydroxychloroquine (10), tacrolimus (3), methotrexate (1), mycophenolate mofetil (2). Changes observed after 12 months included a decrease in LIT from 42.73 to 40.45 and anti-dsDNA antibodies from 49.82 to 35.64 IU/mL. Significant reductions were in PGA 1.27 to 0.46 and GC dosage 6.36 to 4.18 mg/day. SLEDAI-2K decreased from 6.0 to 2.0, with improvement in skin rashes. The LLDAS achievement rate increased from 18.2% at baseline to 45.5% at 12 months. [Conclusion] ANI may be effective in reducing GC dosage, lowering PGA and SLEDAI-2K, improving skin rashes, and increasing LLDAS achievement rates in with SLE.

P3-111

Effect of Anifrolumab on Glucocorticoid Reduction and Withdrawal in Patients with Systemic Lupus Erythematosus

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Conflict of interest: None

[Objective] To evaluate the efficacy of anifrolumab (ANI) in patents with systemic lupus erythematosus (SLE) in real clinical practice. [Methods] SLE patients treated with ANI continuously for at least 12 months were included. Clinical information was retrospectively collected and evaluated SLEDAI, daily glucocorticoid (GC) dose, and relapse. [Results] Seventeen female patients were introduced, ANI was introduced as the first molecularly targeted therapy in 7 pts (first group) and 10pts switched from belimumab (switching group). Both, SLEDAI and daily GC dose significantly decreased; 4 (median) to 2, and 5.5 mg to 2.0 mg. In comparison of first and switch group, SLEDAI significantly decreased in the switch group; from 4 [0-8] to 2 [0-8] (P=0.250), 4 [2-8] to 2 [0-5] (P= 0.016), daily GC dose significantly decreased in both groups; 8.0 mg [1.5-30] to 0.0 mg [0-9] (P=0.016), 5.3 [3-14] mg to 3.3 [0-10] mg (P=0.008), and 4 and 1 pt was able to withdraw GC respectively. One relapse due to arthritis was observed in each groups. [Conclusion] Addition of ANI or switching from BEL in patients with residual disease activity allowed for a reduction in disease activity and a reduction or withdrawal of GC doses. In was considered useful particularly in cases of residual disease activity on BEL treatment.

P3-112

A Case of Primary Sclerosing Cholangitis Developing During Rituximab Therapy for Systemic Sclerosis

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Conflict of interest: None

A 78-year-old woman with a history of Raynaud's phenomenon presented with finger swelling one year prior. She was diagnosed with anti-Scl-70 antibody-positive systemic sclerosis (SSc) with diffuse skin sclerosis (mRSS 44). Echocardiography showed elevated TRPG levels with left ventricular diastolic dysfunction, while cardiac MRI indicated myocardial involvement secondary to SSc. Rituximab (RTX) was administered as treatment for progressive skin sclerosis, with four doses given over six months. During this period, there was no significant liver dysfunction. However, four months after completing the second course, she developed right upper quadrant pain, accompanied by elevated liver enzymes. ERCP revealed stenosis of both intrahepatic and extrahepatic bile ducts, characterized by multifocal stricturing and beaded appearance. A liver biopsy ruled out autoimmune hepatitis and primary biliary cholangitis, leading to a diagnosis of primary sclerosing cholangitis (PSC). Treatment with ursodeoxycholic acid resulted in gradual improvement of liver enzyme levels. **Clinical significance:** The development of PSC during B-cell depletion therapy for SSc is a rare occurrence, providing valuable insights into the potential interplay between autoimmune conditions and B-cell-targeted therapies.

P3-113

A case of anti-eIF2B antibody positive systemic sclerosis with interstitial lung disease and dermatomyositis successfully treated with combination immunosuppressive therapy after improvement of thrombotic microangiopathy

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Conflict of interest: None

[Case] A 45-year-old female was diagnosed with diffuse cutaneous systemic sclerosis, dermatomyositis, and interstitial lung disease (ILD) four years prior. She was positive for anti-eIF2B and anti-SS-A antibodies. Having been stable on prednisolone (PSL) 0.5 mg/kg/day and tacrolimus (Tac), her condition worsened one year prior. Adding 5 sessions of cyclophosphamide did not work, and she was hospitalized in May. Steroid pulse therapy and Tac dose increase to 10 mg were done. Then she developed thrombotic microangiopathy (TMA). We discontinued Tac and initiated plasma exchange, resulting in rapid improvement. Then mycophenolate mofetil (MMF) was started and increased to 3 g. ILD became stable, but myositis persisted. In July, rituximab (RTX) was added. ILD improved, but creatine kinase (CK) levels remained elevated. We combined intravenous immunoglobulin therapy in August, which eventually normalized CK levels in October. [Clinical Significance] Efficacy of combined RTX and MMF therapy has been reported for inflammatory myopathies and ILD. It can be also effective in anti-eIF2B-antibody positive cases. Relationship between the antibody and TMA may need further clarification.

P3-114

Treatment of nintetanib for interstitial lung disease associated with systemic sclerosis

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Conflict of interest: None

Objective. To analyze the results of the use of nintetanib in SSc-ILD. Methods. Thirteen patients who were introduced nintetanib for SSc-ILD were included in the study. Results. The mean age at the time of introduction of nintetanib was 62 years, and the duration of disease was 10.4 years. The skin score was 10, and the forced vital capacity was 1.84 L. The starting dose of nintetanib was 300 mg in 8 patients and 150 mg in 5 patients. Prednisolone was used in 77% and other immunosuppressive agents in 85% of patients. About 15% had diarrhea, nausea, or other gastrointestinal symptoms within 3 months of starting nintetanib, and 8% had liver damage. Three patients discontinued nintetanib within one year of starting nintetanib due to side effects. Clinical symptoms and respiratory function tests improved markedly in only one case. Overall, there was a decrease in prednisolone use and KL-6 levels after one year. Discussion. Adverse effects within 3 months of nintetanib initiation were no more common than those seen in the results of the nintetanib post marketing surveillance. Proactive screening was considered important so that nintetanib could be introduced before lung function declined.

P3-115

A case of anti-PM-Scl 75/100 antibody-positive systemic sclerosis/polymyositis overlap syndrome treated with rituximab and mycophenolate mofetil

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Conflict of interest: None

[Case] A 54-year-old woman had stiffness in both fingers for two years, and swelling of the hands and general fatigue for two months. On examination, she had skin sclerosis involving both hands, and skin biopsy findings were consistent with systemic sclerosis. She also had interstitial lung disease (ILD). ILD was mainly composed of NSIP on CT and cryobiopsy, with some findings of OP. In addition, CK and aldolase levels were elevated, and MRI showed fasciitis in the flexor muscles of the thigh. Then, autoantibody testing using the indirect fluorescent antibody method revealed both anti-PM-Scl 75 and anti-PM-Scl 100 antibodies were positive. Therefore, we diagnosed her with systemic sclerosis/polymyositis overlap syndrome and carried out remission induction therapy using only rituximab (RTX). RTX improved her skin sclerosis, and we then chose mycophenolate mofetil. [Discussion] Anti-PM-Scl antibodies have been reported to be associated with systemic sclerosis/polymyositis overlap syndrome and anti-PM-Scl antibody-positive patients often have ILD. However, the optimal medication is still unknown. In this case, we did not use glucocorticoids, considering the risk of inducing renal crisis. We report on this case, including its clinical course and a literature review.

P3-116

Association of NCF2 missense variant with systemic sclerosis in a Japanese population

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Conflict of interest: Yes

[Objectives] *NCF1* and *NCF2* genes encode components of NADPH oxidase (NOX2) complex. We previously reported association of *NCF1* missense variant, p. Arg90His, with systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) in a Japanese population (Yokoyama et al., 2019). In addition, we recently detected association of *NCF2* p. Arg395Trp with SLE. In this study, we examined whether *NCF2* variants are associated also with SSc. [Methods] Association between three *NCF2* missense variants, p. Lys181Arg, p. Thr279Met and p. Arg395Trp, with SSc was performed on 315 Japanese patients. Allele frequency data on approximately 60,000 controls (60KJPN) registered in the Japanese Multi Omics Reference Panel (jMorp) were used as controls. [Results] Significant association of *NCF2* variants with overall SSc was not detected. However, when the patients were classified by clinical phenotypes or autoantibodies, significant association of p. Arg395Trp with anti-centromere antibody (ACA) positive SSc was detected (P: 0.020, odds ratio: 2.03, 95% confidence interval: 1.10-3.72). [Conclusion] Significant association between *NCF2* missense variant with ACA-positive SSc was detected in the Japanese population, supporting a role of NOX2 complex variants in susceptibility not only for SLE but also for SSc.

P3-117

A case of diffuse cutaneous systemic sclerosis (dcSSc) with a single positive for anti-uncoupled-Ro52 antibody

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Conflict of interest: None

[Case] 57-year-old female [Chief complaint] Dyspnea [Current medical history] She was aware of Raynaud's phenomenon since X-2. In X-1,

she started to suffer from dry cough and dyspnea. In January X, her skin hardening began to appear on the whole body. In February X, she took a chest CT scan and blood test at our hospital. It showed bilateral lower lobe interstitial pneumonia and high KL-6 level. The mRSS score was 28 and we diagnosed her with dcSSc. The major antibodies of dcSSc are all negative, so we looked at another antibody with EUROLINE test, which revealed a single positive for anti-uncoupled-Ro52 antibody. 10 mg prednisolone (PSL) and mycophenolate mofetil were started. She was discharged thanks to respiratory symptoms improved. However, in April X, she was re-admitted due to worsening dyspnea and skin sclerosis. 30 mg PSL, rituximab and nintedanib were started. After that, the progression of symptoms was slowed down. [Clinical Significance] We have experienced a case of dcSSc with a single positive for anti-uncoupled-Ro52 antibody. It has been reported that patients with the antibody alone are more likely to develop interstitial pneumonia and have a poorer prognosis than those who had another antibody, so we need to check this antibody if the major antibodies are negative.

P3-118

Esophageal Dilation in Scleroderma Indicates Poor Prognosis

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Conflict of interest: None

Objective: To investigate the relationship between esophageal diameter measured by CT and nutritional status, lung lesions, and prognosis. Subjects: Twenty scleroderma patients treated at our department from April 2016 to August 2024 who completed follow-up. Methods: Esophageal diameters were measured on chest CT at three levels: A (cervical esophagus), B (pulmonary vein), and C (diaphragm). Results: The average age was 66.75 years (SD 14.95), with 2 males and 18 females; 9 had diffuse scleroderma and 11 had limited scleroderma; 9 had interstitial pneumonia. Esophageal diameters were A: 8.3 mm (SD 10.3), B: 15.0 mm (SD 0.20), C: 14.1 mm (SD 11.1). Correlation coefficients between albumin and esophageal diameter were showing an inverse correlation for A and B with albumin values. Correlation coefficients between BMI and esophageal diameter were indicating a weak inverse correlation. In survivors, esophageal diameters were A: 5.25 mm, B: 10.4 mm, C: 11.5 mm; in deceased cases, they were A: 15.5 mm, B: 25.8 mm, C: 20.1 mm, with significantly higher values for A and B in deceased cases. Conclusion: Esophageal diameter was associated with malnutrition and prognosis, reflecting gastrointestinal lesions in scleroderma.

P3-119

Clinical Investigation of Anti-RNA Polymerase III Antibody-Positive Cases in Our Hospital

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Conflict of interest: None

Objective: Anti-RNA polymerase III antibody (anti-RNAPIII) is specifically detected in systemic sclerosis (SSc). This study examined its clinical features, including its presence in other autoimmune diseases. **Methods:** We analyzed anti-RNAPIII-positive cases from our hospital, focusing on underlying diseases and clinical features. **Results:** From December 2010 to June 2024, 2556 cases were tested for anti-RNAPIII, and 53 (2.1 %) were positive (15 males, 38 females). The average age was 66.8 for males and 62.6 for females. Of the 53, 41 (77.4%) had SSc: 22 (53.7%) with diffuse cutaneous SSc (dc-SSc) and 19 (46.3%) with limited cutaneous SSc (lc-SSc). Interstitial pneumonia was found in 32 cases (78.0%), digital ulcers in 10 (24.4%), pulmonary arterial hypertension (PAH) in 5 (12.2%), and renal crisis in 2 (4.88%). Additionally, 12 had other diseases: Sjögren's syndrome (4), rheumatoid arthritis (2), systemic lupus erythematosus (1), mixed connective tissue disease (1), and 3 others. Malignancies were seen in 10: 3 with dc-SSc, 6 with lc-SSc, and 1 with RA. **Conclusion:** Anti-RNAPIII-positive SSc was linked to dc-SSc and renal crisis, as previously reported. However, lc-SSc and other autoimmune diseases had higher incidences of malignancy and PAH.

P3-120

Evaluation of predictive factors for progression of SSc-ILD with anti-RNA polymerase III antibodies positive based on HRCT scoring

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Conflict of interest: None

[Objective] To evaluate predictive factors for progression of anti-RNA polymerase III (RNAPIII) antibody positive SSc-ILD using HRCT scoring. [Subjects and Methods] 26 consecutive cases of anti-RNAPIII antibody positive SSc-ILD. HRCT scoring was evaluated by semi-quantitatively calculating ground-glass opacity (GGO) score and fibrosis score using the chest CT score by Kazerooni et al. [Results] Among 11 patients (PPF group) who developed progressive pulmonary fibrosis (PPF) during the observation period and 15 patients (non-PPF group), the fibrosis score of the left lower lobe at the time of SSc-ILD diagnosis was 1 (0.67-1) in the PPF group and 0.67 (0.33-0.67) in the non-PPF group, which was significantly higher in the PPF group (P=0.013). In the group with a left lower lobe fibrosis score higher than 0.67 (high fibrosis group; 10 cases) and the group with a left lower lobe fibrosis score of 0.67 or less (low fibrosis group; 16 cases), there were significantly more men in the high fibrosis group (P=0.041), and the KL-6, Cr, and mMRC dyspnea scale were also significantly higher (P=0.018, 0.035, 0.039). [Conclusion] The left lower lobe fibrosis score (>0.67) at the time of diagnosis of anti-RNAPIII antibody positive SSc-ILD may be a predictor of ILD progression.

P3-121

The safety and efficacy of long-term use of avacopan (AVA) in patients with microscopic polyangiitis and granulomatosis with polyangiitis (single-center case series)

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Conflict of interest: Yes

[Objectives] To examine the safety and efficacy of AVA for MPA/GPA. [Methods] We investigated the medical records of 14 cases of MPA/GPA who were observed for more than 52 weeks from the start date of the AVA prescription until October 2024. [Results] Patient background: the remission/re-remission induction in 5 patients (MPA 2, GPA 3) was the average 74.2 years old, BVAS 13.4, PSL 40.0 mg/day. Concomitant immunosuppressants were 3 RTX, 1 IVCY, and 1 AZA. Maintenance in 9 (MPA 6, GPA 3) was 69.1 years old, BVAS 1.0, PSL 9.8 mg/day, and maintenance immunosuppressants were 5 RTX and 2 AZA. As of week 52, nine patients continued AVA (1 relapse; mean PSL of patients who achieved remission/re-remission was 9.3 mg, mean PSL of patients who maintained remission was 4.8 mg), and five patients discontinued (2 liver dysfunction, one death by asphyxiation, one insufficient effect, one transfer to another hospital). Between week 52 and the final observation, there was one relapse and two serious infections (1 death). [Conclusion] A decrease in BVAS was confirmed with the use of AVA. Attention must be paid to liver dysfunction in the early course of treatment. In the long term, RTX may be combined to maintain remission, so attention must be paid to infectious diseases.

P3-122

Two Cases of Microscopic Polyangiitis with successful Perioperative Management through Steroid Reduction Achieved by the Addition of Avacopan

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Conflict of interest: None

[Introduction] We report two cases of microscopic polyangiitis (MPA) in which perioperative management was favorable with the use of avacopan. [Case 1] A 30-year-old woman. Diagnosed with Graves' disease at age 27. Treated with propiothiouracil (PTU) due to thiamazole and potassium iodide allergy. Proteinuria, swelling and pain in the lower legs, and positive MPO-ANCA were observed, and PTU-induced MPA was diagnosed. Remission was induced with prednisolone (PSL) 30 mg/day and rituximab (RTX). Avacopan was started and the dose of PSL was reduced to 10 mg/day. Total thyroidectomy was performed approximately 3 months after the start of treatment. [Case 2] A 72-year-old woman. Diagnosed with MPA at age 70. During maintenance therapy with PSL 10 mg/day, bilateral peroneal nerve palsy occurred, and relapse of MPA was diagnosed. Remission was induced with PSL 50 mg/day and RTX. At this time, early gastric cancer was diagnosed. Avacopan was started and the dose of PSL was reduced to 12.5 mg/day. Gastrectomy was performed approximately 3 months after the relapse. [Discussion] The possibility of safe and rapid steroid reduction prior to surgery by using avacopan in combination was suggested.

P3-123

The efficacy and clinical analysis of Avacopan in the treatment of ANCA-associated vasculitis: a single center experience

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Conflict of interest: None

[Objectives] ANCA-associated vasculitis (AAV) treatment methods have improved prognosis. Since 2022, Avacopan (AVA) has been used to treat AAV. We evaluated its efficacy and analyzed AAV patients in our department. [Methods] We evaluated 12 AAV patients (6 males and 6 females) who received AVA treatment from June 2022 to August 2024, including the BVAS, clinical analysis, and glucocorticoid (GC) reduction after 24 weeks. [Results] 12 AAV patients, 9 MPA (all MPO-ANCA) and 3 GPA (all PR3-ANCA), received AVA in 2 newly diagnosed, 2 relapsed and 8 maintenance phases. The mean age was 76.2 years, disease duration was 1.7 years, GC dose was 17.5 mg/day, and immunosuppressive drugs were used in 7 patients. Interstitial pneumonia, nephritis, neuropathy affected 75% (7/12), 50% (6/12), and 41.7% (5/12) of patients. After 24 weeks of AVA treatment, BVAS, CRP, ANCA, serum Cr, and GC dose changed: -3.11 ± 5.19, -1.2 ± 2.23 mg/dL, -34.5 ± 65.9 U/mL, -0.02 ± 0.23 mg/dL, -8.8 ± 10.6 mg, and KL-6 145.8 ± 92.8 U/mL in patients with interstitial pneumonia. Two patients discontinued AVA due to hepatotoxicity and one patient required rituximab. [Conclusion] AVA may not be effective in the treatment of AAV-ILDs, but it has significantly reduced GC dose, and a rapid GC reduction effect is expected.

P3-124

Study on the Optimal Glucocorticoid Dosage When Using Avacopan

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Conflict of interest: None

[Objectives] Avacopan has been proposed as a steroid-sparing treatment for ANCA-associated vasculitis (AAV), but the optimal regimen remains uncertain. Based on our institution's experience, this study aimed to determine the optimal glucocorticoid (GC) dose when using avacopan. [Methods] We retrospectively reviewed cases of AAV patients treated with avacopan at our Hospital from April 2023 to September 2024. [Results] Four cases were included, with patients aged 50s to 80s (1 male, 3 females), all positive for MPO-ANCA. Avacopan was continued for 52 weeks in two cases; one case discontinued due to rash and another due to liver dysfunction. GC doses were increased in two cases following avacopan discontinuation and in one case due to relapse. [Conclusion] The ADVOCATE trial showed similar renal function improvement between GC and non-GC groups after 4 weeks, suggesting that GC-free treatment might be challenging in severe cases. Our experience suggests that appropriate avacopan use may reduce cumulative GC exposure. We recommend using GCs according to the PEXIVAS protocol for the first 4 weeks, followed by a rapid taper. For AAV cases treated with avacopan, an accelerated GC taper, rather than complete GC elimination, may safely reduce cumulative GC exposure in severe disease.

P3-125

The effectiveness and safety of rituximab in maintenance therapy for microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA)

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Conflict of interest: Yes

[Background] MPA and GPA have shown dramatic improvements in remission rates with induction therapy. However, the high relapse rate remains a significant issue. Although RTX shows higher sustained remission rate comparative to azathioprine (N Engl J Med 2014; 371: 1771-80), since that study focused on GPA or PR3-ANCA-positive patients, which differs from the population of Japanese patients, raising questions about applicability in Japan. [Objective] To evaluate the effectiveness and safety of RTX in maintenance therapy in our hospital. [Methods] MPA/GPA patients in our hospital who were newly diagnosed or had severe relapse were classified by maintenance therapies. Severe infection rates and relapse-free survival rates were compared. [Results] 80 MPA/GPA patients in our hospital were included in analysis. Severe infections by 48 and 104 weeks occurred in 1 case (7.1%) and 0 case (0%) respectively in the RTX group, compared to 3 cases (7.6%) and 4 cases (10.5%) respectively in the non-RTX group. At 104 weeks, relapse-free survival rate was 100% (9 cases) in the RTX group and 92.1% (35 cases) in the non-RTX group. [Discussion] The effectiveness and safety of RTX in maintenance therapy were shown in MPA/GPA patients in our hospital.

P3-126

Combination therapy of rituximab with avacopan for microscopic polyangiitis and rapidly progressive glomerulonephritis with difficult-to-treat rheumatoid arthritis (D2TRA): A Case Report

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Conflict of interest: None

Case Report: A 67-year-old woman had been treated for difficult-to-treat rheumatoid arthritis (D2TRA) with sulfasalazine and tacrolimus after three biologics failed. Her serum creatinine was around 0.5 mg/dL up to two months before admission. Urine sediment analysis initially showed hematuria. After a month, her creatinine level worsened to 0.99 mg/dL with proteinuria and glomerular hematuria, and MPO-ANCA reached 1200 U/mL. A renal biopsy confirmed crescentic glomerulonephritis. On admission, creatinine was 2.05 mg/dL. After half-dose intravenous methylprednisolone pulse therapy (500 mg/day for 3 days), she was switched to oral prednisolone 50 mg/day. From day 5 and 6, rituximab (375 mg/m^2/week, total 4 times) and avacopan (60 mg/day) were administered, respectively. On day 18, creatinine improved to 0.91 mg/dL, and MPO-ANCA decreased to 200 U/mL, with normalized inflammatory markers. She was discharged on day 27, with no clinical flare after early tapering of prednisolone. Conclusion: We reported a case of microscopic polyangiitis and rapidly progressive glomerulonephritis with D2TRA. Rituximab therapy combined with avacopan can effectively treat renal involvement, regardless of comorbid D2TRA.

P3-127

Large Vessel Vasculitis Detected during MPO-ANCA Re-elevation and Treated with Rituximab in a Patient with Microscopic Polyangiitis

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Conflict of interest: None

A 75-year-old man presented with numbness and muscle weakness in both legs. Based on elevated MPO-ANCA, proteinuria, and peripheral neuropathy, he was diagnosed with microscopic polyangiitis (MPA). Remission was achieved with prednisolone 30 mg/day, allowing a gradual reduction to 5 mg/day. 8 years later, MPO-ANCA re-elevated without exacerbation of existing symptoms. One year later, he reported hypertension, and blood pressure measurements revealed significant differences between arms (left 162/107 mmHg, right 186/117 mmHg). Contrast CT showed left subclavian artery occlusion and left common carotid artery wall thickening. PET-CT demonstrated increased FDG uptake in both the left common carotid and right subclavian arteries, leading to the diagnosis of large vessel vasculitis. Remission induction therapy with prednisolone 60 mg/day and rituximab was initiated. Although rituximab was discontinued after three courses due to COVID-19, MPO-ANCA normalized and carotid artery wall thickening improved. This case demonstrates large vessel vasculitis diagnosed during MPA course without typical small vessel vasculitis exacerbation. Reports of rituximab use for MPA with large vessel involvement are limited, and this case suggests its potential efficacy.

P3-128

A case of polyarteritis nodosa with multiple ulcers on the lower leg and necrotizing soft tissue infection

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Conflict of interest: None

The patient is a 65-year-old woman. She presented to our department with leg edema and ulcer. Echocardiography revealed heart failure due to old myocardial infarction, which was the cause of the leg edema. A skin biopsy revealed vasculitis, and a diagnosis of polyarteritis nodosa was made and the patient was admitted to the hospital. The patient was treated with prednisolone 55 mg and IVCY 800 mg, and was discharged. However, after discharge from the hospital, the patient presented to the clinic with fever and leg pain. Based on elevated white blood cell counts, the patient was considered to have an infected leg ulcer. He was judged to have necrotizing soft tissue infection and underwent surgical debridement in addition to TAZ/PIPC administration. New ulcers were observed on the lower leg, so IVCY 800 mg/2 weeks 3 times was administered; AZA was also introduced, and the appearance of new ulcers subsided. We experienced a case of polyarteritis nodosa with multiple ulcers on the lower leg and necrotizing soft tissue infection. Because polyarteritis nodosa is difficult to evaluate because of the lack of specific biomarkers, and because it is often difficult to treat the patient when infection occurs, we report here a case of polyarteritis nodosa with a review of the literature.

P3-129

A case of microscopic polyangiitis with severe liver injury due to avacopan

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Conflict of interest: None

A 77-year-old woman was referred to our department with edema and pain of both lower legs and renal dysfunction. Urinary protein and occult blood were positive, MPO-ANCA was 243.0 IU/mL, and a renal biopsy revealed pauci-immune crescentic glomerulonephritis, leading to a diagnosis of microscopic polyangiitis (MPA). Remission induction therapy was performed with prednisolone, rituximab, and avacopan. Sixty-three days after the administration of avacopan, blood tests showed elevated levels of T-bil (10.5 mg/dl), AST (219 U/l), and ALT (311 U/l). Avacopan was discontinued, and imaging tests such as abdominal ultrasound, CT, and MRCP revealed no abnormalities in the biliary system. Ursodeoxycholic acid was administered, but jaundice worsened. A liver biopsy revealed lymphocytic infiltration in the portal vein area and cholestasis in hepatocytes, suggesting drug-induced liver injury. The dose of prednisolone was increased, and liver injury slowly improved. Liver dysfunction and jaundice nearly normalized about two months after discontinuing avacopan. Avacopan is a newly developed selective C5a receptor inhibitor, and information on its safety is limited. Avacopan-induced liver injury may be frequent in Japanese, and careful consideration is required regarding applicable cases and dosage.

P3-130

Two cases of ANCA-positive EGPA with glomerulonephritis

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Conflict of interest: None

[Case 1] A 41-year-old female presented with fever, bilateral lower limb muscle weakness, diminished Achilles tendon reflexes, and pericardial effusion. She had asthma and was diagnosed with eosinophilia and EGPA. MPO-ANCA was over 1000 IU/mL. After starting prednisolone (PSL) at 40 mg/day, renal impairment was noted, raising suspicion of RPGN due to proteinuria, hematuria, and abnormal casts. Kidney biopsy confirmed pauci-immune crescentic glomerulonephritis. Following three courses of PSL pulse therapy, she was started on PSL at 60 mg/day, leading to rapid renal function improvement. She was discharged in good condition, remaining relapse-free. [Case 2] A 60-year-old male was admitted with fever, muscle pain, and dyspnea. With a history of asthma and eosinophilic sinusitis, he was diagnosed with EGPA, presenting with pneumonia and eosinophilia. MPO-ANCA was positive. Kidney biopsy confirmed crescentic glomerulonephritis. Treatment with PSL at 60 mg/day improved renal function, and he is tapering successfully. [Discussion] EGPA with glomerulonephritis is a serious complication. Although renal involvement is rare, its severity necessitates further research in Japan. Early diagnosis and steroid therapy are crucial for improving outcomes in patients with renal impairment due to EGPA.

P3-131

A case of suspected viral myocarditis after methylprednisolone pulse therapy and rituximab treatment for ANCA-associated vasculitc otitis media

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Conflict of interest: None

Clinical significance: When administering rituximub (abbreviated as RTX), follow-up including viral myocarditis was considered necessary. Case: 68 year-old female Medical history: Asthma, primary biliary cholangitis, atrial fibrillation, In X-18, she suffered sudden hearing loss in her left ear, History: In X-23, she was treated for Graves' disease, and then glucocorticoids (abbreviated as GC) for suspected ANCA-associated vasculitis. In X-6, she had stopped taking GC. On X, she visited the hospital with severe hearing loss in both ears, and was diagnosed with ANCA-associated vasculitis otitis media (bilateral refractory otitis media, MPO-ANCA+, vasculitis at nasal cavity and ear canal). Methylprednisolone pulse therapy was administered and one course of RTX 500 mg/body, GC 1 mg/kg was administered as posttreatment. Hearing improved to moderate on right. On the 33rd days of hospitalization chest pain developed. An abnormal electrocardiogram (new T wave negative conversion), and cardiac catheterization revealed no abnomalities. The antibody titers for adenovirus type 2 had increased 4 times over a month. The chest pain improved spontanously. The lymphocyte counts had dropped to low values. Discussion: We considered the possibility that viral myocariditis occurred during the course.

P3-132

A case of right lower leg amputation due to gangrene associated with EGPA in an elderly patient who could stop steroid after the introduction of Mopolizumab

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Conflict of interest: None

88 years old man was diagnosed of polymyalgia rheumatica and he was treated by PSL (15 mg/day) in X-7. He had type of 2 Deabetes Mulutis and had been experiencing peripheral numbness in his extremities before visiting our department. We tapered PSL and maintained PSL2 mg/day in X-5. He developed bronchial asthma and blood test showed eosinophilia in X-4. On January X-2, he suffered from biral legs edema and gangrene of right big toe, so he administered to our hospital for detailed inspection. On March X-2, right big toe amputation was performed. The pathology showed fibrinoid necrotizing vasculitis with eosinophil infiltration with skin tissue close to the necrotic area. We diagnosed the patient with EGPA based on the clinical symptoms and histopathological findings. We maintained low-dose steroids and added on azathioprine; AZA because of he required a right rigid amputation due to postoperative necrotic expansion and difficult wound healing. And then, AZA was stopped because of liver dysfunction. On April X-1, we induced Mepolizumab and he could stop steroid. We consider about elderly-onset EGPA with mepolizumab in our hospital.

P3-133

Two cases of polyarteritis nodosa with severe paralysis of the upper limbs due to vasculitis neuropathy, that improved with immunosuppressive drugs and long-term rehabilitation

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Conflict of interest: None

[Case 1] A 59-year-old woman had fever, purpura and muscle weakness in both upper limbs. Biopsies of the leg purpura revealed leukocytoclastic vasculitis in the deep dermis. She had untreated HCV infection and was diagnosed with HCV-associated polyarteritis nodosa (PN), which was treated with antiviral drugs, PSL, IVCY and high-dose immunoglobulin therapy. After treatment and long-term rehabilitation, her upper limb muscle strength improved and she was able to perform activities of daily living. [Case 2] A 77-year-old woman had fever, numbness in her hands and feet, drop foot and paralysis of her fingers. Nerve conduction study showed axonal polyneuropathy, and biopsy of the right sural nerve revealed vasculitis with fibrinoid necrosis in the perineural vessels. The patient was diagnosed as PN, and treated with PSL and IVCY. After treatment and long-term rehabilitation, the patient improved to the extent that she was able to perform activities of daily living, although neurological symptoms remained. [Discussion] About 70% of patients with PN develop peripheral neuropathy. Although severe paralysis of the bilateral upper extremities is rare, both patients showed improvement in activities of daily living after long-term rehabilitation in addition to immunosuppressive therapy.

P3-134

Eosinophilic Granulomatosis with Polyangiitis (EGPA) with severe peripheral neuropathy that responded to treatment with Intravenous Immunoglobulin (IVIg): A Case Report

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Conflict of interest: None

Introduction: During the clinical course of EGPA, peripheral neuropathy is a complication in 90% of patients and can be irreversible. IVIg is one of the treatment options for peripheral neuropathy caused by EGPA. Case: A 53-year-old female suffering from bronchial asthma and eosinophilic chronic rhinosinusitis became aware of numbness in her limbs. A few weeks later, she was rushed to her previous hospital and her blood test showed CRP 13.1 mg/dL and eosinophil count 17,000/μL. She was transferred to our hospital, and nerve conduction study revealed mixed motor and sensory peripheral neuropathy. We diagnosed the patient with EGPA. Her manual muscle test (MMT) scores decreased to 0~2 in the hand and ankle joints and beyond. We introduced prednisolone (PSL) and intravenous cyclophosphamide (IVCY) as remission induction. However, after 4 courses of IVCY, severe neuropathy remained in distal region in her limbs, so we introduced IVIg. After 3 courses of IVIg, MMT scores mostly improved to 4, and she became able to walk with a cane. Conclusion: This case suggests that IVIg has a great possibility of improving not only peripheral neuropathy but also patient's quality of life.

P3-135

A case of microscopic polyangiitis (MPA) with inflammation of the aortic arch to left subclavian artery treated with rituximab

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Conflict of interest: None

A 71-year-old woman was admitted to our department in November of the same year with complaints of fever in the 38 degree range, cervical lymphadenopathy, swelling and burning in both forearms, erythema of the left forearm, and myalgia of the right thigh. Physical examination revealed muscle tenderness from the neck to the shoulders. Blood tests showed the following results: CRP: 4.09 mg/dL, Creatinine: 0.49 mg/dL, CK: 171 U/L, MPO-ANCA: 142.7 U/mL, HLA genetic testing did not reveal any disease-specific genotypes. Contrast-enhanced CT scan showed wall thickening from the aortic arch to the origin of the left subclavian artery. Contrast-enhanced MRI of the chest showed evidence of macroangiitis in the same region and myositis in the left triceps brachii muscle. Head MRI/MRA scan showed scattered high-signal areas in bilateral cerebral white matter on T2WI and FLAIR. Ophthalmological examination confirmed the presence of scleritis. Based on these findings, the patient was diagnosed with microscopic polyangiitis (MPA) complicated by large vessel vasculitis, myositis, cerebrovascular involvement, and scleritis. Treatment was initiated with prednisolone and azathioprine, but due to insufficient response, rituximab was added. After treatment, both symptoms and imaging findings improved.

P3-136

Experience with Avacopan in the induction treatment of remission for ANCA-associated vasculitis at our hospital

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Conflict of interest: Yes

[Objective] In remission induction treatment for MPA/GPA, avacopan, a complement C5a receptor inhibitor, has been reported to be an alternative to high-dose glucocorticoids. [Method] We examine the treatment course and efficacy of avacopan in four cases of AAV remission induction treatment in our department. [Results] All patients were male with MPA, aged 79.3 ± 5.6 years. The organ affected was the kidney, and combined kidney and lung. Avacopan was introduced 35.75 ± 3.19 days after the start of remission induction. The dose of PSL at remission induction was 63.8 ± 6.5 mg/day, and the dose of PSL at the time of avacopan introduction was 22.5 ± 6.7 mg/day. There are two methods for administering RTX in remission maintenance therapy or administration according to the number of CD19-positive B cells. At our hospital, we perform the latter method, and RTX has been administered as remission maintenance therapy in two cases, 479 ± 47 days after administration of RTX in remission induction therapy. [Conclusion] In AAV, which often develops in elderly patients, long-term administration of PSL or RTX carries a high risk of complications, including infection. Administration of avacopan may make it possible to extend the interval between RTX administration in remission maintenance therapy.

P3-137

A case of alveolar hemorrhage due to microscopic polyangiitis successfully treated with avacopan

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Conflict of interest: None

[Case] A 75-year-old man visited an emergency room because of fever and cough for 16 days. He was on warfarin for atrial fibrillation and was treated with an antagonist because alveolar hemorrhage due to PT-INR hyperprolongation. But his oxygenation deteriorated further a few hours later. The patient tested positive for MPO-ANCA (57.2 U/L) and was diagnosed with alveolar hemorrhage due to microscopic polyangiitis (MPA). On X+7 day, rituximab was added. On X+14 day, Abacopan 60 mg bid was added. Immediately oxygenation improved. Six months later, the dose was reduced to 4 mg of PSL. During the course of the disease, CMV antigenemia, lumbar vertebral compression fracture, and steroid diabetes mellitus were observed, but the patient's course was good. [Clinical Significance] There is a lack of evidence for the efficacy of abacopan in induction of remission in severe MPA such as alveolar hemorrhage. In the present case, the combination use of abacopan from the early stage of induction of remission of alveolar hemorrhage allowed the patient to achieve rapid induction of remission. The patient progressed without major complications, and the steroid dose was reduced. We report this case as an effective case of abacopan in a severe disease.

P3-138

A case of eosinophilic granulomatosis with polyangiitis presenting with necrosis of the fingers associated with anti-cardiolipin IgG antibody positivity

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Conflict of interest: None

The patient, a 77-year-old woman, presented with lower leg numbness, left finger/toe discoloration, and bilateral foot drop beginning 3 weeks prior. Initially diagnosed with lumbar spinal stenosis and treated with laminoplasty, her symptoms and finger necrosis progressed, leading to her admission. Based on asthma history, elevated eosinophil count, and polyneuropathy, we diagnosed eosinophilic granulomatosis with polyangiitis (EGPA). She also tested positive for anti-cardiolipin IgG antibodies, though upper limb ultrasound showed no blockage. EGPA treatment included methylprednisolone pulse (1000 mg for 3 days), oral prednisolone (1 mg/kg), and intravenous cyclophosphamide (IVCY), normalizing her eosinophil count and CRP. Despite treatment, finger necrosis continued, prompting warfarin and aspirin due to suspected antiphospholipid antibody syndrome (APS), effectively preventing further spread. Prednisolone was tapered, and mepolizumab added. No EGPA recurrence, impaired blood flow, or new thrombosis has occurred. [Clinical Significance] Finger necrosis with vascular impairment is rare in ANCA-associated vasculitis and may relate to antiphospholipid antibodies. Testing for these and adding anticoagulant or antiplatelet therapy may help prevent vascular impairment.

P3-139

A case of Eosinophilic Granulomatosis with Polyangiitis developed during tezepelumab treatment

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Conflict of interest: None

[Case] A 52-year-old Japanese female had been treated at a local clinic with inhaled medications, leukotriene receptor antagonists, and oral glucocorticoids (GC) for refractory bronchial asthma accompanied by eosinophilia. Two and a half months ago, tezepelumab was initiated, resulting in a marked improvement, and oral GC was discontinued. However, one and a half months ago, she developed limb myalgia, and a month ago, she experienced persistent fever. Eosinophilia (5,852 /μL) and MPO-ANCA positivity (14.0 U/mL) were observed, along with hyperintense areas on T2-weighted MRI of the thigh. A muscle biopsy revealed eosinophil-predominant inflammatory cell infiltration and fibrinoid necrotizing vasculitis, leading to a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). Tezepelumab was discontinued, and treatment with moderate-dose GC, mepolizumab, and intermittent intravenous cyclophosphamide therapy was initiated, resulting in improvement. Subsequently, she developed central retinal artery occlusion and is currently receiving treatment. [Discussion] This is the first reported case of EGPA that developed during tezepelumab treatment. Tezepelumab may not be effective in preventing the onset or controlling the disease activity of EGPA.

P3-140

Anti-Glomerular Basement Membrane Nephritis in a Patient with ANCA-Negative Eosinophilic Granulomatosis with Polyangiitis

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Conflict of interest: None

A 64-year-old female developed chronic sinusitis in 20XX-13 and was referred to our hospital the following year due to fever, edema, numbness, and pain in both lower legs. She was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA); although ANCA was negative, eosinophilia, elevated myogenic enzymes, and diffuse high signals in both leg muscle layers were observed on MRI of the lower limbs. In 20XX-2, she maintained remission on PSL 5 mg/day and MTX 12 mg/week. She experienced fever starting in June 20XX and was brought to our hospital due to rapid renal dysfunction, with BUN at 69 mg/dl and creatinine at 7.82 mg/dl. Based on positive anti-GBM antibodies, she was diagnosed with anti-glomerular basement membrane nephritis. Treatment included glucocorticoid pulse therapy, plasma exchange, and maintenance dialysis. Patients with double-positive ANCA and anti-GBM antibodies have been reported to have a poor renal and life prognosis. Although ANCA-negative EGPA is less likely to cause necrotizing glomerulonephritis than ANCA-positive EGPA, when glomerulonephritis develops in ANCA-negative EGPA, complications such as anti-glomerular basement membrane nephritis should be considered in the differential diagnosis.

P3-141

A case of Eosinophilic Granulomatosis with Polyangiitis complicated by severe renal dysfunction

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Conflict of interest: None

We report a case of eosinophilic granulomatosis with polyangiitis (EGPA) complicated by severe renal faliure. The patient was a 57-year-old man who was under treatment for diabetes. Wheezing and eosinophilia were identified and the patient was referred to our hospital. Inhaled steroids, anticholinergics, and β2-agonist inhalation therapy were initiated but renal dysfunction, fever, purpura on the lower extremities, and peripheral neuropathy began to appear. History of bronchial asthma and eosinophilia, fever, mononeuritis multiplex, purpura, and a high MPO-ANCA

titer, rapidly progressive glomerulonephritis (RPGN) were noted. Skin biopsy revealed eosinophils infiltrating the vascular wall with fibrinoid necrosis, and the patient was diagnosed with EGPA. Remission induction therapy with high-dose steroids and intravenous cyclophosphamide was initiated, resulting in improvement in symptoms, eosinophil count, and renal dysfunction. EGPA complicated by RPGN is considered rare among ANCA-associated vasculitis. In this case, since renal biopsy was performed after the initiation of treatment, it was not possible to determine EGPA's involvement in the renal dysfunction. However, we report this as a case where EGPA may have contributed to RPGN in a patient with diabetic nephropathy.

P3-142

Polyarteritis nodosa (PN) diagnosed due to intra-abdominal hemorrhage caused by a rapidly enlarging ruptured aneurysm of the left gastric artery branch: a case report

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Conflict of interest: None

Case report A 72-year-old woman was admitted to the previous hospital for diarrhea, fever, and high inflammatory response. Contrast-enhanced computed tomography (CECT) showed a posterior mediastinal abscess. However, Antimicrobials were ineffective, so a perivertebral resection was performed, but no pus was got. Pathological examination revealed no Tumors or vasculitis. PET-CT showed no vasculitis. The patient was transferred to our department due to positive MPO-ANCA. Although vasculitis symptoms could not be noted, methylprednisolone 48 mg was started. The fever quickly resolved, but the patient had epigastric pain and hypotension on 4th day of treatment. CECT showed a ruptured aneurysm in the left gastric artery branch, and transcatheter arterial embolization was performed. Angiography showed bead-like aneurysm in the celiac artery branch, which had not been noted on CT, and PN was diagnosed. Cyclophosphamide was also given and achieved clinical remission. Discussion Sometimes we fail to diagnose PN by CECT or PET-CT because CT is less sensitive in detecting aneurysms than angiography. So, even if CECT and PET-CT don't point to an aneurysm, it doesn't rule out PN. In addition, as in this case, it should be noted that PN can cause aneurysm rupture even after the treatment started.

P3-143

A case of eosinophilic granulomatosis with polyangiitis presenting with an anterior mediastinal tumor-like lesion

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Conflict of interest: None

<Case> A 43-year-old woman was referred for epigastric pain, nausea, fever. She had a history of adult-onset asthma with worsening control for the past seven months. She began to have epigastric pain and nausea from six months ago, followed by shoulder and back pain, and fever. Blood tests showed eosinophils at 3022/μL, with negative MPO- and PR3-ANCA. Contrast-enhanced CT revealed a tumor-like lesion in the anterior mediastinum and ground-glass opacities and tumor-like lesions were found in both lungs adjacent to the mediastinal lesion. Biopsy samples from the mediastinal and lung lesions showed eosinophil infiltration, epithelioid granulomas and vascular occlusion. There were no findings suggestive of malignant tumors or infections. The patient was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) and prednisolone at 1 mg/kg/day was initiated. After treatment, the tumor-like lesions in the anterior mediastinum and lungs also gradually shrunk and finally almost disappeared. By 12 months, the prednisolone dose was reduced to 6 mg/day, with no signs of eosinophilia or worsening asthma. It is extremely rare for EGPA to cause tumor-like lesions in the mediastinum, so thorough examination, including histological assessment, is essential.

P3-144

A case of eosinophilic polyangiitis granulomatosa with hypocomplementemia

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Conflict of interest: None

[Case] 76 year old male [Chief complaint] abdominal pain [History of current illness] He had a history of bronchial asthma more than 20 years ago. He was referred to our hospital after antibiotic treatment was started. [Clinical Course] Eosinophil count was increased to 1800/μL on blood test, and upper gastrointestinal endoscopy revealed erythema in the stomach and duodenum. Based on eosinophil counts and pathological findings, the diagnosis of eosinophilic granuloma polyangiitis pellagiosum (EGPA) was made, and treatment was started with prednisone 40 mg. Since the start of treatment, low complement levels were observed with C3 58 mg/dL, C4 5.7 mg/dL, and CH50 <12.0/ML. Protein leak scintigraphy was negative. Complement was normalized at X+2 months after the start of treatment. [Consideration] Complement is generally elevated in EGPA, reflecting inflammation. The patient had no evidence of autoimmune disease causing hypocomplementemia. The hypocomplementemia in this case differed from that of other AAVs. After treatment, the hypocomplementemia resolved. [Conclusion] We experienced a case of AAV with hypocomplementemia. Complement loss improved with the course of treatment. Normalization of complement may be a marker for determining the efficacy of treatment.

P3-145

Two cases of successful slow plasma exchange (PE) in refractory adult-onset Still's disease (AOSD) with rapid reduction of immunosuppressants without relapse

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Conflict of interest: None

[Objectives] We reported slow PE in refractory adult-onset Still's disease (AOSD) of 50 year old females successfully contributed to reduce immunosuppressants rapidly without relapse. [Case 1] One patient received 5-ASA as treatment for inflammatory bowel disease. She developed swelling of the lymph nodes, skin rash on both hands, febrile, and arthralgia for three weeks. She received medication for a cold, but her symptoms did not recover. She was then transferred to our hospital. She was diagnosed as refractory AOSD. She was treated for CyA and IVCY combined with five times of slow PE. Her serum ferritin level decreased from 10181 to 325 ng/ml. The dosage of PSL could be reduced soon only with oral Candidiasis. [Case 2] This patient was diagnosed with AOSD two years prior. She was diagnosed with it again after receiving the Corona virus vaccination. Pulse therapy of mPSL, IVCY and TCZ could not suppress activity. Her serum ferritin titer was 4038 ng/ml. Due to that, slow PE was introduced combining immunosuppressants. Consequently, her disease activity decreased despite tapering immunosuppressants due to infection. [Summary] Slow PE contributed the management of refractory AOSD. slow PE might suppress the dosage and durration of immunosuppressants without any side effects.

P3-146

A Case of Hodgkin Lymphoma Complicated by Adult-Onset Still's Disease with Unmasking of Tattoo-Associated Lymphadenitis

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Conflict of interest: None

Since X-10M, a 34-year-old woman experienced intermittent generalized erythema and joint pain. From X-7M, she developed low-grade fever, followed by peripheral joint pain and myalgia from X-1 month. From X-15D, she presented with neck pain, sore throat, and remittent fever. She was referred to our department. Based on symptoms, elevated WBC, and ferritin levels, adult-onset Still's disease (AOSD) was diagnosed. Treatment with prednisolone (PSL) and cyclosporine A (CyA) was initiated, along with plasma exchange. She had multiple lymphadenopathies, and a biopsy of the right inguinal lymph node confirmed Hodgkin lymphoma. CyA was discontinued, she completed BV-AVD therapy and achieved remission. During chemotherapy, AOSD symptoms recurred, which were managed with PSL and IL-6 inhibitor therapy. A follow-up PET-CT suggested a relapse of lymphoma in the left inguinal and para-aortic regions, and a biopsy was performed. The biopsy site was near a tattoo, and the lymph node appeared bluish, showing only reactive changes. sIL-2R levels remained within the normal range, leading to a diagnosis of tattoo-associated lymphadenitis. As this was not observed during remission, it might have been unmasked by AOSD. We report this case along with a literature review.

P3-147

An Autopsy Case of Adult-Onset Still's Disease with Refractory Hemophagocytic Syndrome Resistant to Intensive Immunosuppression and Plasma Exchange

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Conflict of interest: None

[Case] A forty-year-old male was diagnosed with adult-onset Still's disease (AOSD) based on fever, arthralgia, sore throat, and liver injury three years prior to admission. She was initially treated with prednisolone (PSL) 40 mg/day and tacrolimus, followed by tocilizumab (TCZ). Three months before admission, PSL was tapered off. However, AOSD relapsed one month before admission, reintoradueced with PSL 40 mg/day. However, as a skin rash promptly appeared, she was admitted to the previous hospital. Although glucocorticoid (GC) pulse therapy and TCZ were administered, which were not effective, she was transferred to our hospital. We introduced plasma exchange and cyclosporine. However, as hemophagocytic syndrome appeared, confirmed by bone marrow biopsy, we reinitiated GC pulse therapy with blood transfusions, and granulocyte colony-stimulating factor. But she succumbed to the illness 16 days after admission with no response to these treatments. At autopsy, gastrointestinal hemorrhage and hemophagocytosis in the bone marrow were observed, indicating ongoing high disease activity. [Clinical Significance] This highly refractory AOSD with HPS, confirmed at autopsy despite enhanced treatment emphasizes the need for establishing more effective therapies for managing intractable cases.

P3-148

A case of lower extremity peripheral neuropathy during remission induction therapy for adult-onset Still's disease

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Conflict of interest: None

A 65-year-old man developed fever, arthralgia, and skin redness. He was admitted to the hospital with highly elevated ferritin and CRP. He met Yamaguchi criteria and was diagnosed with adult-onset Still's disease. Laboratory values and subjective symptoms improved after administration of prednisolone 60 mg and cyclosporine 200 mg. However, one week after the start of treatment, he noticed difficulty walking, and three weeks later, he was diagnosed with drop foot due to left deep peroneal neuropathy. Prednisolone was gradually reduced, but MMT of the left tibialis anterior muscle showed a slow improvement trend; within 3 months the values improved from 0 to 2, but no further improvement was observed. Peripheral neuropathy is a rare complication of adult Still's disease. In previous reports, the cause was not clear and only symptomatic and supportive care was reported. Therefore, we did not intensify treatment.

P3-149

Three cases of Adult-onset Still's disease treated with plasma exchange therapy

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Conflict of interest: None

[Background] Many cases report plasma exchange therapy (PE) for Adult-onset Still's disease (AOSD) is effective. We report 3 cases of AOSD treated with PE in our hospital from April 2015 to September 2024. [Case 1] New-onset 78-year-old woman failed treatment of high-dose glucocorticoid (GC) and cyclosporine (CyA). A tocilizumab (TCZ) therapy caused markedly higher level of ferritin (Fr) and coagulopathy. PE improved the Fr level and coagulopathy significantly. [Case 2] New-onset 67-year-old woman failed treatment of high-dose GC and CyA. PE improved disseminated intravascular coagulation syndrome and respiratory failure with ventilatory support due to pericarditis and pleurisy, and resulted ventilator weaning. [Case 3] Relapsed 56-year-old woman responded to high-dose GC therapy. An additional TCZ therapy for reduction of GC worsened the Fr level with coagulopathy. Higher dose of GC was required and caused serious adverse events. PE decreased the Fr level and significantly reduced GC. [Conclusions] We reported 3 cases of AOSD failed to a conventional medication therapy. PE was effective in all cases to manage AOSD and coagulopathy without additional GC and immunosuppressant. PE might be effective for refractory AOSD, especially with coagulopathy or requiring early reduction of GC.

P3-150

Three cases of hemophagocytic syndrome due to adult Still's disease successfully treated with cyclosporine

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Conflict of interest: None

[Introduction] There is limited evidence regarding the efficacy of cyclosporine (CyA) for hemophagocytic syndrome (HLH) due to adult Still's disease (ASD). Here, we report three cases in which HLH relapsed after induction therapy with steroids and tocilizumab (TCZ) or infliximab (IFX), and improved with the use of CyA. [Case 1] A 67-year-old woman was admitted with fever, polyarthritis, and HLH. Treatment was initiated with mPSL 60 mg and IFX, but HLH relapsed when PSL was reduced to 50 mg, and CyA was started after steroid pulse therapy. [Case 2] A 20-year-old woman was admitted with fever, sore throat, polyarthritis, and pericarditis. Treatment was started with mPSL 60 mg and TCZ, but HLH developed when PSL was tapered to 30 mg, and CyA was used in addition to steroid pulses and TCZ. [Case 3] A 51-year-old man was admitted with fever, sore throat, polyarthritis, skin rash. HLH progressed during the use of mPSL 60 mg, and treatment was started with steroid pulses and TCZ, but relapsed when PSL was tapered to 40 mg, and CyA was used. [Conclusion] There are some cases of ASD that progress to HLH despite treatment with steroids and biological agents. This suggests that CyA may be a treatment option for refractory HLH cases, and we report this case together with a literature review.

P3-151

A case of adult-onset Still's disease who developed macrophage activation syndrome after tocilizumab administration

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Conflict of interest: None

A 62-year-old woman was referred 3 years ago for recurrent arthritis and erythema, but her symptoms resolved spontaneously. Two years ago, erythema reappeared, and a skin biopsy suggested sarcoidosis. Arthritis recurred 1 year ago and improved with colchicine. Two months ago, she developed a fever, pharyngitis, arthritis, and erythema. A skin biopsy showed keratinocyte necrosis but no granulomas. Elevated ferritin led to a diagnosis of adult-onset Still's disease (AOSD). Prednisolone (PSL) (0.6 mg/kg) improved her symptoms, and 1 month later, tocilizumab (TCZ) was started. However, ferritin levels increased, and thrombocytopenia developed, raising suspicion of macrophage activation syndrome (MAS). PSL was increased to 1 mg/kg, TMP-SMX was stopped, and cyclosporine was added, allowing PSL tapering. IL-18 and IL-6 levels before starting TCZ were 65,100 pg/mL and <1.5 pg/mL, respectively. In cases of AOSD with subsequent onset of MAS following TCZ, it has been reported that elevated inflammatory markers at baseline require attention. However, this case showed no such increase. Conversely, it was also reported that MAS cases exhibit suppressed baseline IL-6 pathways, consistent with our findings. Caution may be warranted when starting TCZ in patients with low baseline IL-6 levels.

P3-152

Two cases of adult-onset Still's disease complicated with macrophage activation syndrome successfully treated with plasma exchange

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Conflict of interest: None

[Introduction] There is no standard treatment for adult-onset Still's disease (AOSD) complicated with macrophage activation syndrome (MAS). We have observed two cases of AOSD complicated with MAS in our hospital in which simple plasma exchange (PE) was effective. We report a retrospective comparison with the other four cases (non-PE group) treated without PE. [Case 1] A 56-year-old woman. AOSD complicated with MAS. She rapidly improved with methylprednisolone (mPSL), prednisolone (PSL) 40 mg, and PE, and tocilizumab (TCZ) was introduced. [Case 2] A 78-year-old woman. Treatment was started with PSL 50 mg for AOSD, but she developed MAS and improved with mPSL and PE. After starting TCZ, MAS recurred, and treatment was again started with mPSL and PE. [Result] Comparing the period from the start of treatment to discharge with non-PE group (listed as median [quartile]), case 1 had a shorter period, and case 2 had a similar period to non-PE group despite a relapse of MAS (case 1 16 days, case 2 48 days, non-PE group 48 [35-62] days). The total amount of PSL after 3 months tended to be lower in case 1 and case 2 (case 1 2120 mg, case 2 3200 mg, non-PE group 3895 [3477-4142] mg). [Conclusion] PE for MAS may lead to rapid improvement of the condition and a reduction in the GC dosage.

P3-153

A case of relapsing polychondritis presenting with skin arteritis during treatment for pulmonary cryptococcosis, suspected to be associated with immune reconstitution inflammatory syndrome

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Conflict of interest: None

Case: A 63-year-old male diagnosed with relapsing polychondritis a year ago was treated with PSL 10 mg, MTX 10 mg, and ADA 40 mg biweekly. He developed a cough for two weeks, followed by fever and dyspnea. He was diagnosed with pneumonia, and MTX and ADA were discontinued. Levofloxacin was started, but his symptoms worsened. A CT scan revealed heterogeneous infiltration and small nodules in the left lower lobe. Elevated serum cryptococcal antigen levels and a CT-guided biopsy confirmed *Cryptococcus neoformans*, leading to a diagnosis of pulmonary cryptococcosis. On the 5th day of hospitalization, fluconazole was initiated, resulting in rapid defervescence. However, on day 23, he developed fever again, along with multiple subcutaneous nodules. Suspecting IRIS due to the discontinuation of immunosuppressive therapy, high-dose PSL 60 mg was started, which led to prompt symptom resolution. He improved and was discharged on day 68. A biopsy of the nodules showed neutrophilic infiltration, confirming skin arteritis. IRIS can occur during cryptococcal infections or after stopping immunosuppressive medications, requiring careful monitoring. This case illustrates the potential for arteritis in relapsing polychondritis and discusses the possibility of VEXAS syndrome.

P3-154

A case of anti-Mi-2 antibody-positive dermatomyositis showing VEXAS syndrome-like condition, with characteristic PET-CT findings

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Conflict of interest: None

A 67-year-old man was referred to our hospital due to facial rash and limb muscle pain and high CK levels. He was diagnosed with anti-Mi-2 antibody-positive dermatomyositis. He was treated with PSL, tacrolimus, methotrexate, and IVIG, and his symptoms improved. Shortly after discharge, he was readmitted because of fever, painful erythema on the face and limbs with elevated CRP. Steroid pulse therapy rapidly reduced his fever. However, fever recurred when PSL was tapered to 60 mg/day, and PSL 90 mg/day was required to relieve the fever. PET-CT revealed numerous nodular accumulations in the nasal mucosa and skin of the limbs. Skin malignant tumors and intravascular lymphoma were suspected, and biopsies were performed on the skin, nasal septum, and earlobes, which showed no malignant findings. Bone marrow biopsy revealed myelodysplastic syndrome, with vacuolated bone marrow cells, but no mutations were found in the UBA1 gene. Considering VEXAS-like clinical presentation, tocilizumab was introduced, resulting in a favorable response and enabling PSL tapering. Recent reports have described cases of VEXAS-like symptoms without UBA1 mutations. This case highlights the potential involvement of unidentified mutations contributing to the observed phenotype.

P3-155

A case of VEXAS syndrome due to macrocytic anemia and thrombocytopenia 3 years after the diagnosis of recurrent polychondritis

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Conflict of interest: None

[Case] A 69-year-old man visited to our hospital due to pharyngeal pain and redness of the left auricular cartilage. He was diagnosed with recurrent polychondritis (RP) presenting chondritis, conjunctivitis and polyarthritis. There was no macrocytic anemia or thrombocytopenia. Treatment with prednisolone (PSL) was started. Since flared-up of RP observed, methotrexate and tocilizumab were added. Mild macrocytic anemia and thrombocytopenia appeared after 3 years of the diagnosis with RP. He was referred to the hematology department for the examination. Vacuoles in myeloid progenitor cells were observed by bone marrow examination, and a diagnosis of VEXAS syndrome was made. [Discussion] VEXAS syndrome can present with chondritis, and many cases meet the diagnostic criteria for RP. A recently reported algorithm to identify polychondritis complicated with VEXAS syndrome proposed the importance of concomitant hematological abnormalities. In this case, there was no macrocytic anemia or thrombocytopenia at the diagnosis of RP, and there were few findings to suspect VEXAS syndrome. Even in patients without hematological abnormalities at the onset of RP, the possibility of developing VEXAS syndrome should be noted especially in elderly men with high inflammatory state and poor RP control.

P3-156

A Case of VEXAS Syndrome Diagnosed During Follow-up for Suspected Relapsing Polychondritis

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Conflict of interest: None

Case: An 81-year-old male Chief complaints: Recurrent fever and fatigue Present illness: Nine years ago, the patient had pain, redness, and swelling in both auricles, which resolved. He later experienced recurrent episodes and polyarthralgia in his fingers. Evaluated for suspected relapsing polychondritis, he did not receive a definitive diagnosis. Elevated inflammatory markers were noted, and treatment with prednisolone at 30 mg/day improved symptoms, but they recurred upon tapering below 10 mg/day. In April of X year, he was admitted due to fever, fatigue, and loss of appetite. Clinical Course and Discussion: Fever recurrence and increased inflammatory markers with prednisolone tapering suggested an autoinflammatory syndrome. No skin manifestations were observed, but macrocytic anemia developed. The patient had diverse symptoms: male sex, older age, chondritis, thrombocytopenia, myelodysplastic syndrome, thrombosis, and pneumonia raised suspicion for VEXAS syndrome. Genetic testing revealed a mutation in the UBA1 gene, confirming the diagnosis. Conclusion: This case emphasizes the need to consider VEXAS syndrome in patients with varied symptoms. Genetic testing identified a UBA1 gene mutation, leading to diagnosis. We report the associated pathological findings.

P3-157

A case of VEXAS syndrome with complete remission treated with glucocorticoids and tacrolimus

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Conflict of interest: None

[Case Presentation] The patient was an 81-year-old man who was treated for type B liver cirrhosis, postoperative liver cancer, and postoperative left kidney cancer. He was admitted due to persistent fever and anemia. CT scan showed pneumonia, and he was treated with antibiotics. His condition did not improve. He had bilateral auricular chondritis, arthritis and costochondritis. He was diagnosed with recurrent polychondritis. Although treatment with 15 mg prednisolone (PSL) quickly improved the arthritis and chondritis, worsened as PSL was tapered off. The addition of tacrolimus (TAC) improved and allowed PSL taper. Thrombocytopenia appeared at the same time as the inflammatory response improved. The diagnosis of VEXAS syndrome was confirmed with peripheral blood genetic testing somatic variant detected in the UBA1 gene. [Clinical Significance] Glucocorticoids are known to be effective in VEXAS, however, relapse with tapering is often difficult to treat. There is no consensus on effective medications. IL-6 inhibitors and JAK inhibitors are considered as a potential therapeutic option. On the other hand, there are few reports on the use of TAC. We report on the efficacy of TAC for VEXAS syndrome in this case, with a review of the literature.

P3-158

Circulating tumor necrosis factor-a DNA are elevated in psoriasis

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Conflict of interest: None

Increased serum or plasma TNF-a levels are considered to be biomarkers of psoriasis. Circulating cell-free DNA (cfDNA) originates from apoptotic or necrotic cells and reflects the severity of cellular damage. The aim of this study was to investigate whether the TNF-a gene is present in the cfDNA, and whether its levels can be utilized as a biomarker for patients with psoriasis. cfDNA was isolated from serum samples of 79 patients with psoriasis vulgaris and 29 with psoriatic arthritis. The levels of TNF-a in the cfDNA were assessed by droplet digital polymerase chain reaction. In this study, we made two novel findings. First, circulating TNF-a DNA levels in the cfDNA were significantly higher in patients with psoriasis than in healthy controls. In addition, the area under the curve was 0.91, suggesting that serum TNF-a DNA levels are effective as a diagnostic biomarker. Second, the levels of TNF-a DNA copies in the cfDNA were positively correlated with the Psoriasis Area and Severity Index (PASI) score in the group of patients with a PASI score higher than 10. Generally, a PASI score of more than 10 is defined as severe psoriasis; therefore, the levels of TNF-a DNA copies in the cfDNA could be a biomarker for severity in patients with severe psoriasis.

P3-159

Risk Factors Associated with Relapse during Glucocorticoid Tapering in Patients with Polymyalgia Rheumatica

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Conflict of interest: None

[Objectives] To investigate factors associated with relapse in patients with polymyalgia rheumatica (PMR) undergoing glucocorticoid (GC) tapering. [Methods] 32 patients diagnosed with PMR who attended our outpatient clinic regularly between June 2023 and August 2024 were assessed. Disease activity was evaluated periodically using PMR-AS score. Relapse was defined by worsening muscle pain or elevated inflammatory markers requiring GC dose escalation or immunosuppressant addition, or by an increase in PMR-AS from <7 to ≧10. Univariate and logistic regression analyses were performed to identify relapse-related factors. [Results] 7 patients relapsed during the observation period. Comparison of the relapse and non-relapse groups showed no significant differences in disease duration, age, history of PMR recurrence, or concomitant immunosuppressant use. A strong correlation was observed between RAPID3 and PMR-AS at relapse (ρ=0.78, p=0.04). [Conclusion] No significant factors were identified as associated with relapse in PMR patients undergoing GC tapering. However, the strong correlation between RAPID3 and PMR-AS supports RAPID3's potential utility as an adjunct tool in assessing relapse and disease activity in PMR.

P3-160

A case of rituximab induced serum sickness

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Conflict of interest: None

[Case] 93 y.o. woman [CC] Arthralgia [HPI] The patient was referred to our department for one day course of multiple arthralgia. Twelve days prior, rituximab (RTX) and dexamethasone were first administered for a relapse of mantle cell lymphoma. Physical exams revealed arthritis in both shoulder joints and peripheral joints. Ultrasonography showed tenosynovitis in the wrist joint. On the same day, she developed a high fever and rash on the back and lower legs. Lab tests showed elevated inflammatory markers and a low C4 level. Rheumatoid factor, anti-CCP, anti-nuclear, and anti-SS-A antibodies were negative. A diagnosis of rituximab induced serum sickness (RISS) was made. The patient was treated with prednisolone for one week. She has had no relapse since RTX was discontinued. [Discussion] RISS is a delayed hypersensitivity reaction that appears one to two weeks after RTX administration. This patient developed the classic triad of fever, rash, and arthralgia. Also, hypocomplementemia, a common laboratory feature of the disease, was observed. RISS is more likely to occur in patients with autoimmune diseases or hematological malignancies. The disease worsens when RTX is re-administered. RISS is a rare but practice-changing side effect of RTX.

P3-161

A case of TAFRO syndrome with thrombocytopenia treated with cyclosporine, rituximab, and eltrombopag

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Conflict of interest: None

[Case] A 42-year-old woman was referred to our hospital for a thorough examination because she had fever of 38°C for 4 weeks, white blood cell count 7700/μL, CRP 25 mg/dl, that did not improve after administration of ceftriaxone. Contrast-enhanced CT scan showed multiple enlarged lymph nodes, ascites, and hepatosplenomegaly. Lymph node and bone marrow biopsies ruled out malignant lymphoma, leading to the clinical diagnosis of TAFRO syndrome. On day 5 of admission, the platelet count decreased from 150,000 to 70,000/μL, and she was treated with corticosteroid pulse therapy and prednisolone 1 mg/kg as post-therapy. However, on day 15, the platelet count dropped to 35,000/μL, and we decided to administer cyclosporine, rituximab, and eltrombopag. Three weeks later, the platelet count increased to 100,000/μL without platelet transfusion. [Disscussion] Thrombocytopenia in TAFRO syndrome is often severe, prolonged, and refractory to blood transfusion. The mechanism of thrombocytopenia is unknown, but an immune thrombocytopenic purpura (ITP)-like mechanism is also considered. In TAFRO syndrome with thrombocytopenia, early introduction of rituximab, eltrombopag and cyclosporine, which are also drugs for ITP, may avoid refractory thrombocytopenia to blood transfusion.

P3-162

A case of TAFRO syndrome occurring during remission of systemic lupus erythematosus

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Conflict of interest: None

A man in his 80s was diagnosed with systemic lupus erythematosus (SLE) in X-5 on the basis of febrile, pleural effusion, thrombocytopenia, lymphocytopenia, positive antinuclear antibody, positive anti-U1-RNP antibody, positive anti-cardiolipin antibody, and hypocomplementemia, and was started on methylprednisolone pulse therapy, high-dose glucocorticoids, and tacrolimus. In August, X, abdominal discomfort appeared, and the patient was admitted to our hospital. At that time, he was transferred to our department because of thoracoabdominal effusion and severe thrombocytopenia. The patient was started on antimicrobials and prednisolone 20 mg/day in combination with intravenous immunoglobulin therapy. Methylprednisolone pulse therapy was administered, but there was no improvement in thrombocytopenia. Bone marrow puncture confirmed microfibrosis of the bone marrow, and the diagnosis of TAFRO syndrome was made based on symptoms of thrombocytopenia, generalized edema, renal dysfunction, and splenomegaly. Although male patients with SLE in elderly-onset may have an atypical course, the possibility of TAFRO syndrome should be considered when the patient presents with pleural effusion and severe thrombocytopenia during remission and inadequate response to immunosuppressive therapy.

P3-163

A case of VEXAS syndrome diagnosed due to recurrent fever, high CRP levels, and dermatitis

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Conflict of interest: None

The patient, a 77-year-old man, experienced fever, headache, limb myalgia, and redness in both upper limbs with high CRP levels around 12 months ago. Lumbar puncture, head MRI, and chest/abdominal CT showed no significant findings, and the symptoms improved with ceftriaxone. Similar symptoms reappeared at 9 months and responded to amoxicillin-clavulanic acid. At 6 months, anemia and neutropenia led to a diagnosis of myelodysplastic syndrome (MDS). Three months prior, he developed redness in both upper limbs, sore throat, and headache, which improved with celecoxib. One month prior, he had migrating limb and trunk pain, unresponsive to prednisolone. PET-CT was performed but showed no findings as symptoms had subsided. In month X, the patient developed redness, swelling, and pain in his right eyelid and ankle and redness in the nasal ala, prompting hospitalization. Examination showed signs of chondritis, and VEXAS syndrome was suspected due to recurrent fever, high CRP, systemic inflammation, chondritis, lymphadenopathy, and MDS. *UBA1* mutation analysis confirmed a somatic mutation, leading to a VEXAS syndrome diagnosis. Described in 2020, VEXAS is characterized by fever, cytopenia, bone marrow dysplasia, chondritis, and vasculitis. This case is presented with a literature review.

P3-164

Two Cases of Sarcoidosis with a Wide Range of Symptoms

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Conflict of interest: None

[Case 1] A 57-year-old female was diagnosed with uveitis in Year X-6. CT revealed mediastinal lymphadenopathy, and a biopsy confirmed the diagnosis of sarcoidosis. PET-CT demonstrated uptake of the parotid gland, liver, and spleen in addition to the lungs. She was initiated with prednisolone at 30 mg/day, which was later tapered off. In Year X, she was referred to our department with a diagnosis of cardiac sarcoidosis. Treatment was initiated with prednisolone at 30 mg/day and methotrexate at 6 mg/week. [Case 2] A 52-year-old female presented with joint pain, skin rash, and pain in both lower extremities for three months in Year X. Ophthalmologic examination revealed angle nodules, and CT showed multiple granular shadows, nodules, and masses. There was redness of peripheral joints and erythema in both lower legs, and MRI of the lower legs revealed widespread patchy high signal changes. Skin biopsy confirmed non-caseating epithelioid cell granulomas. She was diagnosed with sarcoidosis and was initiated with prednisolone at 40 mg/day and methotrexate at 8 mg/week. The treatment has been effective. [Discussion] In a previous report, 5 organ lesions were reported in 7.5% of cases and 6 lesions in 3.7% of cases. We consider these cases to be valuable and report their clinical course.

P3-165

Fever of unknown origin due to Weber-Christian disease

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Conflict of interest: None

[Present History of the Disease] Patient described fever from June Year X, which was diagnosed as COVID-19. As his fever hadn't alleviated, he was introduced to our hospital on 20th July Year X and consequently hospitalized. Blood test showed CRP 21.0 mg/dl, enhanced CT scan revealed splenomegaly and high-density deep lipid concentrations in anterior mediastinum, pancreatic tail and left lower limb. He also complained painful swelling in the left thigh with erythema, which found to be fat necrosis and panniculitis with neutrophil infiltration by biopsy. Afterward, since novel pericardial fluid appeared, we diagnosed him as Weber-Christian Disease and started to treat by prednisolone (PSL) 60 mg/day (1 mg/kg/day). We reduced the dose of PSL by 3 days but flared up when we decreased PSL to 20 mg/day. We increased PSL up to 60 mg/day, followed by decrease 10 mg/day per 2 weeks and additional treatment with Cyclosporine, resulting in alleviation of his fever. He was discharged with PSL35 mg/day. [Clinical Implications] We encountered this rare Weber-Christian Disease, whose evidence-based treatment has not been identified, and further accumulation of case reports is necessary for the better understanding. Here we report clinical course of this patient with literature-based assessment.

P3-166

A case of SAPHO syndrome complicated with pericarditis and pleurisy

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Conflict of interest: None

[Case] Woman in her 70s [Chief complaint] Fever, Cough [Present medical history] She was diagnosed with SAPHO syndrome and treated with MTX 8 mg/week and SASP 1000 mg/day. In Y-1, X, she developed a cough. She was treated medically for asthma, but her symptoms did not improve and she also had back pain, so she was prescribed prednisolone 30 mg/day for 5 days, and her symptoms improved. After the prednisolone was discontinued, she came to our hospital with back pain and fever from Z-4, Y. Blood tests showed WBC 10430/μL, CRP 14.06 mg/dL, and she was admitted to the hospital on Y/Z. Imaging examination revealed pericardial and left pleural effusion, and pleurodesis was performed, which revealed exudative pleural effusion. Bacterial culture was negative and there was no evidence of malignancy. She was treated with NSAIDs, but her symptoms did not improve. First, we considered infection and started antibacterial therapy, but no effect was observed, and prednisolone 40 mg/day was started as a treatment for pericarditis and pleurisy due to SAPHO syndrome. Pericardial and pleural effusion improved markedly and the patient was discharged. We report a case of SAPHO syndrome with reduced pericardial effusion and pleural effusion after steroid therapy, including a review of the literature.

P3-167

Clinical characteristics of six experienced cases of TAFRO syndrome

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Conflict of interest: None

[Objectives] TAFRO syndrome is a systemic inflammatory disease with thrombocytopenia, anasarca, fever, renal dysfunction, and organomegaly. TAFRO syndrome associated with idiopathic multicentric Castleman disease (iMCD) is called iMCD-TAFRO or called TAFRO without iMCD. However, information on the clinical features is scarce due to the rarity of the disease. The study was to clarify the clinical features of TAFRO syndrome. [Methods] This is a medical-record based review study. We enrolled patients diagnosed with TAFRO at our department until October 2024. [Results] Two patients with iMCD-TAFRO and four patients with TAFRO without iMCD were included in this study. All patients had fever, renal dysfunction, and anasarca. Thrombocytopenia was observed in five patients except one patient with iMCD-TAFRO. Serum IL-6 was elevated in one patient with iMCD-TAFRO (28.0 pg/mL), while it was elevated in all patients with TAFRO without iMCD (10.1-102.0 pg/mL). Hypergammaglobulinemia and anti-SS-A antibody positivity were observed only in one case of iMCD-TAFRO. [Conclusion] All patients with TAFRO without iMCD had elevated serum IL-6 levels. Although it has been reported anti-SS-A antibody positivity is likely to be seen in TAFRO without iMCD (Sci Rep. 2024; 14: 2889), this was not true for our cases.

P3-168

A case of relapsing polychondritis involving large airway without auricular and nasal cartilage inflammation

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Conflict of interest: None

A 47-year-old male with a 3-month history of dry cough, hoarseness, and elevated CRP level was referred to our hospital for further evaluation. There were no signs suggesting auricular or nasal cartilage inflammation. CT scan revealed thickening of the tracheal and bronchial walls. Laryngological examination showed edema in the arytenoid and vocal cords. Bone scintigraphy and MRI indicated costochondritis. Bronchoscopy revealed mucosal swelling in the trachea and bronchi. Biopsy of airway epithelia showed nonspecific inflammation, with no findings suggestive of amyloidosis or vasculitis. Due to safety concerns, cartilage biopsy was not performed. Clinical diagnosis of relapsing polychondritis was made and treatment was started with glucocorticoid pulse therapy, followed by high-dose glucocorticoids and intermittent intravenous cyclophosphamide. The therapy improved clinical symptoms, decreased CRP level, and improved tracheal wall thickening on CT and MRI. [Discussion] Diagnosing relapsing polychondritis without nasal or auricular cartilage inflammation can be challenging. In this case, the combination of CT, bone scintigraphy, and MRI provided evidence suggesting cartilage inflammation in the trachea and costal cartilage junction, leading to diagnosis.

P3-169

An intractable sarcoidosis case with rare central nervous involvement

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Conflict of interest: None

[Background] The central nervous system is infrequently involved in patients with sarcoidosis (SARC). [Case] 49 year-old male was diagnosed as pulmonary SARC at the year X-16. In the year X-7, systemic erythema appeared and the diagnosis of skin SARC was made based on the biopsy. Topical glucocorticoid (GC) followed by 20 mg/day of prednisolone (PSL) was started. In the year X-2, while taking 6 mg/day, he developed diabetes insipidus and bilateral temporal hemianopsia. Brain MRI suggested a pituitary gland lesion. GC pulse therapy resulted in inprovement. But after PSL was tapered to 5 mg/day, visual field defect reappeared. He was referred to our hospital for further evaluation. [Clinical Course] At the initial visit, bilateral temporal and horizontal heminopsia was observed. Brain MRI showed hypothalamic, optic chiasm and basilar lesions and multiple nodules on the pia mater. Spinal MRI also showed an intraspinal lesion from 6th to 10th thoracic segment. Spinal fluid test showed elevation of the levels of ACE, IgG and soluble IL-2R. After the GC pulse therapy, 60 mg/day of PSL was followed, which resulted in improvement [Discussion] We experienced a quite rare SARC case involving optic chiasm, pia mater and intraspinal lesion that successfully responded to GC.

~~P3-170~~

~~**Systemic Multiple Nodules in a Rheumatoid Arthritis Patient Possibly Associated with Cutibacterium acnes Infection: A Case Report**~~

~~Kahori Ishida, Kohei Tsujimoto, Atsuko Tsujii, Reo Shiratani, Kenichiro Hori, Makiko Ikoma, Eri Itotagawa, Yasuhiro Kato, Masayuki Nishide, Masashi Narazaki, Atsushi Kumanogoh~~
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~~Conflict of interest: None~~

~~52-year-old female with RA was treated using methotrexate and etanercept. In August X-1, nodular erythema appeared on the left thigh and disappeared spontaneously. In September, after stopping etanercept, a painful mass appeared in the left parotid gland, and although repeated biopsies were performed, the diagnosis could not be determined as only inflammatory granulation tissue was found. The mass continued to grow, and gradually the patient began to have trouble opening her mouth. In January of year X, methotrexate was discontinued, but there was no improvement. In March, PET-CT scan showed abnormal accumulation in the left parotid gland, lungs, and subcutaneous nodules in the buttocks, and the patient was admitted. Since Cutibacterium acnes was detected in the culture of the left parotid gland and the nodule in the buttocks, we administered penicillin and some shrinkage of the nodule in the front of the left ear was observed, but the other nodules did not change and the opening disorder did not improve. Prednisolone 30 mg was started and the opening disorder improved. In addition to, a simple chest and abdominal CT scan~~

showed that the nodules had shrunk. (1177 characters)

P3-171

A Case of Relapsing Polychondritis Complicated by Polycythemia Vera, Successfully Treated with Ruxolitinib

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Conflict of interest: None

[Case Presentation] A 66-year-old Japanese woman was diagnosed with relapsing polychondritis (RP) based on a history of fever, bronchial wall thickening, airway stenosis upon inhalation, painful erythema, polyarthritis, and internal carotid artery stenosis. Treatment with methylprednisolone (mPSL) pulse therapy, high-dose prednisolone (PSL), and methotrexate were effective; however, it was difficult to taper PSL below 10 mg because of minor flares with skin rashes and arthritis. Two years later, she developed erythrocytosis and was found to have the JAK2 V617F mutation, leading to a diagnosis of polycythemia vera (PV). Subsequently, therapeutic phlebotomy was initiated. At the age of 72, a follow-up MRI revealed arteritis and leptomeningitis due to RP. In response, mPSL pulse therapy, high dose PSL with intermittent intravenous cyclophosphamide (IVCY) were started; however, arthritis and rashes relapsed upon tapering PSL. After discontinuing IVCY, Ruxolitinib was introduced for the management of PV, allowing for a tapering of PSL to 5 mg without recurrence of symptoms. [Clinical Significance] While there are reports of Baricitinib and Tofacitinib being effective for RP, this is the first report indicating the efficacy of Ruxolitinib, a JAK1/2 inhibitor.

P3-172

A case of cutaneous sarcoidosis after remission of primary malignant lymphoma of the thyroid gland

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Conflict of interest: None

[Case] A 72-year-old woman was admitted to our department for fatigue in both lower extremities. In X-10 years, she was diagnosed with Stage IVA primary thyroid lymphoma and received R-CHOP therapy, radiation therapy, peripheral blood stem cell transplantation. The malignant lymphoma (ML) resulted in remission. In September X years, A blood test showed elevated soluble IL-2R of 1691 U/mL, and a relapse of ML was suspected. PET-CT scan revealed abnormal skin and fascia accumulations in the bilateral buttocks and lower extremities. Ichthyosis was observed in her both lower legs. Biopsy of the skin and fascia of the lower leg showed epithelial granulomas and she was diagnosed with cutaneous sarcoidosis. Prednisolone 20 mg/day was initiated, and she is in remission. [Clinical Significance] Complication of ML after sarcoidosis is known and the concept of sarcoidosis-lymphoma syndrome has been proposed. Cases of cutaneous sarcoidosis after ML are rare, with 7 previously reported cases. A review of 8 cases, including our case, showed the mean age of onset was 45.9 years, and the mean time was 2.3 years. Skin findings varied such us erythema nodosum, lipositis, and ichthyosis. When skin findings are seen after ML, sarcoidosis should be suspected and a pathologic examination is important.

P3-173

A case of drug-induced sarcoidosis-like reaction (DISR) with dupilumab

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Conflict of interest: None

[Case] A 72-year-old woman had been treated with corticosteroids for refractory asthma, eosinophilia, and eosinophilic gastroenteritis for 24 years. Treatment with 100 mg of mepolizumab every 4 weeks was initiated in X-2 years, but her hearing and olfaction worsened in X-1 years. In X-7 months, her treatment was switched to dupilumab 300 mg every 2 weeks for eosinophilic otitis media and eosinophilic sinusitis. In X year, the corticosteroid treatment was terminated. Subcutaneous induration in her lower legs and uveitis appeared. The blood levels of sIL2R and ACE were elevated. A biopsy of the lesions confirmed sarcoidosis. Dupilumab was discontinued, and the subcutaneous induration subsequently improved. [Discussion] Several cases of DISR caused by dupilumab have been reported. DISR is believed to be associated with a Th1/Th2 cell imbalance caused by drugs, leading to granuloma formation. Dupilumab is an anti-IL-4/13 receptor monoclonal antibody that promotes the Th1 pathway by inhibiting IL-4 and IL-13, and it may be the causative drug of DISR. DISR can be expected to improve with spontaneous remission or by discontinuing the drug. In some cases, treatment with corticosteroids or other medications may be necessary. DISR should be noted when using dupilumab.

P3-174

Paraneoplastic adult-onset Still's disease-like manifestations caused by mediastinal lymph node adenocarcinoma of unknown primary site

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Conflict of interest: None

[Case] A 73-year old man was admitted to A hospital due to fever, polyarthritis, and erythema on his back. Laboratory findings showed leukocytosis and elevated CRP (31 mg/dL). CT revealed swollen mediastinal lymph node (MLN) and pericardial effusion. Musculoskeletal ultrasound showed active synovitis, tenosynovitis and enthestis. FDG-PET/CT demonstrated high FDG uptake in multiple joints, pericardium, and MLN. EBUS-TBNA of MLN indicated no evidence of malignancy. At this point, he was diagnosed with adult-onset Still's disease (AOSD), and prednisolone was initiated, followed by intravenous tocilizumab therapy. Arthritis and pericarditis tended to alleviate, but swollen MLN remained. We performed a thoracoscopic MLN biopsy considering malignancy. Biopsy specimen indicated adenocarcinoma. We finally diagnosed with paraneoplastic AOSD caused by MLN adenocarcinoma of unknown primary site. Additional examination showed EGFR gene mutation and positive immunostaining of CK7 and TTF-1, and therefore, we started osimertinib according to lung carcinoma treatment. This treatment resulted in reduction of swollen MLN and remission of arthritis and pericarditis. [Conclusion] We would like to discuss the present case of mediastinal lymph node adenocarcinoma presenting paraneoplastic AOSD.

P3-175

A Case of Hypereosinophilic Syndrome (HES) Presenting with Acute Lower Limb Arterial Occlusion

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Conflict of interest: None

Case Presentation: A 57-year-old male presented with one-week history of numbness and pain in both hands and feet. Examination revealed acrocyanosis in all four limbs, severe eosinophilia (6723/μl), and proteinuria (3.3 g/gCre). CT scans showed bronchial wall thickening and reticular shadows in the lungs. CTA showed the peripheral branches of the three main vessels in the lower legs were not visualized. The patient was diagnosed with acute lower limb arterial occlusion due to hypereosinophilic syndrome (HES). Treatment and Course: Treatment with PSL 60 mg was initiated. Peripheral cyanosis improved in all limbs except the left lower limb. About a month after starting treatment, the necrotic area expanded from the left toes to the foot. Salvage was deemed impossible, and below-knee amputation was performed. Pathology revealed thrombus for-

mation in the anterior tibial arteries and veins, and thrombi occluding vessels in the dermis to subcutaneous tissue. No fibrinoid necrosis of blood vessels was observed. Renal pathology showed membranous nephropathy. Clinical Significance: Acute lower limb arterial occlusion and glomerulonephritis are rare organ manifestations of HES. These complications are important in the differential diagnosis of eosinophilic granulomatosis with polyangiitis.

P3-176

A case of palmar fasciitis and polyarthritis syndrome initially diagnosed with rheumatoid arthritis

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Conflict of interest: None

[Case] A 59-year-old male presented with 1 year-long polyarthralgia and contracture. He was referred to our hospital from a local doctor, who diagnosed him with RA but MTX or ETN did not show efficacy. He presented with 15 kg/year weight loss and esophageal cancer was discovered. Contract-enhanced MRI demonstrated enhancement around digital muscles. We diagnosed him with palmar fasciitis and polyarthritis syndrome (PFPAS). [Discussion] PFPAS is one of a rare paraneoplastic syndrome which is characterized by hand flexion contracture, thickening of palmar fascia and symmetrical polyarthritis. This is the second PFPAS case accompanied by esophageal cancer. Skin biopsy reveals fibroblast proliferation, collagen deposition and monocyte invasion but the mechanism is unclear. The efficacy of corticosteroids, NSAIDs and DMARDs is limited. The removeal of cancer improves arthritis but contracture is often irreversible. PFPAS is confusable with RA due to symmetrical digital synovitis, which may cause the delayed diagnosis, and progression of contracture may lead to low PS. [Clinical Significance] PFPAS often precedes initial diagnosis, recurrence and progression of cancer. When encountering RA-like symptoms with contracture or weight loss, rapid investigation of cancer is essential.

P3-177

A case of pyoderma gangrenosum complicated by arthritis

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Conflict of interest: None

[Objectives] Pyoderma gangrenosum (PG) is a relatively rare disease designated as an intractable disease in Japan, with an incidence of 3 cases per million persons per year. PG is a neutrophilic dermatosis, but activated neutrophils can cause arthritis as an extradermal manifestation. We report a case of PG complicated with arthritis treated with adalimumab (ADA). [Case] A 75-year-old man was diagnosed with PG by the dermatology department of this hospital in August X. In December X, he developed polyarthralgia. When she came to our hospital, tenderness was observed in both wrist joints, both ankle joints and both knee joints, and swelling in the left ankle joint. Simple x-rays showed no evidence of erosion or joint destruction. A joint echo showed synovitis in both wrist joints, synovitis in both ankle joints, and edema in the right knee joint. Skin symptoms also improved. [Conclusion] Although no treatment for PG has yet been established, the efficacy of treatment with biologics was reported in 2020, and guidelines for the use of ADAs for PG were established in 2021. In this case, we experienced a patient with arthritis whose skin symptoms did not improve with existing treatment, and both skin symptoms and arthritis improved with the use of ADA.

P3-178

A case of TAFRO syndrome requiring differentiation from systemic lupus erythematosus

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Conflict of interest: None

Case: In June of year X, 24-year-old male developed a fever and general malaise, so he visited his family doctor, and referred to our hospital because he was found to have thrombocytopenia. In arrival, there was a decrease in two types of blood cells, and mild renal dysfunction. CT scan showed bilateral pleural effusion and generalized lymphadenopathy. A bone marrow biopsy showed no abnormal cells, ruling out a hematological disorder. Autoantibodies were measured, and the patient tested positive for ANA and positive for anti-ds-DNA IgG antibodies, with low serum complement levels. The patient was diagnosed with SLE, with the 2019 ACR/EULAR classification criteria for SLE. The patient was given PSL, IVCY and TAC. After treatment, gradual recovery of blood cells was observed. Furthermore renal biopsy was performed. Edematous swelling of endothelial cells and mesangial cells was observed, and no immune deposits were observed, so the patient was diagnosed with TAFRO syndrome. Discussion: SLE and TAFRO syndrome have many similar findings, and it is difficult to diagnosis in case that autoantibodies are positive. In this case, we started treatment as SLE, but after a renal biopsy, we diagnosed the patient with TAFRO syndrome. We report on this case, including a literature review.

P3-179

A case of TAFRO syndrome-like symptoms during treatment of Sjogren's syndrome

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Conflict of interest: None

<Case> A 62-year-old woman. She had Raynaud's phenomenon, symptoms of stasis, and interstitial pneumonia since her 40s. 53 years old, she was diagnosed with Sjogren's syndrome due to positive anti-SS-A/B antibody. 4 months ago, she developed worsening arthralgia, and 2 months ago, bilateral neck and inguinal lymph node enlargement appeared. Fever, thrombocytopenia, pleural effusion, and renal dysfunction were observed, and TAFRO syndrome was suspected due to the absence of malignant findings on lymph node biopsy. Renal dysfunction and thrombocytopenia resolved spontaneously, but enlarged lymph nodes, urinary protein and occult blood, and low-grade fever persisted, and anti-RNP antibody positivity was also observed. Renal biopsy revealed membranous proliferative glomerulonephritis, and treatment with prednisolone 1 mg/kg and cyclosporine was initiated. The fever, thrombocytopenia, urinary protein and occult blood, and effusion improved. <Discussion> TAFRO syndrome can be caused by malignant tumors, autoimmune diseases, and infectious diseases, and autoimmune diseases such as systemic lupus erythematosus should be ruled out. We report a case of a patient with primary Sjögren's syndrome presenting with symptoms similar to TAFRO syndrome, along with a review of the literature.

P3-180

Four cases of eosinophilic fasciitis diagnosed based on hypereosinophilia and MRI findings

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Conflict of interest: None

Eosinophilic fasciitis (EF) is a rare disease that presents with edematous sclerosis and joint contractures, and requires differentiation from other diseases. We report 4 cases of EF diagnosed by edema, eosinophilia (Eos) of the peripheral blood, and MRI. [Patients] 2 males and 2 females (median age 41 years). [History] 2 patients had asthma and 1 had sinusitis. [Physical examination] 4 patients had edema of the extremities, 3 patients had arthralgia of the hands. [Examination] (Median) Eos was 5191/μL, IgE 123 IU/ml, TARC 24185 pg/ml, sIL-2R 1615 U/ml. All patients were negative for various autoantibodies. MRI showed high intensity signal along the fascia on STIR in all patients, tendinitis in 3 cases. 1 patient underwent myofascial biopsy for histologically confirmed diagnosis, and 3 patients were diagnosed with EF based on Eos and MRI. [Treatment] All

patients received mPSL pulse + high-dose oral steroids + early rehabilitation. All patients showed rapid decrease in Eos, rapid disappearance of edema, and MRI showed improvement. [Conclusion] Hypereosinophilia with edema often recalls eosinophilic angioedema, but history, physical examination, and MRI lead to the diagnosis of EF. EF is a systemic disease, and high-dose steroid is associated with early recovery of the patient's ADL.

P3-181

A case of Sarcoid-like Myositis

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Conflict of interest: None

[Case] A 76-year-old female presented with a 17-day history of swelling and pain in both forearms, followed by finger extension difficulty. The pain has spread, making it difficult to stand and impaired finger dexterity. MMT was 4/5 at triceps, 2-/5 at etextensor digitorum, 4/5 at flexor digitorum profundus muscle, and 4-/5 at quadriceps. Blood tests showed that Ca 12.9 mg/dL, Alb 3.7 g/dL, CK 810 U/L, aldolase 36.0 U/L, lysozyme 20.4 μg/mL, and 1,25-$(OH)_2$ vitamin D 173 pg/mL (Normal range 20-60). MRI showed high STIR signals in the triceps, forearm extensors, and quadriceps. Triceps muscle biopsy showed muscle fiber necrosis and granulomatous lesions with giant cells. In the absence of other organ involvement, a diagnosis of Sarcoid-like Myositis was made. She was started on methylprednisolone 60 mg/day, which resulted in a rapid improvement in CK and Ca levels, accompanied by a gradual recovery of muscle strength. The patient was able to walk independently, and subsequently, the finger extension impairment is gradually improving. [Discussion] In this case, granulomatous / giant cell myositis that manifested with acute onset muscle weakness and was accompanied by hypercalcemia. Similar cases have been reported as Sarcoid-like Myositis. We report a case with a literature review.

P3-182

A 79-year-old woman with a muscle weakness diagnosed with myasthenia gravis and autoimmune neutropenia due to antineutrophil antibodies

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Conflict of interest: None

[Medical history] A 79-year-old female. She had difficulty straightening her back and distal leg muscle weakness and low white blood cell count, She visited our department for suspicion of SLE, IIM and SSc due to positive anti-Centromere antibodies. [Physical findings] She had no Raynaud's phenomenon, shortened lingua frenulum, nail cuticle and periungual abnormalities, MRSS all 0, MMT all 5/5, no muscle pain, no swollen, tender joints, no skin rash. [Laboratory findings] WBC 2300/μL, Neut 26.0%, CK 766 IU/L, Myoglobin 325.8 ng/mL, Aldolase 13.2 U/L, ANA Centromere 1280x, anti-Centromere antibody 240 U/mL, anti-Jo-1 antibody 1+, anti-AchR antibody 1.9nMOL/L [Clinical Course] CT showed muscle atrophy of both lower legs. The symptoms were worse in the evening and the walking distance was reduced. Moreover she also had ptosis, respiratory muscle fatigue, anti-AchR antibodies, so she was diagnosed with myasthenia gravis (MG). She had anti-neutrophil antibodies, no abnormalities in the bone marrow, so she was diagnosed with autoimmune neutropenia (AN) due to anti-neutrophil antibodies. [Discussion] Initially, SSc, SLE, and IIM were suspected, but further examination led to a diagnosis of MG and AN due to antineutrophil antibodies. Cases of MG and AN was considered to be rare and valuable.

P3-183

An Effective Case of Early Plasma Exchange in a Patient with TAFRO Syndrome

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Conflict of interest: None

A 59-year-old female. The patient was referred for evaluation of fever and lower leg edema with elevated inflammatory markers. Lab tests showed CRP 26.2 mg/dL, IL-6 310.0 pg/mL, and VEGF 4755.7 pg/mL. CT revealed pleural and abdominal effusion, retroperitoneal lymphadenopathy, and adrenal infarction. The platelet count dropped to 90,000/μL, and progressive renal impairment led to a diagnosis of TAFRO syndrome. Treatment with GC and TCZ was initiated; however, the platelet count decreased to 49,000/μL, and worsening effusion caused respiratory failure. Hemodynamic instability necessitated drainage of pleural effusion, daily PEx and HD, combined with TAC. Daily PEx led to decreased inflammatory markers, and improved respiratory function, stabilizing hemodynamics. After stopping PEx, the patient's condition remained stable. TAFRO syndrome is a systemic inflammatory disease that can lead to rapid organ failure. There is no established treatment, and cases achieving remission with GC alone are rare. Severe cases require combination therapy with GC, RTX, or TCZ, and some may involve PEx. PEx may serve as adjunct therapy until the effects of immunosuppressants are seen; early initiation in severe cases may help reduce inflammatory cytokines and improve the disease course.

P3-184

Analysis of patients with human adjuvant disease in our institution

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Conflict of interest: None

[Objectives] Human adjuvant disease (HAD) is condition in which foreign substances, such as paraffin or silicone, remain in the body long-term and may trigger connective tissue diseases (CTDs) or similar pathological states. It is difficult to be diagnosed, and that can be refractory. This study aims to elucidate the clinical features of HAD cases at our institution. [Methods] We retrospectively analyzed and compared the clinical characteristics of four cases of HAD diagnosed in our department from January 2016 to December 2023, with an average onset age of 56.5 ± 26.2 years. [Results] The patients developed diseases such as rheumatoid arthritis, systemic scleroderma-like syndromes, discoid lupus erythematosus, and microscopic polyangiitis, respectively. The interval between foreign substance injection/implantation and disease onset was 26 ± 18.7 years. None of the cases underwent surgical removal. On the other hand, symptoms were ameliorated by treatment with immunosuppressive and symptomatic therapies, and all patients remain under ongoing follow-up. [Conclusion] Even if a typical CTD can't be diagnosed, when symptoms and test results suggest a condition related to HAD, it's necessary to consider treatment strategies based on the suspected diseases in addition to foreign body removal.

P3-185

Clinical characteristics of polymyalgia rheumatica with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Polymyalgia rheumatica (PMR) may be difficult to differentiate from late-onset rheumatoid arthritis (LORA) but there are few PMR patients complicated with RA. We investigated clinical characteristics of PMR patients with RA at our hospital. [Methods] Of the 118 patients diagnosed with Bird's criteria or 2012 EULAR/ACR criteria from January 2015 to March 2024, 11 patients with RA (9.3%) were examined. Seronegative RA patients were excluded. [Results] The average of age was 79.0±8.7 years for 4 males and 7 females. The average levels of CRP, ESR,

RF, ACPA and MMP-3 were 7.27±4.13 mg/dL, 91.0±25.5 mm/h, 166.5± 106.7 IU/mL, 639.3±524.4 U/mL and 372.5±434.6 ng/mL, respectively. Peripheral arthritis developed in 7 cases. The initial dose of prednisolone (PSL) was 13.6±3.7 mg/day. 5 cases (45.5%) relapsed, and no cases achieved PSL-free remission in 1 year. 4 cases (36.4%) had serious infection, and 2 cases were diagnosed as malignant tumor. HBV reactivation occurred in 1 case treated with TCZ. [Conclusion] It is necessary to treat with DMARDs for RA during PSL tapering and it should be especially careful about the complication of infection.

P3-186

A case of polymyalgia rheumatica without headache in which large vessel vasculitis was diagnosed

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Conflict of interest: None

[Case] 77-year-old male [Chief complaint] Pain in the neck, shoulders, and both thighs [Present illness] X-1 month, the patient visited our clinic with pain in the neck and both shoulders. CRP was 7.13 mg/dL, and was diagnosed with polymyalgia rheumatica (PMR). Prednisolone (PSL) 15 mg/day was started, but the inflammatory response did not improve, and in month X, pain in the neck and shoulders remained, and muscle pain in the left upper arm was also observed. CRP was 6.88 mg/dL, and FDG-PET/CT showed abnormal accumulation in the descending thoracic aorta. The patient was diagnosed with large vessel giant cell arteritis (GCA) as well. The patient strongly resisted steroids, and was treated with tocilizumab (TCZ) alone (240 mg/month). Symptoms improved, and all FDG-PET/CT findings became negative, and the disease progressed. [Discussion] GCA occurs in elderly people, High-dose steroids are highly effective, but problems such as increased blood sugar, blood pressure, and intraocular pressure can occur. It has been suggested that TCZ monotherapy may also be an option.

P3-187

The usefulness of MRI images of the upper limbs in patients with eosinophilic fasciitis

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Conflict of interest: None

We report on the usefulness of upper limb MRI in cases of EF that we have experienced in our department. [Subjects] Four cases of eosinophilic fasciitis. [Methods] We evaluated the areas of edema seen on MRI of the upper limb (mainly the forearm to the hand). [Results] Case 1: There were high intensity areas (HIA) on T2-weighted fat-suppressed images (T2WI-FatSat) around the flexor tendons of the second flexor carpi radialis, abductor pollicis longus and extensor digitorum longus in the carpal tunnel. Case 2: At the MIP joint level, there is a HIA around the flexor tendons of the third finger on T2WIFatSat. There is fluid accumulation around the flexor and extensor tendons of the carpus. Case 3: At the carpal tunnel level, there is a HIA around the flexor tendons of the long thumb and deep flexor tendons on STIR. There is a HIA around the extensor tendons of the dorsal hand on STIR. Case 4: There was thickening of the transverse carpal ligament (under GC treatment). [Conclusion] MRI is a non-invasive examination that is useful for confirming the presence or absence of tenosynovitis when differentiating between diseases such as scleroderma and eosinophilic angioedema. In order to prevent any after-effects, strong treatment including GC pulse therapy is necessary.

P3-188

Two Cases of Neurological Complications with Herpes Zoster in Rheumatoid Arthritis Patients on JAK Inhibitors

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Conflict of interest: None

[Case 1] A 75-year-old woman with rheumatoid arthritis (RA) who had started upadacitinib 15 mg/day one month prior was admitted with herpes zoster (HZ) on her face and right auricle, and intravenous acyclovir (ACV) was initiated. She subsequently developed difficulty swallowing with soft palate deviation and right vocal cord paralysis, which led to a diagnosis of lower cranial nerve palsy (IX and X) associated with HZ. Despite three weeks of ACV treatment, her dysphagia persisted. [Case 2] A 61-year-old woman with RA who had started filgotinib 100 mg/day eight months prior was admitted with disseminated HZ affecting her left gluteal region, back, and both upper arms, and intravenous ACV was started. She developed numbness, pain, and weakness in her left leg. Sensory loss in the L4-S1 dermatomes and absence of the left patellar reflex were also observed, leading to a diagnosis of segmental zoster paresis. Following intravenous glucocorticoid pulse therapy, her motor function improved. [Discussion] Although few cases have been reported, JAK inhibitors may increase the risk of neurological complications with HZ. Preventive measures, including vaccination, along with early diagnosis and appropriate treatment, are recommended.

P3-189

Experience with Herpes Zoster Vaccine in Rheumatoid Arthritis Patients Receiving JAK Inhibitors

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Conflict of interest: None

[Objectives] We investigated the vaccination status of the recombinant zoster vaccine (RZV) and its preventive effect against herpes zoster (HZ) in rheumatoid arthritis (RA) patients receiving Janus kinase inhibitors (JAKi). [Methods] A total of 63 patients (mean age 67 ± 13.7 years) who initiated JAKi and continued attending our department between January 2014 and October 2024 were included. The incidence of HZ was compared between patients who received the RZV and those who did not. [Results] Out of the 63 patients, 18 (28.5%) developed HZ (mean age of 67 ± 15.4 years). 2 patients experienced HZ within one month of starting JAKi; both were on prednisolone (PSL) 10 mg/day or more. 23 patients received the RZV, and 2 (8.7%) developed HZ. These cases occurred in patients over 75 years old, both with prior exposure to biological agents, and one was taking PSL at 5 mg/day for organizing pneumonia. The risk of developing HZ was higher in the non-vaccinated group, with an odds ratio of 5.85 (95% CI: 1.20, 28.51), indicating a notable preventive effect of the RZV. [Conclusion] Elderly RA patients, particularly those using glucocorticoids, should be closely monitored for the development of HZ when starting JAKi therapy. The RZV appears to be effective in reducing the incidence of HZ.

P3-190

Safety and Efficacy of the Recombinant Zoster Vaccine in Patients with Rheumatic Diseases in Our Department, and Assessment of Trends in Antibody Titers

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Conflict of interest: None

[Objectives] To assess the safety and efficacy of the recombinant zoster vaccine (RZV) in patients with rheumatic diseases and to measure VZV IgG production using EIA. [Methods] We conducted a retrospective analysis of adverse reactions and herpes zoster (HZ) incidence among patients receiving RZV. IgG levels were measured at three points: before vaccination, after the first dose, and after the second dose, involving 41 cases to evaluate variations by HZ history, treatment, and age. [Results] Among 136 patients, two developed HZ-one shortly after the first dose and anoth-

er one month after the second. Most adverse reactions were mild; however, one patient was hospitalized for worsening nephropathy. IgG levels in 41 patients were 22.1±27.8 pre-vaccination, and post-vaccination levels were 59.2±46.1 and 121.8±85.4, showing significant increases. Pre-vaccination IgG levels did not significantly differ by HZ history, but post-vaccination levels were higher in patients with HZ history ($P < 0.05$). No significant differences were noted based on treatment type or age. [Conclusion] RZV is effective in patients with rheumatic diseases, irrespective of treatment regimen, with adverse events remaining within acceptable limits.

P3-191

Examining the impact of herpes zoster on disease activity and treatment of rheumatoid arthritis - analysis using the NinJa database

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Conflict of interest: None

[Objectives] To examine the impact of herpes zoster (HZ) on disease activity and treatment decisions in patients with rheumatoid arthritis (RA). [Methods] RA patients in NinJa2021 were split into 215 with HZ and 17,028 without HZ. Background characteristics and treatments were compared between the two groups. Among the HZ cases, 207 were tracked the following year to analyze the use and continuation rates of b/tsDMARDs and HZ vaccination history. [Results] Significant differences were found between HZ and non-HZ groups in age, CDAI, HAQ-DI, glucocorticoids (GC) use, and tsDMARDs use. The associations with GC and tsDMARDs use remained statistically significant after adjustments. No significant differences were found in CDAI and HAQ-DI in HZ patients across years. Of the 207 HZ cases, 72 were using b/tsDMARDs at the time of HZ onset; 62 continued treatments, while 10 discontinued. Disease worsening was noted in 40.3% of patients who continued b/tsDMARDs compared to 70.0% who discontinued. Among those who continued, 9 vaccinated patients had no recurrence, while 2 unvaccinated patients did. [Conclusion] Discontinuation of b/tsDMARDs following HZ onset may exacerbate RA activity, while continuing b/tsDMARDs carries a risk of recurrence. Vaccination may help continue b/tsDMARDs safely.

P3-192

A case of elderly-onset Epstein-Barr virus (EBV) activation in Systemic Lupus Erythematosus (SLE)-like symptoms

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Conflict of interest: None

A 65-year-old man was referred to the hospital on X day with the chief complaint of edema and dyspnea. He was admitted to the hospital for treatment of heart failure. He also had enlarged lymph nodes and nephrotic syndrome, decreased platelet count, pericardial effusion, anti-nuclear antibody (HOMO) 160x, anti-ssDNA antibody, anti-U1RNP antibody, weakly positive anti-MPO-ANCA, positive immune complex, and hypo complementemia. He fulfilled the criteria for SLE classification, but was also suspected to have malignant lymphoma due to high sIL2R and LDH levels. Lymph node biopsy was performed, which showed numerous EBER ISH-positive cells in germinal centers and between follicles, and blood EBV was 8000 copies/ml, suggesting a reactive lesion caused by EBV. Malignant lymphoma was negative, and nephrotic symptoms and laboratory findings improved only with treatment for heart failure (EF 25%). Three months later, EBV levels in the blood were less than sensitive, and anti-ssDNA antibody, anti-U1RNP antibody, and anti-MPO-ANCA/FEIA were all negative. Careful follow-up is needed to monitor the dynamics of EBV. In the case of atypical autoimmune disease-like symptoms, the possibility of EBV activation should be kept in mind.

P3-193

A case of pneumocystis pneumonia during remission induction therapy for microscopic polyangiitis thought to have triggered alveolar hemorrhage

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Conflict of interest: None

Case: An 87-year-old woman was diagnosed with microscopic polyangiitis based on positive MPO-ANCA, interstitial pneumonia, rapidly progressive glomerulonephritis, and high inflammatory response in July X. She was started on PSL 30 mg/day and rituximab 480 mg/week. CRP levels improved and urine protein became negative, so PSL was tapered to 15 mg/day. However, sputum became bloody, and CRP increased to 6.08 mg/dL. CT showed new reticular shadows, and ampicillin-sulbactam was started for bacterial pneumonia. The inflammatory response was mild with no worsening of symptoms, but CT on day 33 showed partial enlargement of the infiltrate and ground-glass opacities in the right lung. The prophylactic administration of atovaquone was started on day 29. On the 41st day, sputum Carini DNA was found positive, and next day, hemosiderin phagocytosis in the sputum was confirmed. CT showed a reduction in ground-glass opacities and infiltrates and the inflammatory response became negative, so the dose of PSL was not increased. Clinical significance: We have experienced a case of alveolar hemorrhage during treatment of microscopic polyangiitis. The clinical course of the patient suggests that PCP may have triggered the alveolar hemorrhage, and early prophylactic treatment was necessary.

P3-194

Incidence and potential control of pneumocystis pneumonia among rheumatoid arthritis patients in a community-oriented hospital

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Itakura Hospital

Conflict of interest: None

[Background] Although there is a growing shift of patients with rheumatoid arthritis (RA) from tertiary medical centers to regional hospitals, concerns are expressed about their management ability for uncommon complications represented by pneumocystis pneumonia (PCP). [Methods] RA patients receiving immunosuppressive therapy (IST) that developed PCP during 2020-2023 were carefully scrutinized. RA patients on IST that visited our clinic on arbitrary days of the week in August 2022 were followed up for 8 months and checked for their clinical details, PCP incidence, and matters related to its prophylaxis. [Results] Out of three PCP cases that were identified, all were on MTX and IST, two had preexisting lung disease (preLD) and two had lymphopenia <500. RA patients on IST in ambulatory-care setting consisted of 37 with prophylaxis and 80 without it. Two (2.5%) of the latter developed PCP while none with prophylaxis did. PCP prophylaxis (n=37) comprised 6 weekly, 18 bi-weekly, 4 triweekly and 3 daily TMP-sulfa at introduction, while the regimen was modified in two afterwards. [Conclusion] Low-dose TMP-sulfa was considered effective for prevention of PCP in RA patients, and its safety ensures benefit to community-based medical practitioners.

P3-195

Verification of improvement of the Hand Joint destruction by Strengthening and Stretching for Rheumatoid Arthritis of the Hand (SARAH) exercises in patients with RA

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Medicine, Osaka Medical and Pharmaceutical University, Takatsuki, Osaka

Conflict of interest: None

[Objectives] There is still limited information and specific tools available to encourage an active approach to hand rehabilitation in RA patients. This study examined the effect of SARAH (Strengthening and Stretching for Rheumatoid Arthritis of the Hand) exercise on reducing joint destruction. [Methods] 43 RA patients [9.3% male, 90.7% female, age 65 years (58-73)] were instructed in SARAH exercises to their hand joints and to prevent misuse and overuse. Total Sharp Score (TSS) of the hand before and 52 weeks after the intervention. Approved by the Research Ethics Review Committee of Kyoto University Hospital (C1464). [Results] The disease duration was 4 years (2-14). Treatments included MTX 69.7%, PSL 4.6%, JAK 27.9%, and Bio 13.9%. Before the intervention, grip strength 18.9 (10.4-22.3) kg on the right and 16 (12.2-21.7) kg on the left; pinch strength 3.9 (2.9-5.5) kg on the right and 3.9 kg (3.1-5.2) on the left. Hand TSS was 9 (4-21) to 10 (3-24) after 52 weeks. Δ hand TSS $\leqq$ 0.5 was observed in 97.5% of patients. 40 out of 41 showed inhibition of joint destruction progression. 34 patients (79%) continued self-exercise for 12 weeks following the intervention. [Conclusion] SARAH exercises may be effective in inhibiting the progression of joint destruction in the fingers of RA patients.

P3-196

Survey on Patient Understanding After Medication Guidance on Methotrexate

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Azuma Rheumatology Clinic

Conflict of interest: None

[Objectives] This study aims to assess patients' understanding after medication guidance and improve future instruction. [Methods] From October 21 to 29, 2024, a non-face-to-face survey was conducted on 61 randomly selected patients aged 20 to 80 who were attending our hospital and taking MTX. [Results] Among those who received explanations about MTX, 5 patients (8%) reported they had not received any explanation, and 3 patients (5%) indicated they did not understand the explanation. Only one patient across all age groups reported that someone else managed their medication. Overall, 57% understood the function of folic acid, but this was only 37% among those aged 60 to 80. (1) The average understanding of MTX (9-point scale) and (2) the necessity for discontinuation (5-point scale) were as follows: for those in their 20s to 40s, the scores were (1) 8, (2) 2.9; for 50s to 60s, (1) 7.28, (2) 2.4; and for 70s to 80s, (1) 3.95, (2) 1.05. [Conclusion] Understanding of MTX decreases with age, while the perceived necessity for discontinuation remains low across all age groups, especially among older adults. To maximize treatment effectiveness and ensure the safe continuation of MTX, it is essential to provide regular medication guidance, regardless of age or duration of use.

P3-197

Evaluation of administrative staff in patient satisfaction based on questionnaire for patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objective] As a rheumatology facility certified by the Japan Society of Rheumatology, our hospital is working as a multidisciplinary team to provide medical care and care for patients with RA. In this study, we conducted a questionnaire survey for RA patients visiting our hospital to clarify the role of administrative staff in patient satisfaction. [Methods] A questionnaire survey was conducted from October 2023 to January 2024 among 237 RA patients on an outpatient basis at our hospital, and the response rate was 86.1% (204 patients). [Results] 87.8% of the patients answered "Yes" to the question "Are you glad you received medical treatment at our hospital?". In the univariate analysis, seven items were cited as questions related to the answer "yes", and the results of the multivariate analysis showed a significant relationship between three of the seven items: "the therapeutic drug is effective", "there is a sufficient explanation from the doctor", and "there is a sufficient explanation from the administrative staff". [Conclusion] Analysis of the results of a questionnaire survey from RA patients visiting our hospital revealed that "sufficient explanation from the administrative staff" is one of the evaluations of the hospital.

P3-198

Efforts to improve team medical care by rheumatology consultants at our hospital

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Toyo Hospital, Tokushima, Japan

Conflict of interest: None

[Objectives] To clarify the role of rheumatologists (hereafter referred to as "specialists"), a multidisciplinary team that responds to the diverse needs of patients with collagen vascular disease (hereafter referred to as "CVD") in collaboration with rheumatologists. [Methods] We investigated changes in the treatment and care of CVD patients in each department and hospital as a whole before and after the assignment of specialists to our hospital. [Results] Until now, medical treatment and care for CVD patients have been mainly carried out within each department, but after placement, specialists will take the lead. Specifically, the establishment of CVD consultation services by administrative staff and MSWs, medication guidance and self-injection guidance by nurses and pharmacists, and outpatient rehabilitation and foot care by nurses and PT/OTs are mentioned. [Conclusion] Progress has been made in building a team medical system that can provide medical care and care for CVD patients through multidisciplinary collaboration and hospital-wide practice.

P3-199

Challenges faced by MSW through the care of patients with rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR)

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Toyo Hospital, Tokushima, Japan

Conflict of interest: None

[Objective] To clarify the challenges by MSW at a medical care facility involved in the care of elderly patients with combined RA and PMR. [Case] This is a medical institution with an outpatient clinic for RA and a 50-bed long term care ward. The patient was an 83-year-old woman with a 20-year history of RA. In November in X-1, she was referred from another hospital due to increasing polyarthralgia, and was diagnosed with RA flare-up, PMR complication, and compression fracture of the lower thoracic spine. She was treated with steroids and IL-6 inhibitors. Because the patient was elderly, lived alone, and had a low income, we provided care with an emphasis on caregiver support, daily living support, and intervention for financial problems. In June in X, a policy was decided to provide support toward the goal of supporting the patient's admission to a long-term care facility where long-term treatment and continuous medication treatment are possible, as well as support for the use of the welfare system for daily life. [Conclusion] As MSW, I was able to establish a system that responded to changes in the medical conditions and care environment of elderly rheumatic disease patients by actively communicating with the patients' families and other support personnel.

P3-200

How do rheumatoid arthritis patients cope with difficult-to-control disease activity?

Emi Motoki
Hashimoto Clinic for Rheumatic Diseases

Conflict of interest: None

[Objectives] This study explores how RA patients, who are resistant to treatment and unable to control their disease or symptoms, endure their condition and maintain their quality of life, using the concept of Sense of

Coherence (SOC). [Methods] This is a case study involving a 75-year-old female patient with a 20-year history of RA. The disease activity could not be managed with pharmacological treatment. Over six months, semi-structured interviews, DAS28, functional disability, HAQ, and SOC scores were collected at each visit. The interview content was transcribed verbatim, and themes were extracted by comparing them with the progression of each score. [Results] From the participant's narrative, several themes emerged: exchanging information with fellow patients to understand her body and environment; creating the capacity to cope with symptoms with family support; maintaining a relationship with healthcare providers for ongoing consultation; and the importance of appearing "normal" externally, which helps clarify self-image and alleviate frustration with treatments. [Conclusion] Patients cultivate SOC by engaging in dialogue with their own bodies and attempting to reinterpret their situations positively.

Morning Seminar

MS1-1

Understanding the Mechanisms of Psoriatic Arthritis: From Inflammation to Comorbidities

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Conflict of interest: Yes

Psoriatic arthritis (PsA), characterized by skin symptoms and arthritis, has increasingly been recognized as a systemic disease. Approximately 72.9% of PsA cases follow a psoriasis-first pattern, where skin symptoms preceded arthritis, making diagnosis relatively straightforward when skin manifestations are present. However, multi-center studies have reported that about 11% of PsA cases present as arthritis-first, which poses significant diagnostic challenges. These cases may be misdiagnosed as seronegative RA or osteoarthritis, highlighting the importance of examining not only joint symptoms but also skin and nail changes specific to PsA in routine clinical practice. Inflammatory cytokines, particularly IL-23 and IL-6, play a central role in the pathogenesis of PsA. This inflammation extends beyond the joints and skin, impacting systemic health. PsA patients exhibit a higher prevalence of metabolic syndrome, diabetes, and obesity (elevated BMI) compared to those with psoriasis alone. This presentation will explore the underlying reasons for these comorbidities and their impact on disease activity and overall management strategies for PsA. Understanding the interrelationship between PsA, its comorbidities, and diagnostic challenges is essential for formulating effective treatment strategies. This lecture aims to provide a comprehensive perspective on PsA management, addressing both systemic inflammation and the associated clinical complexities.

MS1-2

Treatment Strategies for Psoriatic Arthritis Based on Pathophysiology: Perspectives on JAK and IL-23 Inhibitors

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Department of Orthopedics, Rehabilitation, Rheumatology & Psoriasis Center, Nippon Life Hospital, Japan

Conflict of interest: Yes

Psoriatic Arthritis (PsA) is an inflammatory disease characterized by skin and joint symptoms. PsA combines psoriasis, a skin disorder, with arthritis, affecting approximately 14.3% of psoriasis patients according to a multicenter survey by specialists in Japan. PsA pathogenesis is believed to involve the overproduction of various inflammatory cytokines, including IL-23, which activate different immune cells. Currently, PsA lacks established diagnostic criteria, making differential diagnosis from related conditions essential. While 72.9% of PsA cases present initially with psoriasis, making the diagnosis relatively straightforward, 11.0% begin with arthritis symptoms alone, as reported in a multicenter survey by specialists. This suggests that cases diagnosed as seronegative arthritis, such as seronegative RA or OA, may actually be PsA. Therefore, in daily practice, it is crucial to assess not only arthritis but also the presence of skin and nail symptoms. As with other rheumatic diseases, advancements in Biologics have significantly improved PsA treatment options. According to GRAPPA and EULAR recommendations, biologics are key therapeutic options for PsA. Given that PsA often presents with various domains of symptoms, treatment choices should be tailored to specific domains. PsA can also present with numerous comorbidities and extra-articular symptoms, necessitating a cross-disciplinary approach involving rheumatologists, dermatologists, and other healthcare professionals. The humanized anti-IL-23p19 monoclonal antibody (Risankizumab), approved for PsA in March 2019, and the JAK inhibitor (Upadacitinib), approved in June 2021, are now in clinical use. This seminar will explore treatment strategies for PsA (Psoriatic Arthritis) with a focus on Upadacitinib and Risankizumab.

MS2

Hypogammaglobulinemia in the Treatment of Rheumatic Diseases; Is the Management of gamma-Globulin Levels Important?

Tomonori Ishii

Hematology and Rheumatology Department, TOHOKU Medical and Pharmaceutical University, Sendai, Miyagi, Japan

Conflict of interest: Yes

Immunoglobulin replacement therapy has been established as a treatment for hypogammaglobulinemia in primary immunodeficiency diseases. Among the most evident diseases requiring this treatment is X-linked agammaglobulinemia. According to Japan's 2020 clinical practice guidelines, the target trough level for serum IgG is recommended to be maintained at 700 mg/dL or higher. In cases of secondary immunodeficiency with hypogammaglobulinemia caused by underlying diseases, the decline in γ-globulin levels may result either from the underlying disease itself or from the treatment. Knowledge about transient hypogammaglobulinemia induced by treatment has gradually accumulated. For instance, hypogammaglobulinemia related to hematopoietic stem cell transplantation has been one of the most studied topics. The infection management guidelines for post-hematopoietic cell transplantation recommend maintaining serum IgG levels between 400 and 500 mg/dL through replacement therapy. Hypogammaglobulinemia associated with rheumatic diseases has also gained attention. The increased use of B-cell depletion therapies, such as rituximab, in rheumatic diseases has led to a growing number of cases presenting with hypogammaglobulinemia, and its association with increased infections has been reported. Before rituximab became widely used, cases of hypogammaglobulinemia due to immunosuppressive therapy often improved with corticosteroid tapering alone. For such transient conditions, the necessity of replacement therapy remains uncertain. However, with the widespread use of B-cell depletion therapies as maintenance treatments, persistent hypogammaglobulinemia has been observed in a certain subset of patients, indicating significant changes in clinical practice. This seminar will discuss the importance of monitoring serum IgG levels during the treatment of rheumatic diseases, the profiles and risk factors of hypogammaglobulinemia, and the current state of immunoglobulin replacement therapy.

MS3

The importance of differential diagnosis in the IgG4-related disease: insights from a second opinion outpatient clinic

Yasufumi Masaki
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Conflict of interest: None

Introduction: IgG4-related disease (IgG4-RD) has been a recognized condition for over 20 years since its first description in 2001, and is included in the Japanese national annual medical licensing examination. While diagnosis of typical cases is usually without challenge, differentiating IgG4-RD from other conditions poses a challenge in atypical cases due to potential involvement of multiple organs throughout the body. Main body: At Kanazawa Medical University Hospital, I manage an outpatient clinic specializing in IgG4-RD. Over the past 10 years, I have evaluated 20 cases referred for a second opinion. Typically, second opinions involve confirming the diagnosis made by the referring institution and discussing treatment strategies with patients. However, in the case of IgG4-RD, the presence of numerous mimicking conditions and the potential for misdiagnosis necessitate a more thorough review. At our clinic, we not only assess clinical information but also reanalyze pathological specimens to confirm the diagnosis, including pathological findings. Through this process, seven out of 20 cases initially diagnosed as IgG4-RD by the referring facilities were found to have different conditions upon reevaluation. Of these, three were ultimately diagnosed as idiopathic multicentric Castleman disease (iMCD), while the others comprised a range of inflammatory diseases. Conclusion: IgG4-RD presents significant diagnostic challenges due to its broad spectrum of differential diagnoses. Even for specialists, borderline cases can be difficult to diagnose. In differential diagnosis, the distribution of organ involvement is important. Another major characteristic of IgG4-RD is its responsiveness to moderate doses of glucocorticoids (0.5-0,6 mg/kg of daily prednisolone), especially in the early stages of treatment. If glucocorticoid therapy proves ineffective, a review of the initial diagnosis is essential. While new therapeutic approaches are anticipated in the near future, insufficient attention to differential diagnosis may lead to diagnostic confusion and compromise patient care.

MS4

The significance of TNF inhibition therapy in the treatment of rheumatoid arthritis

Shintaro Hirata
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Conflict of interest: Yes

The era of molecular targeted therapy for rheumatoid arthritis (RA) in Japan began with the launch of infliximab in 2003. Twenty years have passed since then, and TNF inhibitors, IL-6R inhibitors, CTLA4-Ig, and JAK inhibitors are now available as molecular targeted therapies. Not only have these drugs contributed greatly to improving the outcomes of RA patients, but the verification of their efficacy and safety has also led to a better understanding of the new actions of target molecules, and has brought about a positive cycle of bed-to-bench and bench-to-bed translation. In particular, the TNF inhibitors, the first biological anti-rheumatic drugs, have accumulated a world-class safety profile thanks to the efforts of Japanese rheumatologists, and have contributed to the construction of evidence that forms the cornerstone of RA treatment. TNF inhibitors have expanded their indications to include not only RA, but also other immune-related diseases including spondyloarthritis, Behçet's disease, and inflammatory bowel disease. In this seminar, the significance of TNF inhibitor therapy for RA as a mature treatment method, and consideration about its expected position in the next decade will be discussed.

MS5-1

Treatment Strategies for Rheumatoid Arthritis with Pulmonary Complications

Yasuhiko Yamano
Department of Respiratory Medicine and Allergy, Tosei General Hospital

Conflict of interest: Yes

Lung manifestations in rheumatoid arthritis (RA), such as interstitial lung disease (ILD) and bronchiectasis, significantly impact both prognosis and treatment choices. Recently, the presence of lung involvement has been recognized as a major risk factor for difficult-to-treat RA (D2TRA), making treatment strategies for RA with lung complications a critical challenge. As lung disease has been reported as a leading cause of death in RA patients, comprehensive management from early stages is essential. Optimal management of RA with lung complications requires screening strategies for early detection, assessment and monitoring of ILD reversibility and progression risk, and measures against critical complications including acute exacerbation. Understanding the pathological mechanisms of RA-ILD is crucial for addressing these challenges. RA-ILD has long been characterized by the presence of lymphoid follicles (iBALT) around the lesions. Autoantibodies are produced within iBALT through interactions between T cells and B cells. Indeed, anti-citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) have been identified as independent risk factors for the development of ILD and airway lesions in RA. ACPA is known to be involved in both RA disease activity and joint destruction progression, making it a significant factor in both RA and ILD pathogenesis. Recently, increasing attention has been focused on the pathological significance of "cellular and destructive bronchiolitis" in RA-ILD, where local inflammatory responses mediated by iBALT lead to destruction of existing bronchioles and alveoli, contributing to honeycomb lung formation. In this seminar, we will discuss the latest insights and practical therapeutic strategies for the aforementioned clinical challenges, taking into account these pathological mechanisms of RA-ILD.

MS5-2

Draft strategy for the treatment of elderly RA based on JCR Guideline 2024

Yuko Kaneko
Keio University

Conflict of interest: Yes

Rheumatoid arthritis is an autoimmune disease, mainly characterized by chronic destructive synovitis, which causes irreversible deformity and

functional decline due to joint destruction if not treated appropriately at an early stage. The advent of methotrexate and molecular-targeted drugs that directly inhibit pathologically relevant molecules has markedly improved the treatment of rheumatoid arthritis and has made it possible to aim for 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 patients in their 60s and 70s, and the number of elderly-onset rheumatoid arthritis (LORA) cases has been reported to be increasing in Japan. The elderly have impaired physiological function, cognitive function, and motivation for treatment, and are at increased risk for drug treatment, including drug adherence, changes in blood levels due to impaired renal function, and infections due to excessive immunosuppression. However, inadequate arthritis control can lead to rapid ADL decline, especially in the elderly, and can exacerbate the risk of infection and cognitive decline. The treatment of LORA patients with both of these 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 opinions from over 1000 rheumatologists regarding their current views on the treatment of elderly-onset RA, problematic comorbidities, and how to deal with specific cases. In this presentation, I will discuss the issues in the treatment of patients with LORA and the management of complications such as renal insufficiency, interstitial pneumonia, and chronic infections that require special consideration due to the high rate of complications in elderly RA patients, while explaining the key points of the 2024 edition of the Rheumatoid Arthritis Treatment Guidelines and using data from our hospital. The following is a discussion of the management of patients with LORA, including the data from our hospital.

Luncheon Seminar

LS1

Usefulness of IL-6 receptor inhibitors in the treatment of rheumatoid arthritis

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Conflict of interest: Yes

If you were limited to one biological antirheumatic drug (bDMARD) available at your facility for the treatment of rheumatoid arthritis (RA), what would you choose? Interleukin (IL)-6 is a major amplifier of inflammation, and inhibition of IL-6 action leads to a reduction in the progression of inflammation-induced organ damage. Sarilumab (SAR) binds with high affinity to the IL-6 receptor and maintains >95% receptor occupancy, especially at the primary dose of 200 mg every other week. SAR 200 mg every other week has shown benefit in a variety of RA patients including those showing inadequate response to conventional synthetic DMARDs (csDMARDs) such as methotrexate and to tumor necrosis factor (TNF) inhibitors, and IL-6 receptor inhibitors have also been reported to be useful in patients with difficult-to-treat (D2T) RA. Safety has been shown to be comparable to that of TNF inhibitors, although more caution for infectious events is required than with TNF inhibitors. Our analysis of global studies has shown that SAR improves disease activity and anemia in anemic RA patients, that it is equally effective as a monotherapy or in combination with MTX and other csDMARDs. Furthermore, SAR showed favorable tolerability in postmarketing surveillance (PMS) in Japan including in elderly RA patients. In this seminar, I would like to present such numerous evidences and verify the usefulness of SAR in the treatment of RA.

LS2

Efficacy and Safety of JAK Inhibitors for the Management of Rheumatoid Arthritis: Structural and Clinical Remission With Filgotinib

Gerd R Burmester[1,2,3]
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Conflict of interest: None

On behalf of Gilead Sciences K. K and Eisai Japan K.K., please join us for an engaging luncheon seminar chaired by Prof Takao Koike, where Prof Gerd Burmester will explore the latest advances in management of rheumatoid arthritis (RA), the role of janus kinase (JAK) inhibitors in the treatment of moderately to severely active disease, and current international guidance on their use in clinical practice. He will also discuss the latest clinical and real-world insights on filgotinib, a once-daily oral JAK inhibitor, and its position among the JAK inhibitor class and within the broader treatment landscape for RA. Prof Burmester will review the latest EULAR recommendations and JCR guidelines on the clinical use of JAK inhibitors for the management of RA. He will highlight the importance of appropriate therapeutic intervention during the window of opportunity to prevent structural damage and the development of difficult-to-treat RA, and help achieve treatment goals, in line with the treat-to-target strategy. He will discuss the latest clinical trial and real-world evidence for the efficacy of filgotinib 200 mg in combination with methotrexate (MTX) in achieving clinical and structural remission and improving patient-reported outcomes (eg, pain, physical function), particularly in MTX-IR patients. The safety profile of filgotinib will also be discussed in the context of overall safety of JAK inhibitors in RA. The presentation will also review the impact of patient characteristics in treatment selection, including patient groups who may be good candidates for receiving filgotinib. The presentation will be followed by a brief Q&A.

LS3

Bone Metabolism Abnormalities in Rheumatic Diseases and Their Management: Insights for Rheumatologists Based on the Updated Guidelines for Glucocorticoid-Induced Osteoporosis

Kosuke Ebina[1,2]

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Conflict of interest: Yes

Rheumatic diseases, such as rheumatoid arthritis (RA), are associated with enhanced bone resorption, suppressed bone formation, and systemic bone loss from the early stages of disease, driven by inflammatory cytokines. These processes have been shown to correlate with an increased risk of fractures and progression of joint destruction. Inflammatory cytokines, including interleukin (IL)-17, tumor necrosis factor-alpha (TNF-α), and IL-6, produced by inflammatory cells in affected joints, stimulate the expression of receptor activator of nuclear factor κB ligand (RANKL) by osteoblasts and synovial fibroblasts. This not only leads to systemic bone loss but also promotes local bone erosion. Additionally, anti-citrullinated peptide antibodies (ACPAs), a specific autoantibody in RA, are known to enhance osteoclast differentiation. Other contributing factors, such as menopause and immobility due to joint destruction, further drive RANKL expression and bone resorption by osteocytes and osteoblasts. On the other hand, TNF-α and glucocorticoids inhibit the Wnt signaling pathway, which is essential for bone formation. Consequently, RA patients exhibit a characteristic bone microarchitecture with increased cortical bone resorption from the inner cortex, caused by osteoclast activation during menopause and inflammation, combined with reduced periosteal apposition due to glucocorticoid use and inflammation, resulting in thinning and porosity of the bone. To prevent the progression of bone and joint destruction associated with systemic and periarticular bone loss, it is critical to control inflammation early, prevent joint destruction progression to maintain physical function, minimize glucocorticoid use when possible, and ensure adequate levels of vitamin D and calcium. Furthermore, selecting appropriate medications based on the patient's bone metabolic status is essential. This presentation will review the mechanisms of bone destruction in rheumatic diseases, strategies to address these challenges, and provide an overview of the updated 2023 guidelines for glucocorticoid-induced osteoporosis.

LS4

The role of JAK Inhibitors in rheumatoid arthritis: Insights from the FIRST registry

Satoshi Kubo
Department of Molecular Targeted Therapies, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan

Conflict of interest: Yes

Rheumatoid arthritis, characterized by synovitis, leads to irreversible joint destruction and organ damage, significantly impairing an individual's activities of daily living and impacting society. In Japan, four classes of molecular targeted therapies are approved for treatment: JAK inhibitors, CTLA4-Ig, anti-IL-6 receptor antibodies, and TNF inhibitors. According to the European Alliance of Associations for Rheumatology recommendations and Japan College of Rheumatology guidelines, phase I utilize methotrexate MTX-based therapies, advancing to molecular targeted therapies in Phase II if initial treatments fail. Achieving clinical remission or maintaining clinical low disease activity by Phase II is crucial for improving patient quality of life. Since 2003, when TNF inhibitors were first approved in Japan, we have been registering rheumatoid arthritis patients in the FIRST registry and exploring better treatment strategies. Recent clinical trials have shown that multiple JAK inhibitors, including upadacitinib, surpass the efficacy of other biological DMARDs. Timely use of JAK inhibitors may enhance overall remission rates; however, careful management of potential adverse events is essential. This lecture will explore the strategic use of JAK inhibitors in Phase II and the management of associated adverse events.

LS5

Treatment for Eosinophilic granulomatosis with polyangiitis (EGPA): Up-to-date

Ken-ei Sada
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Conflict of interest: Yes

Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss syndrome, was first described in 1951 by Churg and Strauss as a syndrome characterized by preceding bronchial asthma or refractory eosinophilic sinusitis, followed by an increase in peripheral blood eosinophil counts and subsequent vasculitic symptoms. It was later discovered that a subset of patients with Churg-Strauss syndrome tested positive for antineutrophil cytoplasmic antibodies (ANCA). Consequently, in the 2012 revised Chapel Hill Classification Criteria, Churg-Strauss syndrome was renamed EGPA and categorized as an ANCA-associated vasculitis. In EGPA, the frequency of ANCA positivity (mainly myeloperoxidase [MPO]-ANCA) is relatively low compared to other ANCA-associated vasculitides, being approximately 30-40%. Clinical features vary depending on the presence or absence of ANCA, reflecting a mixture of eosinophilic and vasculitic inflammation. Patients with ANCA-positive EGPA are more likely to develop neurological and renal involvement compared to ANCA-negative patients, who, in turn, exhibit a higher frequency of cardiac involvement. The Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis published treatment recommendation in 2020 based on existing clinical evidence. This recommendation highlighted the use of common vasculitis therapeutic options, such as glucocorticoids and immunosuppressants like cyclophosphamide, as well as the positioning of mepolizumab, an anti-interleukin-5 (IL-5) monoclonal antibody, which targets the eosinophilic inflammation. Since the evidence review for this recommendation, six years have passed, during which new findings from randomized trials and observational studies have emerged. As a result, a revision of the recommendation is currently underway. This seminar will review the standard treatments outlined in the 2020 recommendation and examine the latest insights that may inform future updates to therapeutic approaches.

LS6-1

Future Prospects of Still's Disease Treatment Based on the History of sJIA

Masaki Shimizu
Department of Pediatrics, Neonatal and Maternal Medicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo (ISCT)

Conflict of interest: Yes

Systemic juvenile idiopathic arthritis (sJIA) was originally reported as Still's disease in 1897. Currently, s-JIA is classified as a subtype of JIA. 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). 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. Regarding diagnosis, serum IL-18 concentration is significantly increased in both diseases, and its usefulness as a diagnostic biomarker has been attracting attention. Regarding treatment, biological agents targeting IL-1β and IL-6 have been clinically applied and have shown dramatic effects. In the United States, Induction therapy without glucocorticoids is performed for sJIA in the absence of macrophage activation syndrome. Meanwhile, although it is rare in Japan, the occurrence of interstitial lung disease associated with sJIA has become a new problem in Europe and the United States. In the future, it is desired that pediatric rheumatologists and adult rheumatologists will work together and promote research in order to develop more effective and safe therapeutic strategies that take into account seemless transitional care and lifelong care.

LS6-2

Future Prospects of Still's Disease Treatment from Latest AOSD Therapies

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Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Conflict of interest: Yes

Adult-onset Still's disease (AOSD) is a rare disease, with a prevalence of 3.7 per 100,000 people, and it is thought to involve both autoinflammation and adaptive immunity in its pathogenesis. Due to its similarities with systemic juvenile idiopathic arthritis (sJIA), recent trends abroad are moving towards unifying AOSD and sJIA under the umbrella of "Still's disease". In both diseases, biomarkers indicating activation of M2 macrophages, such as serum ferritin and heme oxygenase-1, as well as markers of inflammasome activation, including IL-18 and gasdermin D, are commonly elevated. For AOSD diagnosis, the Yamaguchi criteria are often used, requiring exclusion of malignancies, infections, and other connective tissue diseases. Of note, recently identified congenital or acquired NLRC4-autoinflammatory disease, which present with symptoms similar to AOSD and elevated IL-18 and ferritin, have become important differential diagnoses. In managing AOSD, attention must be given to the risk of macrophage activation syndrome (MAS), a serious complication. Meta-analysis conducted at our department revealed that leukocytosis, neutrophilia, high CRP, and hyperferritinemia are associated with MAS risk when using anti-IL-6 receptor antibodies. Therefore, it is recommended to first control inflammation adequately with glucocorticoids and immunosuppressive agents before introducing anti-IL-6 receptor antibodies during highly active phases. Additionally, in Europe, anti-IL-1 antibodies are used alongside anti-IL-6 receptor antibodies, which may prompt considerations for their role in future treatment guidelines in Japan. This seminar will explore future treatment strategies for AOSD, tailored to disease pathogenesis and inflammatory states.

LS7-1

Tofacitinib in the treatment of rheumatoid arthritis*: Insights from the real world data

Ryu Watanabe
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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has significantly advanced with the introduction of biologic agents and Janus kinase (JAK) inhibitors, rendering remission a feasible therapeutic goal. The 2019 update of the EULAR recommendations advocated for the addition of a biologic or JAK inhibitor in patients exhibiting an inadequate response to methotrexate (MTX). However, findings from the ORAL Surveillance study identified advanced age and a history of smoking as risk factors for adverse events associated with JAK inhibitors. Consequently, the EULAR recommendations 2022 update advised the administration of biologic agents in such patients, reserving JAK inhibitors for consideration only after thorough risk assessment. This underscores the necessity of tailoring drug selection based on individual clinical profiles and conducting comprehensive risk evaluations prior to initiating therapy to optimize RA management. It is also recognized that approximately 5-20% of RA patients develop difficult-to-treat RA (D2T RA), characterized by persistent disease activity despite treatment with multiple biologic agents and JAK inhibitors. Analyses of real-world data from the Kyoto University KURAMA cohort and the Kansai multicenter ANSWER cohort have identified high disease activity at baseline, concomitant pulmonary involvement, and elevated rheumatoid factor (RF) levels as predictive factors for D2T RA. High RF levels have been shown to correlate with type I interferon and may contribute to treatment resistance; JAK inhibitors that can regulate type I interferon may be an optimal treatment option not only for patients with established D2T RA but also for those with predicted D2T RA. This presentation aims to review the latest information on tofacitinib, with a focus on real-world data, including insights from the ANSWER cohort, and to discuss recent developments in RA treatment strategies. *Rheumatoid arthritis with inadequate response to existing therapy

LS7-2

Total Management of the Rheumatoid Foot - Including Perioperative Management of JAK Inhibitors

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Conflict of interest: None

Foot disorders associated with rheumatoid arthritis (RA), referred to as "rheumatoid foot", significantly reduce patients' quality of life, making their management a critical issue for rheumatologists. Various treatment options are available for rheumatoid foot, including foot care, orthotic therapy, rehabilitation, and surgery. When managing rheumatoid foot, it is essential not only to adhere to clinical guidelines but also to carefully listen to the patient's preferences and challenges in daily life to establish an individualized treatment plan. By addressing specific daily activity issues and incorporating the patient's pain complaints into the treatment strategy, it is possible to improve patient satisfaction and contribute to a better quality of life. Surgical options are considered when conservative treatments are ineffective. Joint-preserving surgery is selected for deformities in the forefoot, while joint fusion or total ankle replacement is chosen for hindfoot disorders. Surgical intervention is one of the most advanced areas of RA surgery in recent years, with further improvements in outcomes anticipated. The use of Janus kinase (JAK) inhibitors in RA patients is an effective measure for controlling arthritis symptoms; however, evidence regarding postoperative complications remains limited. Existing studies on the impact of JAK inhibitors on wound healing and infection rates have yielded insufficient data. Perioperative discontinuation of JAK inhibitors is often recommended to minimize risks, though concrete evidence regarding optimal discontinuation protocols is also scarce. The appropriate cessation period varies depending on the patient's condition and the type of surgery, necessitating flexible case-by-case management. In this lecture, I will present the current knowledge on perioperative management of JAK inhibitors and share practical examples of comprehensive, patient-centered approaches for the treatment of rheumatoid foot.

LS8

Better treatment for more patients! ~Making the option of a biosimilar more accessible~

Yasushi Kondo
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Conflict of interest: None

The treatment of rheumatoid arthritis (RA) has made dramatic progress over the past two decades, and a variety of treatment options have emerged. However, the medication costs required for treatment are high, amounting to more than 30,000 yen per month for biologic agents (bDMARDs) and more than 40,000 yen per month for JAK inhibitors (tsDMARDs) when 30% co-payment is made against a median household income of 4.05 million yen in Japan in FY2023. In addition, there are cases of treatment-resistant RA (D2TRA) whose symptoms do not improve despite guideline-based management, and a review of data from our institute revealed that half of these cases had difficulty in intensifying treatment due to economical reasons. (The EULAR definition of D2TRA excludes cases that are difficult to treat for financial reasons.) This data suggests that there are potentially more patients with RA who 'do not receive good treatment' than we thought. In addition, national healthcare expenditure and the ratio to GDP in Japan are increasing, and musculoskeletal and connective tissue diseases, including RA, are the third largest group of diseases category, after cardiovascular diseases and tumours. Therefore, a health economic assessment of RA treatment is crucial not only for the patient burden, but also for the improvement of healthcare financing on a national level. In this setting, the use of bio-similars (BS) of biologicals is expected to significantly lower the cost of treatment for individual RA patients, increase access to optimal treatment for all patients, and potentially improve patient adherence to RA treatment. In this seminar, we would like to discuss RA treatment in the context of healthcare costs on a patient and also country levels, and reconsider the option of BS, which may bring better treatment to many rheumatology patients.

LS9

Treatment Strategies for CTD-PAH Considering Concomitant Respiratory Diseases: Including experiences with Selexipag

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Conflict of interest: Yes

Connective tissue disease-pulmonary arterial hypertension (CTD-PAH) is a disease with a poor prognosis, necessitating early diagnosis and appropriate treatment. One of characteristics of CTD-PAH is the frequent coexistence of interstitial lung disease (ILD). When considering pulmonary vasodilator therapy for CTD-PAH, presence of coexisting respiratory disease must be considered due to the potential mismatching ventilation-perfusion in such cases. In patients with PH and concomitant respiratory disease, it is crucial to differentiate between the predominance of Group 1 PH (PAH) and Group 3 PH before starting pulmonary vasodilator therapy. Because effective pulmonary vasodilators for Group 3 PH are currently limited, management of the underlying disease including oxygen therapy is mainly conducted. However, the 2022 ESC/ERS guideline allows individual consideration of pulmonary vasodilator therapy in PAH with concomitant respiratory disease. However, it is important to note that all pulmonary vasodilators may worsen oxygenation in PAH patients with concomitant respiratory disease. Therefore, this risk should be carefully considered when selecting a therapy. In this presentation, treatment strategies for CTD-PAH with concomitant respiratory disease will be discussed including a approach for differentiating between Group 1 PH and Group 3 PH in patients with concomitant respiratory disease and PH and experiences of selexipag treatment, from pulmonologist's perspectives. Group 3 PH: PH associated with lung diseases and/or hypoxemia.

LS10

Challenges in Rheumatoid Arthritis Treatment and Expectations for JAK Inhibitors

Shingo Nakayamada
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Conflict of interest: Yes

Early and appropriate treatment with conventional synthetic DMARDs (csDMARDs) such as methotrexate (MTX) and biological DMARDs (bDMARDs) has made remission an achievable goal in rheumatoid arthritis (RA). However, about 40% of patients fail to achieve remission, highlighting the issue of difficult-to-treat RA (D2T RA). Factors such as comorbidities that limit early treatment intensification and the aging of the RA population contribute to the development of D2T RA, highlighting a critical unmet need in RA management. Janus kinases (JAKs) are central to cytokine signaling, regulating immune responses, lymphocyte differentiation, and inflammatory processes. JAK inhibitors modulate multiple pathways involved in RA pathogenesis, demonstrating efficacy comparable to or exceeding that of bDMARDs. Nonetheless, safety concerns, including cardiovascular events and malignancy risks, necessitate meticulous risk management. Peficitinib, a pan-JAK inhibitor, targets all JAK family members (JAK1, JAK2, JAK3, TYK2) and suppresses cytokine signaling to mitigate RA-related inflammation. Subgroup analyses from a Phase 3 trial (CL-RAJ4) demonstrated efficacy across diverse patient populations, including differences in MTX dosage and age. In this seminar, we would discuss the challenges in RA treatment, including D2T RA, and explores the potential of JAK inhibitors to address unmet needs, supported by evidence from the FIRST registry to guide future treatment strategies.

LS11

Optimal Treatment Strategies in Rheumatoid Arthritis with Poor Prognostic Factors for Joint Destruction: Key Considerations from the Perspectives of Rheumatology and Nephrology Specialists

Yuji Nozaki
Department of Hematology and Rheumatology, Kindai University Hospital, Osaka, Japan

Conflict of interest: Yes

In rheumatoid arthritis (RA), key prognostic factors for joint destruction include seropositive status, elevated inflammatory markers, early joint damage, and failure of at least two csDMARDs (Ann Rheum Dis, 2020). For patients with these risks, early methotrexate (MTX) intervention is crucial for controlling disease activity. However, many patients face limitations in MTX dosing or show resistance to bDMARDs. Disease activity in RA is also linked to organ issues such as renal and lung impairment, making early remission or low disease activity an essential treatment goal. Elderly RA patients have an elevated risk of chronic kidney disease (CKD), lung disease, and cardiovascular complications. eGFR is typically used in clinical settings to adjust drug dosages based on renal function, but factors like age, sex, and muscle mass can introduce error. In cases where eGFR may be inaccurate, cystatin C-based eGFR (eGFRcys) is preferred, although it has its own limitations. Janus kinase (JAK) inhibitors (tsDMARDs) have been conditionally approved for Phase II use, with patient selection being key. Data from the 2024 Japan College of Rheumatology's ANSWER cohort indicated that early remission within three months of b/tsDMARD initiation improved renal outcomes significantly over two years compared to patients with higher disease activity. Upcoming data in 2025 is expected to show that JAK inhibitors are particularly beneficial for patients with multiple poor prognostic factors. With careful patient selection, JAK inhibitors may help achieve early low disease activity and long-term organ protection. This presentation will discuss JAK inhibitors' role for RA patients with poor prognostic factors, focusing on organ protection and renal function evaluation from rheumatology and nephrology perspectives.

LS12

For the standardization of the treatment for the interstitial lung disease (ILD) in Systemic Sclerosis (SSc)

Hidekata Yasuoka
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Conflict of interest: Yes

Systemic sclerosis is a prototypic disease with systemic excessive fibrosis. However, it also has microvascular abnormalities and autoimmune features. Even various findings from basic research revealed the aspects of the mechanism of the disease, we have not seized the clue for the entire picture of the disease process. For the treatment of SSc, the direct control of the process of the remodeling is the only way to stop the progression, however, the development of the novel drugs for this purpose is still in the phase of "under construction". Furthermore, we are still struggling with the establishment of the measures for the evaluation of the "effectiveness" of the treatment or "activity" of the disease, which is another burden in our field. These burdens resulted in the delay of the development of novel SSc treatment. However, we attempted a few different approaches to overcome these difficulties. The one is to accomplish the early diagnosis and intervention for SSc, which is at the same phase with other connective tissue diseases, the inflammatory phase, to minimize the damage and the remodeling. Also, the setting of the treatment goal is another important challenge. We usually expect to have the "improvement" as an outcome by the treatment. But in the fibrotic diseases, we realized that it is better for us to accept to have the concept of "slowing down the progress" as a new outcome. Combined with the discovery and development of the novel drugs, we are having substantial progress of the clinical trials for SSc, especially in the field of interstitial lung disease, which resulted in the deepening of the re-understanding of the pathogenesis simultaneously. In this lecture, I am going to summarize the progress in our field, mainly focused on to the interstitial lung disease, discussing with the recent revision or the development of the guidelines and recommendation.

LS13

Diagnosis and Treatment of Connective Tissue Disease Related TMA - Differences from Complement Mediated TMA (aHUS)-

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Conflict of interest: Yes

Thrombotic microangiopathy (TMA) is a group of disorders characterized by the three main symptoms that are microangiopathic hemolytic anemia, thrombocytopenia, and organ damage due to microcirculatory disturbances. Well-known diseases included in TMA are thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS). TTP is thought to occur when the activity of ADAMTS13, a von Willebrand factor (VWF) cleaving enzyme, is significantly reduced to less than 10%, leading to the development of TMA due to the inability to cleave ultra-large VWF multimers. TTP can be congenital, associated with an ab-

normality in the ADAMTS13 gene, or acquired, with a marked reduction in ADAMTS13 activity due to autoantibodies against ADAMTS13. Among the cases of acquired TTP, some involve connective tissue diseases such as SLE, and these are diagnosed as secondary acquired TTP. HUS is most commonly seen in cases related to Shiga toxin-producing E. coli (STEC) infections, known as STEC-HUS, which often presents with diarrhea. HUS without diarrhea used to be called atypical HUS (aHUS), but abnormalities in complement-related factors were discovered among these cases, leading to the term complement-mediated TMA being used to describe aHUS. It is believed that in many cases, patients with a predisposition, such as complement gene abnormalities, develop the condition when triggered by factors like influenza infection. Among the secondary TMAs that occur in association with various diseases, connective tissue disease-related TMA is the most frequently observed in our collection of cases. In connective tissue diseases, SLE and systemic sclerosis are common, but we have experienced that the type with a marked reduction in ADAMTS13 is more common in SLE and less common in systemic sclerosis. One of the mechanisms predicted for the onset of connective tissue disease -related thrombotic microangiopathy (TMA), where ADAMTS13 activity is not significantly reduced, is the imbalance in the enzyme-substrate ratio due to a marked increase in von Willebrand factor (VWF) antigen. Additionally, thrombus formation due to blood flow disturbances caused by vasculitis is considered one of the triggers for connective tissue disease-related TMA.

LS14

Treatment of rheumatoid arthritis from the perspective of medical economics

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Conflict of interest: Yes

The introduction of biological DMARDs (bDMARDs) has resulted in significant advances in treatment strategies for rheumatoid arthritis (RA). On the other hand, rising RA care costs have caused concern, placing a heavy burden on society as well as patients with RA. The IORRA study has also shown that RA patients' financial burden is increasing and that direct and indirect costs associated with progression of functional impairment or decline in quality of life. These suggested that inhibiting the progression of functional impairment through aggressive control of RA may help reduce lifetime RA care costs. I also would like to share the results of the impact of RA on employment. Pharmacoeconomics is the scientific discipline that evaluates both the clinical benefits and economic effectiveness of a drug to determine whether it is worth the cost. We have analyzed the cost-effectiveness of bDMARDs in the treatment of RA and found that the use of bDMARDs in Japanese RA patients is acceptable in the long term from an economic perspective. Biosimilars are approved only if biosimilarity (equivalence/homogeneity) is demonstrated in terms of quality, efficacy, and safety in comparative studies with reference products. Approved biosimilars are drugs that can be used in appropriate patients in the same way as the reference products. In the Nordic countries, reference products are being switched to biosimilars in principle as a national policy. Infliximab BS, Etanercept BS, and Adalimumab BS are available biosimilars currently approved for RA in Japan. Because the cost of biosimilars is now approximately 40-60% of the reference product, it is expected that biosimilars will become available in patients with RA for whom bDMARDs have been economically difficult to introduce. At this seminar, I would like to share the health economic issues and the importance of pharmacoeconomic evaluation in RA, and then explain the expectations and challenges regarding biosimilars.

LS15

Treatment Strategies for Pulmonary Lesions Complicated by CTD

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Conflict of interest: Yes

Pulmonary involvements in collagen disease are very diverse and can be caused by a variety of factors, including the underlying treatment agents, and infections. An important aspect of the diagnosis of pulmonary lesions in collagen disease is to determine whether or not they are related to primary CTD. In addition, pulmonary lesionss in CTD can involve all parts of the lung. In other words, the pulmonary parenchyma, interstitium, bronchi, pleura, blood vessels, and many other areas can be affected, so it is necessary to accurately diagnose pulmonary lesions. To diagnose CTD associated lung lesions, it is necessary to understand that the frequency and characteristics of pulmonary lesions differ depending on the underlying disease. The most frequent primary disease-related lung lesion associated with CTD is interstitial pneumonia (ILD). The classification of collagen disease-associated interstitial lung disease (CTD-ILD) has been discussed according to the classification of idiopathic interstitial pulmonary disease (IIP), although the pattern often appears mixed. Among CTD-ILDs, ILDs associated with rheumatoid arthritis (RA), systemic sclerosis (SSc), ANCA-associated vasculitis (AAV), and dermatomyositis/polymyositis (IIMs) are of particular concern in clinical practice. In recent years, evidence for the efficacy of nintedanib, an antifibrotic agent, as a novel treatment strategy for these ILDs has been accumulating. In addition to ILD, alveolar hemorrhage (AH) and pulmonary hypertension (PH) are also important pulmonary complications that determine the prognosis of patients. In this seminar, we will review pulmonary lesions associated with collagen disease and discuss treatment strategies for pulmonary lesions associated with collagen disease, focusing on ILD, including immunosuppressive agents and antifibrotic agents.

LS16-1

Sjögren's syndrome from the perspective of a diagnostic radiologist

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Conflict of interest: None

How many doctors actively use imaging examinations in the clinical practice of Sjögren's syndrome (SS) ? This has always been of concern to me, as I have made imaging diagnosis of SS my life's work. As you know, since the ACR criteria for SS (2016), imaging examinations are not included in the global diagnostic and classification criteria at all. This means that SS can be diagnosed without any imaging examinations. The revised Japanese criteria for SS (1999) include X-ray sialography and salivary gland scintigraphy as imaging examinations, but they are used much less frequently throughout the country. However, it would be premature to conclude that imaging examinations are completely unnecessary in the clinical practice of SS. This is because imaging examinations provide us with as much or more information as any other examinations included in the diagnostic and classification criteria. The most representative of such imaging examinations are salivary gland ultrasonography and MRI, which are non-invasive imaging methods. Salivary gland ultrasonography has attracted worldwide attention as a simple, inexpensive and versatile imaging method in the diagnosis of SS. In recent years, the OMERACT (Outcome Measures in Rheumatology) group proposed a consensus definition of abnormal findings and a semi-quantitative scoring system based on it, which has accelerated the trend towards standardisation. In addition, MRI can be used in conjunction with routine MRI scans plus MR-sialography to simultaneously assess the glandular parenchyma and the ductal system. This is a major advantage over other imaging modalities and its objectivity and reliability are superior to salivary gland ultrasonography. If you have access to these imaging modalities, I would urge you to make active use of salivary gland ultrasonography and MRI. I would also like to ensure that the information obtained from both examinations is well understood and used in the clinical practice of SS. In this lecture, I would like to explain the key points of SS diagnosis in salivary gland ultrasonography and MRI in an easy-to-understand manner. In addition, I would like to discuss the core of SS from the perspective of diagnostic imaging, including our latest research results.

LS16-2

Cutting edge of diagnosis and treatment for interstitial lung disease (ILD) associated with Sjögren's syndrome

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Conflict of interest: Yes

Primary Sjögren's syndrome (pSS) is linked to pulmonary manifestations, such as airway disease and ILD, in 20-30% of cases. In this seminar, we will discuss 1) epidemiology and clinical features of SS-ILD, 2) pathophysiology of SS-ILD, 3) practice in our department, and 4) treatment strategies and evidence suggested by recommendations and guidelines. 1) The systematic review (SR) by EULAR reported CT findings in pSS patients with pulmonary manifestations: airway disease 50%, interstitial change 49%, and honeycombing 13%, as well as histopathology: NSIP 45%, UIP 16%, and LIP 15%. An Italian SR showed cumulative incidence of ILD in pSS who had no history of ILD as 10% at 1 year and 20% at 5 years after diagnosis of pSS. On the other hand, ILD preceded pSS in 10-51% of cases. Anti-SS-A/B antibodies are included in IPAF criteria. Progressive fibrosing (PF) ILD accounted for 21.7% of SS-ILD cases, with 3-year survival rates of 82.4% compared with 100% in non-PF-ILD cases. Advanced age, impaired pulmonary function, extensive CT findings, high PCO2, severe reticulation, and fibroblastic foci were identified as poor prognostic factors of pSS-ILD. 2) In SS-ILD, $CD4^{+}$T cells and epithelial cells contribute to specific chronic inflammation like salivary glands, resulting in self-perpetuating fibrosis in which myofibroblasts play important roles. 3) In our 22 cases of pSS with lung involvement, glucocorticoids (GC) were started or increased in 13 cases. Among 9 cases who underwent CT reassessment after GC treatment, 5 cases showed lesion progression. Nintedanib (NTD) was added to GC and immunosuppressants (IS) for our pSS-ILD cases with impaired pulmonary function. 4) EULAR recommendations and Sjögren's Foundation consensus guideline suggest GC as 1st-line, IS such as AZP or MMF (off-label) as 2nd-line, and CY and RTX (off-label) for refractory and severe cases. Consensus guideline and latest ACR/CHEST guideline suggest NTD when fibrosis progresses despite immunosuppressive therapy.

LS17

Modern Management of Rheumatoid Arthritis With JAK Inhibitors: Evidence for the Clinical Utility of Filgotinib

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Conflict of interest: None

On behalf of Gilead Sciences K.K. and Eisai Japan K.K., please join us for an interactive, discussion-based session chaired by Prof Motomu Hashimoto. This event will include a short presentation from Prof Gerd Burmester followed by a panel discussion with Japanese experts Profs Mitsuhiro Akiyama, Tadashi Okano, and Kosaku Murakami. Key topics in the session will include: (a) the evolution of the role of janus kinase (JAK) inhibitors in the treatment of moderately to severely active RA, (b) the latest EULAR recommendations and JCR guidelines on the clinical use of JAK inhibitors and the importance of appropriate therapeutic intervention during the window of opportunity to prevent structural damage and the development of difficult-to-treat RA, and (c) how a treat-to-target strategy can help achieve optimal patient outcomes. The session will highlight the clinical utility of filgotinib, a once-daily oral JAK inhibitor approved for the treatment of RA, in achieving clinical and structural remission and improving patient-reported outcomes, particularly in MTX-IR patients. It will also review the impact of patient characteristics in the selection of therapy, including patient groups who may be good candidates for receiving filgotinib, and how to ensure effective treatment of active disease while balancing efficacy and safety. Prof Burmester and the panel experts will discuss these key topics and share their clinical perspectives on the use, efficacy, and safety of filgotinib, as well as its position in the RA treatment landscape.

LS18-1

Unmet needs on the treatment of lupus nephritis

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is a typical systemic autoimmune disease. Lupus nephritis is one of the most frequent organ involvement in SLE patients. The underlying pathogenesis of the disease is inflammation and dysfunction of multiple organs as a result of autoimmunity. It is true that the prognosis of patients with severe organ involvement in SLE, including lupus nephritis, improved markedly since the establishment of treatment with high-dose glucocorticoids, a non-specific but potent anti-immunological and anti-inflammatory therapy. However, when the complications of long-term high-dose glucocorticoids are added to the inherent chronic organ iinduction and maintenance with immunosuppressive drugs have been practiced, and treatment pronvolvement of SLE, the prognosis in terms of morbidity is not favourable. In recent years, remission tocols that improve prognosis with minimise complications have been discussed. Currently, non-glucocorticoid drugs approved for the treatment of SLE in Japan include cyclophosphamide, azathioprim, hydroxychloroquine, belimumab and anifrolumab. Tacrolimus, mycophenolate, mizoribine, rituximab and voclosporin are also added for lupus nephritis. How would these be appropriately selected and combined with glucocorticoids? The guideline for the treatment of SLE, developed by the JCR and the MHLW Research Group (Autoimmunity Group), was published in 2019 and is currently undergoing further revision work. In this guideline, recommendations were developed for lupus nephritis based on the results of a systematic review and meta-analysis. Taking into account of the essence of this guideline plus the latest evidence, we would like to consider the best possible management of lupus nephritis at present.

LS18-2

The Frontline of Lupus Nephritis Treatment: The Significance of Triple Therapy with Voclosporin

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Conflict of interest: Yes

The treatment of active proliferative lupus nephritis (LN) has been based on the results of the ALMS trial, which established glucocorticoid (GC) + mycophenolate mofetil (MMF) or GC + intravenous cyclophosphamide (IVCY) as the standard therapies. However, the complete remission rate in the ALMS trial was less than 10% at six months, highlighting the need for more effective treatments. Numerous clinical trials have since been conducted to evaluate the combination of novel molecular-targeted drugs with standard therapies, but most have not succeeded. Amid these efforts, two treatment strategies have demonstrated efficacy. The first involves the use of the anti-BlyS antibody belimumab (BLM) in the BLISS-LN trial, which showed the utility of triple therapy with GC + MMF + BLM or GC + IVCY + BLM. The second is triple therapy using calcineurin inhibitors (CNIs). In a multicenter trial in China, tacrolimus (TAC) was employed, while an international multicenter trial utilized voclosporin (VCS). Notably, the AURORA1 trial compared GC + MMF + VCS with GC + MMF + placebo. The primary endpoint, complete renal response at 52 weeks, was achieved in 40.8% of the VCS group compared to 22.5% in the placebo group (odds ratio 2.65, 95% CI 1.64-4.27), demonstrating significant superiority. Additionally, the subsequent AURORA2 extension trial confirmed the long-term safety and efficacy of continuing treatment for 24 months. Based on this evidence, the 2023 EULAR recommendations for SLE and the 2024 KDIGO LN guidelines now recommend triple therapies-GC + MMF + BLM and GC + MMF + CNI-as first-line options alongside standard treatments. Furthermore, the 2024 ACR LN guidelines, presented in November, explicitly endorse only triple therapies such as GC + MMF + BLM or GC + MMF + CNI as first-line treatments. This lecture will focus on the triple therapy of GC + MMF + VCS, providing an in-depth discussion of emerging treatment strategies for LN.

LS19

The Future of Rheumatoid Arthritis Treatment with JAK Inhibitors: The Role and Potential of Baricitinib Based on RA Pathophysiology and Real-World Evidence, Including Post-Marketing Surveillance

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic disease characterized by synovitis and joint destruction caused by aberrant immune activation. Despite the availability of various biological agents, some patients remain difficult to manage, with complications such as organ damage. Baricitinib, a JAK inhibitor, has shown accumulating efficacy and safety in randomized controlled trials (RCTs) and real-world evidence (RWE). This lecture aims to identify optimal patient profiles for baricitinib treatment, integrating data from a three-year post-marketing surveillance (PMS) and insights into RA pathophysiology and its mechanism of action. RA is driven by abnormal activation of the JAK-STAT signaling pathways, promoting overproduction of inflammatory cytokines such as interleukin-6 (IL-6) and interferons (IFNs). Baricitinib targets JAK1 and JAK2, effectively suppressing these pathways to control inflammation and prevent joint destruction. Its inhibition of GM-CSF is also expected to help manage pain. Baricitinib is suited for patients with insufficient responses to DMARDs or biologic agents. In Phase 2 of RA management, it should be considered for those with poor prognostic factors, including rapid joint destruction, older age, frailty, autoantibody positivity, organ dysfunction, or difficult-to-treat rheumatoid arthritis (D2TRA). Post-marketing surveillance in Japan revealed that baricitinib does not significantly increase risks associated with JAK inhibitors, such as malignancies, major adverse cardiovascular events (MACE), or thrombosis, suggesting a favorable safety profile in Japanese patients. This presentation will summarize the efficacy and safety evidence for baricitinib and discuss its role in RA treatment, focusing on patient profiles based on disease pathophysiology and comorbidity risks.

LS20

Evolving Rheumatoid Arthritis Treatment Strategies -The Role of JAK Inhibitors-

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Conflict of interest: Yes

The advent of biologics has led to a paradigm shift in rheumatoid arthritis (RA) treatment, enabling clinical, structural, and functional remissions. With the introduction of oral JAK inhibitors in Japan about ten years ago, remission treatment options have expanded, and a standard regimen has been established. However, achieving and maintaining remission in practice remains insufficient, and Treat to Target (T2T) presents ongoing challenges. The safety of JAK inhibitors gained attention after the ORAL Surveillance study, leading the 2022 EULAR recommendations to advise considering risks when using JAK inhibitors in Phase II. Japan's 2024 rheumatoid arthritis guidelines incorporate research evidence and all-case post-marketing surveillance (PMS) results. Japan's 2024 rheumatoid arthritis guidelines incorporate research evidence and all-case PMS results of JAK inhibitors. In Phase II of the therapeutic algorithm, JAK inhibitors are recommended with bDMARDs. Short-term, TNF inhibitors and JAK inhibitors with MTX show similar efficacy. Long-term, ORAL Surveillance study results indicate a preference for bDMARDs. The long-term utility of JAK inhibitors awaits final PMS results. Upadacitinib (UPA), a JAK inhibitor, targets JAK1 to reduce inflammation by blocking cytokine signaling in RA. Phase III SELECT trials confirmed UPA's efficacy and safety for diverse RA patients, both with csDMARDs, including MTX, and as monotherapy. UPA conducted direct comparisons with biologics across varying patient backgrounds (e.g., inadequate MTX or biologic response). While pooled clinical trial data indicate a higher herpes zoster risk, further evaluation through specific use-results surveys in Japan is needed. In this lecture, I would like to address the importance and strategies for achieving early remission and its long-term maintenance. Additionally, I will consider the clinical significance and safety profile of UPA from the latest evidence including long-term results of Phase III clinical trials, as well as the positioning of JAK inhibitors in RA treatment strategies.

LS21

A Strategy for Preventing Frailty in the Management of Rheumatoid Arthritis: Perspectives on Bone Metabolism and Immune System Regulation

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Conflict of interest: Yes

The World Health Organization identifies 'physical inactivity' as the fourth major global mortality risk after high blood pressure, smoking, and high glucose levels. This is particularly relevant for patients with rheumatoid arthritis (RA), which is associated with increased frailty in aging patients. Frailty, characterized by decreased activity, reduced muscle strength, and slower walking speed, shortens healthy lifespans and increases mortality risk. As populations age, the incidence of RA peaks among individuals in their sixties during the 2020s. Preventing frailty is crucial for enhancing the health span of elderly RA patients, as frailty in RA stems from joint destruction and deformity, and is compounded by muscle weakness, fatigue, reduced activity, slower walking speed, and weight loss. Therefore, 'physical inactivity' resulting from frailty in RA patients is a significant mortality risk. Early detection and medical intervention, through appropriate physical activities, can mitigate the progression of frailty. Patients with RA are prone to "physical inactivity" due to "reversible functional impairments" caused by joint swelling and pain, as well as "irreversible functional impairments" resulting from joint destruction and deformity. The primary treatment goal is to minimize synovitis and prevent damage to bone and cartilage before 'irreversible functional impairments' occur. Inflammatory bone destruction, primarily caused by osteoclasts activated by inflammatory cytokines and autoantibodies, plays a crucial role in the 'irreversible impairments' associated with RA. Our research has identified inflammatory osteoclasts induced by co-stimulation of tumor necrosis factor and interleukin-6, which represents a significant finding. This seminar will explain the onset mechanisms of RA and the progression of inflammatory bone destruction, enhancing understanding of optimal diagnostic and pharmacological strategies to prevent frailty.

LS22

The Pathophysiology and Evolution of Treatment Strategies in Eosinophilic Granulomatosis with Polyangiitis (EGPA): Focusing on the Roles of Eosinophils and ANCA

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Conflict of interest: Yes

Eosinophilic granulomatosis with polyangiitis (EGPA) constitutes a subset of ANCA-associated vasculitis (AAV), which is characterized as a small to medium-vessel necrotizing vasculitis with a high prevalence of anti-neutrophil cytoplasmic antibodies (ANCA) positivity, alongside microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). Among AAV, differential clinical manifestations delineate the specific disease entities: GPA is distinguished by the presence of extravascular necrotizing granulomatous inflammation, whereas EGPA is uniquely characterized by eosinophilic inflammation, setting it apart from other vasculitides. This eosinophilic component necessitates a distinct therapeutic approach for EGPA compared to the other two forms of AAV. Furthermore, EGPA is notable for its lower ANCA positivity rate relative to the other AAV subtypes. Historically clinical trials in AAV reported prior to the year 2000, the primary objective was to enhance survival rates. Those published in the early 2000s focused on mitigating drug toxicity, particularly that associated with cyclophosphamide. These studies aimed to reduce cyclophosphamide exposure while maintaining favorable prognostic outcomes. Trials published post-2010 have increasingly concentrated on strategies to diminish glucocorticoid-related toxicity. One of milestones of such clinical investigational efforts in vasculitis was approval of therapeutic agents targeting interleukin-5 (IL-5), a crucial cytokine in eosinophil biology. This advancement has led to a reduction in long-term glucocorticoid usage

in patients with EGPA. This talk will provide a comprehensive overview of EGPA's position within the spectrum of necrotizing vasculitides, compare and contrast EGPA with other AAV subtypes, elucidate the role of eosinophils in EGPA pathogenesis, and delineate current therapeutic strategies for EGPA management.

LS23-1

Challenges in RA treatment based on real-world data and the role of IL-6 targeted therapy

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Conflict of interest: Yes

The success of biologic DMARDs and JAK inhibitors in the treatment of rheumatoid arthritis (RA) has brought about a paradigm shift in RA management. However, remission is achieved in only about 60% of patients, and 10-20% fall into the category of difficult-to-treat RA (D2T RA). Furthermore, with the aging RA population, the number of cases complicated by interstitial lung disease, renal impairment, and drug-related adverse effects is increasing, making treatment more challenging. Although the range of therapeutic options has expanded in recent years, remission rates have plateaued, and significant unmet needs in RA treatment remain. Effective RA treatment requires the selection of molecularly targeted drugs with distinct mechanisms of action tailored to the most suitable patients. However, no clear criteria currently exist to guide the optimal use of these agents. Additionally, heterogeneity in RA pathophysiology and clinical presentation underscores the importance of carefully considering the unique characteristics of each drug during treatment selection. The pathogenesis of RA involves immune dysregulation driven by dendritic cells, monocytes, T cells, and B cells, as well as joint destruction mediated by osteoclasts. IL-6 is a pro-inflammatory cytokine that plays a central role in the immune and bone metabolism abnormalities. IL-6 contributes to RA pathogenesis through various mechanisms, including the conversion of Treg to Th17 cells, RANKL induction, and activation of osteoclast precursors. The IL-6 receptor antibody tocilizumab has shown efficacy as monotherapy in patients unresponsive to anti-TNF therapy or those unable to use methotrexate, positioning it as a promising option to address unmet needs in D2T RA. In this seminar, we will discuss the multifaceted role of IL-6-targeted therapy in RA treatment and explore its future potential. This discussion will incorporate the latest findings, including data from our registry study.

LS23-2

Chronic kidney disease in patients with rheumatoid arthritis

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Conflict of interest: None

The number of elderly patients with rheumatoid arthritis (RA) is increasing as life expectancy increases, and new strategies are needed to optimize therapy in this population. Limited data are available regarding the treatment of RA in individuals aged 65 years and older due to age-based selection criteria or because such patients often have comorbidities, factors which restrict their inclusion in intervention studies. Furthermore, management of RA in elderly individuals is challenging owing to comorbidities and frailty, requires appropriate tailoring of the aggressiveness of the therapeutic approach. Most of the elderly patients have problems in drug metabolism includes decline in renal function and impaired digestion and absorption. Approximately one-fourth of patients with RA develop chronic kidney disease (CKD), a higher rate than that of healthy individuals. The causes of kidney diseases in RA vary, but most cases can be categorized into two types: chronic inflammation, including secondary renal atherosclerosis and amyloidosis, and drug-induced kidney diseases. Since it is difficult to increase the dose of methotrexate in RA patients with CKD for its toxicity, adding other disease-modifying anti-rheumatic drugs is sometimes necessary in clinical settings. Since a number of studies have addressed CKD is one of the risk factors for severe infection, careful attention needs to be paid for preventing CKD progression in clinical practice of RA. Additional considerations include the emerging role of sodium-glucose cotransporter-2 (SGLT2) inhibitors, though their efficacy and safety remain uncertain in rheumatic diseases due to limited trial data. This overview aims to integrate novel therapies, including angiotensin receptor neprilysin inhibitors (ARNIs) and Hypoxia-inducible factor-prolyl hydroxylase (HIF-PH) inhibitors, into a practical CKD management framework for rheumatic care. Here, we discuss therapeutic strategy for RA patients to prevent CKD progression.

LS24

Clinical significance of indirect fluorescent assay in systemic autoimmune rheumatic diseases ~ Usefulness of ICAP classification in clinical practice ~

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Conflict of interest: Yes

Antinuclear antibody (ANA) testing is essential when systemic autoimmune rheumatic disease (SARD) is suspected. Indirect fluorescence assay (IFA) is used as a screening test to suspect specific SARD in combination with clinical symptoms and to measure disease-specific antibodies in advance. The International Consensus on ANA Staining Patterns (ICAP) was initiated as a session of the 12th International Workshop on Autoantibodies and Autoimmunity and has since been working to form an international consensus and promote harmonization of cell staining patterns in IFA using HEp-2 cells. It plays an important role in the diagnosis and pathogenesis of SARD. A Japanese-translated ICAP website has been opened (https: //www. anapatterns. org/index. php), which shows 28 staining patterns (the number has increased to 31 in the latest report [*Autoimmun Rev,* 2024]). Note that the autoantibodies shown here include not only intranuclear but also cytoplasmic and nuclear membrane antigens, so it may be better to use the term of anti-cell antibodies rather than ANA. The patterns shown on this website are described as competent and expert levels. Figure of each pattern is accompanied by a comment on its clinical significance. The background to the proposal of this classification is that not only intranuclear antigens but also cytoplasmic antigens have clinical significance (such as anti-synthetase antibodies in idiopathic inflammatory myopathy) and that among speckled patterns, the nuclear dense fine speckled (DFS) type is highly likely to rule out SARD. Furthermore, it is possible that the ICAP anti-cell (AC) classification may influence the classification criteria for SARD in the future or that specific AC classifications mw will predict clinical significance. In this lecture, I would like to discuss the clinical significance of ICAP classification for ANA-IFA testing in daily clinical practice.

LS25-1

Update in PsA management ~from nail to axial joints~

Mitsumasa Kishimoto
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Conflict of interest: Yes

Psoriatic arthritis (PsA) significantly impacts patients' quality of life, and delays in diagnosis can result in progressive joint destruction and long-term disability. Therefore, recognizing the key clinical features of PsA is crucial for early diagnosis and effective management in clinical practice. A comprehensive evaluation across multiple domains-including skin and nail involvement, peripheral arthritis, axial joint lesions, dactylitis, and enthesitis-alongside consideration of comorbidities and complications, is essential. Among these domains, axial joint lesions represent a particularly severe manifestation, yet their prevalence and characteristics remain inadequately understood. Recent findings from the (ASAS-GRAPPA) AXIS study have shed light on the prevalence and clinical characteristics of axial joint lesions in patients with PsA. Concurrently, therapeutic advancements have expanded treatment options, with numerous biologics and molecularly targeted agents, such as JAK inhibitors, now widely accessible. In particular, the IL-17 inhibitor, Ixekizumab has emerged as a promising therapy in the management of multi-domain disease. This presentation will provide an overview of the latest insights into axial joint

lesions in PsA, key diagnostic and differential diagnostic strategies, and an evidence-based evaluation of the efficacy and safety of ixekizumab in addressing this complex condition.

LS25-2

The robust diagnosis and treatment strategy for peripheral psoriatic arthritis in the new era. ~ The longing to make you happy! What Ixekizumab can do now? ~

Kenta Misaki
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Conflict of interest: Yes

Methotrexate (MTX), biologic agents (Bio) and JAK inhibitor (JAKi) are now available in the therapy of psoriatic arthritis (PsA) as well as rheumatoid arthritis (RA). In retrospect, could we imagine such an era would come along to the PsA fields with good outcome for PsA patients? Recently, the novel PsA-treatment strategy such as PASI100 and suppression of bone destruction have gradually suggested as a common sense of PsA outcome. Focused on the preventing bone destruction, it is possible to achieve the similar outcome owing to the earlier usage of MTX, Bio and JAKi to PsA patients like those of RA. One of the reasons above is not only the awesome treatment-agents but also the introduction of musculoskeletal ultrasound (MSUS) to PsA territory. MSKUS make it possible to depict early pathological finding with no harm and contribute the early diagnosis of PsA with precise component detection, finally lead to the early treatment for us rheumatologists. Especially Ixekizumab (IXE), anti-IL-17A antibody launched in 2016, is still fresh in our memory in terms of the noteworthy evidence of achieving PASI100, inhibiting synovitis and suppressive effect of bone destruction overturned conventional acknowledgement by means of Spirit H2H trial (Ann Rheum Dis 2020; 79 (10): 1310-1319). We want to discuss about the pivotal benefits of IXE treatment for peripheral PsA patients and points to consider under the treatment of IXE according to the latest EULAR PsA recommendation.

LS26-1

Treatment Strategies for Rheumatoid Arthritis Focused on Early Remission Induction-Significance of early remission induction by TNF inhibitors-

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by polyarthritis. If appropriate treatment is delayed, fibroblast-like synoviocytes (FLS) in the synovium undergo various modifications, leading to hyperplasia, multilayering, and potentially refractory disease, as reported in the literature. In such synovium, secondary lymphoid tissue-like structures facilitate local lymphocyte education, and hyperplastic FLS release cytokines such as IL-7 and IL-15. Therefore, in the early stages of RA, it is advisable to treat the disease intensively before synovial hyperplasia develops. Once RA is diagnosed, methotrexate (MTX) should be initiated promptly unless contraindications exist, as endorsed by the EULAR 2022 recommendations and the 2024 edition of the Japanese Rheumatoid Arthritis Treatment Guidelines. However, in Japanese patients with ACPA positive RA, only about 30% achieve SDAI remission with the maximum dose of MTX monotherapy, as shown in the placebo arm of the C-OPERA trial, which included all patients with ACPA positive RA. In contrast, the main arm of the same trial, which combined MTX and certolizumab pegol (CZP) from the start, achieved SDAI remission in 60% of patients. This means that 30% of patients with ACPA positivity, a poor prognostic factor in RA, require TNF inhibitor therapy alongside MTX from the early stages of treatment. In this lecture, I will outline the importance of early remission induction with TNF inhibitors, particularly in RA patients with poor prognostic factors (e.g., high RF/ACPA levels, early bone erosions), and the necessity of distinguishing between remission induction therapy and remission maintenance therapy in clinical practice.

LS26-2

Treatment Strategies for Rheumatoid Arthritis Focused on Elevated RF~Precision Medicine with Certolizumab Pegol~

Ryu Watanabe
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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has significantly progressed with the introduction of biologic disease-modifying antirheumatic drugs and Janus kinase (JAK) inhibitors, enabling many patients to attain clinical, structural, and functional remission. Nonetheless, a subset of patients exhibits treatment-resistant RA, termed difficult-to-treat RA (D2T RA), where disease activity remains inadequately controlled despite these therapeutic interventions. To mitigate the development of D2T RA, it is imperative for rheumatologists to carefully monitor patient profiles and optimize treatment strategies. We have previously demonstrated that, utilizing data from the Kyoto University KURAMA cohort and the Kansai multicenter ANSWER cohort, elevated rheumatoid factor (RF) levels are a significant risk factor for D2T RA. Patients with high RF levels not only present with high disease activity and accelerated joint destruction but also exhibit diminished responses to tumor necrosis factor (TNF) inhibitors that contain the Fc region. Certolizumab pegol (CZP) is expected to be beneficial for women of childbearing age due to its lack of an Fc region and has data supporting its placental transfer. The PEGylation of CZP extends its half-life and enhances its hydrophilicity, facilitating higher concentrations at sites of inflammation. Importantly, CZP maintains stable serum levels even in patients with elevated RF, demonstrating efficacy irrespective of RF status. This presentation will critically appraise the evidence supporting the use of CZP, including a comparative analysis with ozoralizumab-a TNF inhibitor which also lacks Fc region-and explore the implications for precision medicine in the management of RA.

LS27

The Role of IL6 in Optimizing Treatment in Patient with Rheumatoid Arthritis

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Conflict of interest: Yes

Rheumatoid Arthritis (RA) is a chronic inflammatory and destructive disease. The phases of its development are now well defined ranging from the mere presence of genetic risk factors to full-blown persistent RA. Interestingly inflammation is already present before arthritis develops making the inflammatory response a driving factor in RA development. We expect that the management of RA will change by testing intervention strategies designed to prevent the development of persistent RA. Inhibition of inflammation is the key target for treatment of RA and sufficient inhibition is often not met with traditional DMARD therapy. IL6 drives inflammation and in daily practice the production of CRP is partly dependent on IL6, thereby making CRP a very good biomarker of a biological pathway that drives inflammation of RA. Sarilumab is a human mAb that binds the IL6R while Tociluzimab is humanized murine mAb binding the IL6R. The efficacy of targeting IL6 in relation to the different outcome measures will be discussed.

LS28-1

A Rare Disease Lurking Around Us: Diagnosis and Treatment of Hypophosphatasemia

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Conflict of interest: None

Chronic pain is a very common complaint and is classified as nociceptive pain, such as in rheumatoid-related diseases and osteoarthritis, neuropathic pain, or nonorganic pain. There are a wide variety of diseases and conditions that cause pain. In many cases, the principal cause of the pain is hard to identify and only symptomatic treatment is provided. Chronic pain of unidentified cause includes osteomalacia associated with vitamin

D deficiency and/or chronic hypophosphatemia. Although osteomalacia is one of the representative metabolic bone diseases, along with osteoporosis, it is relatively rare and not well recognized in clinical practice. Hypophosphatasia (HPP) is a disease that must be differentiated from osteomalacia; however, this disease is more difficult to diagnose because it is more infrequent and is not associated with typical laboratory findings in metabolic bone diseases. Osteomalacia and HPP in adulthood are often misdiagnosed and inappropriately treated as osteoporosis because of low bone mineral density. Hypophosphatasia is a bone and tooth calcification disorder caused by insufficient alkaline phosphatase (ALP) activity and is quite different from osteoporosis, whose primary pathogenesis is mineralized bone loss. The main pharmacological effect of bisphosphonates, which are the standard therapeutic agents for osteoporosis, is to inhibit bone resorption, but there is concern that their chemical structure may contribute to impaired bone mineralization. In fact, there have been many reports of atypical femoral fractures in HPP patients treated with bisphosphonates, so appropriate diagnosis and treatment of HPP is clinically essential. In this presentation, I would like to explain how to proceed with the medical treatment of HPP, a rare disease that lurks close at hand, from the viewpoint of chronic pain and low bone mineral density in the fields of internal medicine and endocrinology.

LS28-2

Diagnosis and treatment of hypophosphatasia in rheumatology outpatient clinic

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Conflict of interest: None

Hypophosphatasia (HPP) is an inherited bone disease with impaired bone calcification due to reduced *ALPL* gene activity encoding tissue non-specific alkaline phosphatase (TNSALP). Previously, severe prognostic cases with bone deformity have been known among neonates. However, milder cases with recurrent fractures, osteoporosis and musculoskeletal pain among adults come to attention these days. Milder cases may develop frequently due to heterozygous genetic mutations, unlike rare severe cases. The main complaints in adult HPP are osteoarticular, such as rheumatic symptoms in 83% of patients and skeletal symptoms in 48%. The causes of pain are presumably multifactorial, including pain derived from osteomalacia, neurotransmitter synthesis through *ALPL* gene expression in the central nervous system, nociceptive pain derived from reduced TNSALP activity, and chronic arthritis caused by calcium pyrophosphate deposition disease. HPP patients may visit rheumatology clinics. Recalling the disease is crucial in noticing low serum ALP levels, obtaining history including family and dental disease, and conducting a genetic diagnosis. Since 2015, an enzyme replacement therapy (ERT, by asphotase alfa) has been approved for HPP including adults, and is expected to improve symptoms such as pain. Here present three cases of HPP (including one suspected) experienced in my outpatient department, with the course after the introduction of ERT. Case 1: A 60-year-old woman with seropositive rheumatoid arthritis, showing markedly low ALP and multiple bone bruises around the ankle, diagnosed through genetic test and conducting ERT for two years. Case 2: A 33-year-old woman detected a gene variant through periodontal disease, easy fatigue, family history of her mother (case 1) and low ALP levels. Case 3: A 50-year-old woman treated to be seronegative rheumatoid arthritis, with intractable polyarthritis and persistently low ALP levels, diagnosed through genetic test and planning ERT.

LS29-1

Superiority of Robotic assisted total hip arthroplasty

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Conflict of interest: Yes

The need to improve the accuracy of implant placement has led to the development of various methods such as navigation and robotic surgery. The accuracy of implant placement was compared between the manual, CT Navigation, and Mako groups. Mako, a robotic-assisted THA, can reproduce preoperative planning more accurately than manual THA and THA with navigation.

LS29-2

Cutting-Edge Total Knee Arthroplasty with CT-based Robotic-Assisted Surgery

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Conflict of interest: Yes

The Mako system, a CT-based robotic system, has revolutionized total knee arthroplasty (TKA) surgeries. This system allows for detailed preoperative planning using the patient's own 3D bone model, improving the accuracy of femoral and tibial component rotation placement, which was challenging with imageless navigation. Compared to 2D images like standing long-leg radiographs, the 3D bone model enables precise measurement of angles between bone functional axes and joint surfaces (such as LDFA and MPTA), facilitating the planning of kinematic alignment surgeries. Additionally, the Mako system can evaluate bone spurs, bone defects, and the alignment between the native patellar groove and the implant's patellar groove, which was not possible before. One notable feature is the ability to perform soft tissue balancing before bone cutting (pre-resection balancing), ensuring proper soft tissue balance through minor adjustments in bone cutting surfaces. This minimizes soft tissue release, such as MCL superficial layer, and allows for minimally invasive surgeries. The CT-based system can accurately replicate the patient's native joint surface inclination as defined by CPAK classification, while maintaining the native joint surface of the distal femur. By finely adjusting the bone cutting surface according to the patient's soft tissue condition, it is possible to achieve functional alignment reflecting individual anatomical characteristics. The robotic arm allows precise bone cutting without the need for cutting guides, enabling safe kinematic alignment TKA with a wider boundary setting. The presentation introduces the overview of functional alignment TKA using the Mako system and explains surgical strategies and their implementation based on the presenter's experience with various cases, including varus, valgus, and severely deformed knees.

LS30-1

Hereditary angioedema (HAE) ~The cutting edge of evolving treatments

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Conflict of interest: Yes

Hereditary angioedema (HAE) is a genetic disorder characterized by recurrent, transient edema affecting various parts of the body. Laryngeal edema, which can cause life-threatening asphyxiation, is a serious complication that must not be overlooked. The pathology involves an overproduction of bradykinin caused by dysfunction of complement C1 inhibitor (C1-INH), leading to increased vascular permeability and edema formation. Additionally, HAE is often associated with autoimmune diseases, which are thought to occur due to the consumption of early complement components, such as C4, resulting from C1-INH dysfunction. As the mechanisms of HAE have gradually been elucidated, treatment options have significantly advanced. In 1990, the first disease-specific treatment in Japan, a human plasma-derived C1-INH preparation, was introduced. It was used as an on-demand therapy for acute attacks and remained the sole treatment option for many years. In 2018, the bradykinin receptor antagonist icatibant was added as another on-demand therapy, expanding the range of treatments available. More recently, several long-term prophylactic treatments have been approved. In 2021, the oral medication berotralstat was introduced, followed in 2022 by lanadelumab, a subcutaneous injection, as well as a human plasma-derived C1-INH preparation for subcutaneous administration. Both berotralstat and lanadelumab inhibit plasma kallikrein, an enzyme responsible for bradykinin production, though they differ in their routes of administration. The introduction of these long-term prophylactic treatments has significantly transformed the therapeutic goals for HAE. Current international and domestic clinical guidelines advocate for a daily life free from the "disease burden". This term refers to the physical, emotional, and social challenges that patients face, regardless of whether they are experiencing an attack. In this presentation, I aim to

use HAE as a model to discuss important points for creating a treatment environment that maximizes patient satisfaction, inviting you to explore these ideas together.

LS30-2

Practice of Hereditary Angioedema

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Conflict of interest: None

Hereditary angioedema (HAE) is a rare disease that causes recurrent attacks of acute angioedema of the skin and mucous membranes, primarily due to quantitative or qualitative abnormalities of 1-inhibitors (C1-INH). The number of patients in Japan is estimated to be 2,500. Its attacks can be accompanied by respiratory and abdominal symptoms and can be life-threatening. Therefore, there is an urgent need for early diagnosis and the establishment of an appropriate medical treatment system. Not only is it essential to raise awareness of this disease in medical settings, including emergency medical care, because of the small number of patients with this disease, but it can also be difficult to differentiate it from other diseases, even if the patient is treated with HAE in mind. In particular, HAE may be accompanied by abnormalities in the complement system, and it is necessary to differentiate it from diseases in which complement is decreased (e.g., systemic lupus erythematosus). In addition, cases of complications of autoimmune diseases have been reported, requiring careful evaluation by clinicians. In addition, type 3 of HAE has been reported to be difficult to diagnose because complement tests are not abnormal. In addition, because the symptoms of HAE are similar to those of anaphylaxis, it is often misdiagnosed in the emergency setting. In fact, there have been cases in which patients with HAE have been treated with adrenaline, which was ineffective and later found to be the cause of the disease. Therefore, there is a need to clarify the methods used to differentiate this disease from anaphylaxis and to widely disseminate these methods to healthcare professionals. This disease occurs from childhood to adulthood, and treatment plans should be tailored to the growth stage of the patient. In particular, it is essential to respond to life events such as puberty, pregnancy and childbirth, as well as stress and changes in the work environment. It is desirable for patients and healthcare professionals to share information together on how to manage seizures during pregnancy and how to respond in the workplace, and to provide appropriate care. Currently, rheumatologists are often involved in the treatment of HAE in Japan, and our hospital has also established a specialized outpatient clinic and accepts many patients. We report on the current status of treatment and guidance surrounding HAE, including data from our hospital, as well as points of differentiation that require attention in daily medical care.

LS31

The crucial role of molecular targeted therapies in managing systemic lupus erythematosus

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE), often cited as the prototype of autoimmune disorder, is characterized by profound immune system dysregulation and diverse organ involvement. The heterogeneity in pathological mechanisms underlying SLE not only influences clinical manifestations among patients, such as organ involvement and treatment responsiveness, but also complicates management strategies. Current therapeutic approaches prominently feature molecular targeted therapies, which focus on B cell activating factor (BAFF), type I interferon receptors, and the B cells themselves. Numerous clinical trials are exploring the potential of these targeted therapies, offering a precision medicine approach that minimizes unnecessary immunological activity and potentially reduces the risk of adverse effects. Conversely, glucocorticoids are the treatment of choice for severe organ damage due to their rapid efficacy. Although short-term use of glucocorticoids has been demonstrated to improve prognosis, prolonged usage can lead to irreversible organ damage. Thus, minimizing or eliminating glucocorticoid use is a critical consideration in SLE management. Achieving this requires an understanding of the cellular and molecular anomalies contributing to the disease's pathogenesis. A pivotal challenge in SLE treatment is the translation of immunological advances, primarily derived from mouse models, into clinical applications. In this presentation, I will discuss the complexity of SLE, highlighting the pivotal role of molecularly targeted therapies and their transformative potential in the management of this multifaceted disease.

LS32-1

AAV treatment with Avacopan in Japan

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Conflict of interest: Yes

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. Furthermore, avacopan, a C5a receptor (C5aR) inhibitor, has been attracting attention as an alternative to GC, which has been the mainstay of treatment. Avacopan is a small molecule with a molecular weight of 581 and is an orally available inhibitor of the receptor for complement C5a (C5aR). A Phase 3 study, the ADVOCATE trial, was conducted. Patients with new or relapsed AAV were randomized in a double-blind fashion to receive either avacopan (avacopan plus GC (placebo)) or control (avacopan (placebo) plus standard PSL), and remission induction therapy with CY or RTX as standard therapy. The primary endpoint was non-inferiority of BVAS remission at 26 weeks (72.3% vs. 70.1%) and at 52 weeks (65.7% vs. 54.9%) in the Avacopan and control groups, respectively ($p<0.0001$). % vs. 54.9% at 52 weeks ($p=0.0066$), respectively. However, there is no clear consensus on the use of avacopan other than in remission induction therapy. However, there are various clinical questions such as how avacopan should be used in clinical practice and in which patients it has the greatest potential. In this seminar, I will focus on the current status of diagnosis and treatment in MPA and GPA, as well as data on avacopan use in Japan, and discussing future strategies for avacopan use.

LS32-2

Complement inhibition with avacopan in the treatment of ANCA associated vasculitis. From clinical trials to real world experience to practical use in the clinic

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Conflict of interest: Yes

Patients with ANCA associated vasculitis (AAV) continue to suffer from an increased risk of the adverse outcomes of mortality, end stage kidney disease and infective co-morbidities. Avacopan, an oral complement C5 receptor antagonist has the potential to improve these outcomes through better disease control and reduced glucocorticoid exposure. The development of avacopan in the clinical trial, ADVOCATE, focused on the two major AAV subgroups: microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), and recruited 330 patients with a new diagnosis or at the time of relapse, but excluded those with severe kidney failure (GFR < 15 ml/minute) or hypoxic lung hemorrhage. Patients were followed for one year. In addition to showing an improvement in sustained remission, ADVOCATE demonstrated benefits with avacopan on disease relapse, glucocorticoid toxicity, quality of life and recovery of kidney function. Since the launch of avacopan in North America and Europe we now have three years of real world experience. Published results of this experience have validated the efficacy and safety of avacopan and have added additional data supporting the use of avacopan in AAV indications not studied in ADVOCATE, especially severe kidney failure, lung hemor-

rhage, refractory disease and longer term administration after one year. In addition, prospective data from both avacopan and non-avacopan treated AAV patients is being collated in the AVACOSTAR registry. Following review of this experience, the practical use of avacopan in the clinic will be discussed including specific indications, management of concomitant medications and disease and adverse event monitoring.

LS33-1

Role of Imaging in Understanding the Pathophysiology of Psoriatic Arthritis (PsA) and Practical Application of T2T Strategy to Achieve Treatment Goals

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Conflict of interest: Yes

Psoriatic arthritis (PsA) is a heterogeneous disease with various clinical manifestations that requires early diagnosis and appropriate treatment selection. Recently, treatment targets such as Minimal Disease Activity (MDA) have been established for PsA based on the Treat-to-Target (T2T) guidelines proposed for the management of spondyloarthritis (SpA). However, in clinical practice, achieving these targets can be challenging, particularly regardingthe timing of treatment escalation. Imaging plays a crucial role in PsA management. Specifically, musculoskeletal ultrasound (MSUS) is used to evaluate peripheral arthritis, while MRI is utilized for axial arthritis assessment, facilitating differential diagnosis and demonstration of disease activity. I will focus on the role of imaging in PsA, from diagnosis to monitoring of disease activity, and examine how MSUS and MRI assessments contribute to the T2T strategy. This approach enables accurate assessment of disease activity and helps identify the optimal timing of treatment escalation. This session focuses on the role of imaging diagnostics (X-ray, MSUS, and MRI) in PsA diagnosis and disease activity monitoring. I will examine PsA pathology and discuss the implementation of effective T2T strategies utilizing imaging diagnostics. According to EULAR 2023 recommendations, Phase II involves treatment with methotrexate (MTX) or other csDMARDs, with treatment escalation to biologics or JAK inhibitors recommended in Phase III if no improvement is seen after 3 months or if treatment goals are not achieved within 6 months. In this session, I will focus on upadacitinib, a JAK inhibitor, and explore its utility in PsA patients. Referencing clinical trial data, I will propose treatment strategies based on individual pathological assessment using MSUS and MRI.

LS33-2

Mechanistic insights into the roles of the JAK-STAT pathway for the development of spondyloarthritis

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Conflict of interest: Yes

Ankylosing spondylitis (AS) is a chronic, inflammatory disease of the axial spine (spondyloarthritis (SpA)), characterized by ectopic bone formation, fusion of multiple vertebrae, and ankylosis. It has been reported that the BMP, Wnt, and Hedgehog signaling pathways regulate osteoblast differentiation and calcification, which result in the fusion of the spine in AS. The human leukocyte antigen (HLA) class I molecule HLA-B27, which is strongly associated with the development of AS, has recently been reported to be involved in osteogenesis and cytokine production in AS. Various cytokines and immune cells are involved in inflammation and bone formation. Although the clinical effectiveness of blocking the JAK-STAT pathway in treatment of AS established the significance of JAK in the pathogenesis of AS, the mechanistic insights into the roles of JAK for inflammation and bone formation remain unclear. AS is a seronegative chronic arthritis, which is typically associated with low back pain in young patients, but the clinical diagnosis of AS is not easy because of the lack of sensitive and/or specific biomarkers. Additionally, it is difficult to observe the sclerotic lesions in the sacroiliac joint by the X-rays in the early stages. To exclude PsA, IBD-associated arthritis and other orthopedic disorders, interprofessional collaboration among rheumatology, orthopedics, dermatology, gastroenterology, and rehabilitation medicine is required to improve the clinical outcome in AS patients. In this talk, the mechanistic insights into the roles of inflammatory cytokines and the JAK-STAT pathway for the pathogenesis and ossification of AS will be introduced. Additionally, the therapeutic strategy for AS on the basic of the ASAS-EULAR recommendations for the management of axial SpA: 2022 update and the clinical evidence of the JAK inhibitor Upadacitinib will be shown.

LS34-1

Sjögren's syndrome: disease overview and disease burden

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Conflict of interest: Yes

Sjögren's syndrome (SS) causes exocrine disorders due to immune abnormalities. Approximately 68,000 patients have been confirmed, with a male-to-female ratio of 1:17, and 19,000 patients have been issued specific disease benefit certificates. Factors associated with the long-term prognosis of SS include male gender, high disease activity, and positive cryoglobulin. In terms of disease burden, SS has symptoms in multiple organs, and there are many organ disorders that are not included in the evaluation items of the EULAR Sjögren's syndrome Disease Activity Index (ESSDAI). A report in the Japan Sjögren's Syndrome White Paper 2020, edited by the Japan Sjögren's Syndrome Patient Association, revealed that there are concerns about the impact on daily life and career choices, as well as the worsening of the condition and incurability. It was also pointed out that sufficient explanations and treatment plans are not provided in response to patients' wishes. It was also revealed that it takes an average of 3 years and 6 months from the first consultation to diagnosis. The 1999 revised criteria of the Ministry of Health, Labor and Welfare are used to diagnose SS, and two or more of four items must be met to confirm the diagnosis, but multiple medical departments must be visited. The ACR/EULAR criteria classify SS as a condition with a score of four or more out of nine, and there are exclusion criteria. Although the ACR/EULAR criteria have a high diagnostic sensitivity, it has been reported that the Ministry of Health, Labor and Welfare criteria are superior in terms of specificity. In addition, the 1999 criteria include tests that are less frequently performed, and it has been reported that the diagnosis of SS can be improved by adding salivary gland ultrasound instead of invasive lip biopsy. As a key point for early diagnosis of SS, it has also been reported that there are slight differences in the way symptoms appear around the age of 50 as early symptoms of onset.

LS34-2

Molecular mechanisms of pathogenesis in Sjögren's syndrome (SS) from the perspective of dysregulated acquired immunity

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Conflict of interest: None

In this seminar, we will discuss the pathogenic roles of 1) autoantibodies, 2) autoantigens specific T cells, and 3) $CD8^+$memory T cells and $CD8^+$Treg in SS. 1) Anti-SS-A (Ro52/60) antibody (Ab) is adopted in diagnostic and classification criteria for SS. Recently, Ro52 (TRIM21) has been reported to function as an intracellular Fc receptor, playing a role in regulation of innate immune responses and B cell differentiation. In SS, it was reported that anti-Ro52 Ab contributed to increased disease activity and severity of glandular lesions via upregulation of IFN pathway. We previously revealed that the effect of anti-M3 muscarinic acetylcholine receptor (M3R) Ab on salivary secretion via M3R might be altered according to their epitopes in SS. 2) In SS, salivary glands infiltrating T cells could induce activation and proliferation of B cells, and differentiation into plasmacytes, as well as contribute to apoptosis of glands cells. We showed that M3R reactive Th1 and Th17 were detected in peripheral blood, and M3R reactive Th17 associated with disease activity and an-

ti-M3R Ab in SS. Moreover, we confirmed that M3R reactive T cells could develop autoimmune sialadenitis in mice. We recently revealed that peripheral Tfh significantly increased in SS compared with HC, and peripheral Tfh1 and Tfh2 frequently shared TCR repertoire with labial salivary gland (LSG) infiltrating T cells. The genome-scale platform to identify the epitopes recognized by $CD4^+$T cells has been newly developed, reporting the novel autoantigens in SS. 3) scRNA-Seq of LSG in SS revealed that $CD8^+$T cells exhibit greater clonal expansion compared to $CD4^+$T cells, the presence of $CD69^+CD103^-CD8^+GZMK^+$tissue-resident memory T cells was identified, and this subset showed a significant positive correlation with focus score of LSG. We demonstrated that CDK8/19 inhibitor had the potential to convert $CD8^+$memory T cells into $CD8^+$Treg which decreased in SS, and this conversion could contribute to regulation of SS.

LS35-1

Key points of the '2025 guide for the diagnosis and treatment of interstitial lung disease associated with connective tissue disease'

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Conflict of interest: None

The diagnosis and treatment of connective tissue diseases (CTD) have advanced significantly in recent years, leading to improved patient outcomes. However, challenges remain, particularly with interstitial lung disease (ILD), which is a critical prognostic factor in these patients. A key issue in managing CTD-ILD is the differing perspectives of rheumatologists and pulmonologists; while rheumatologists focus on CTD, pulmonologists assess ILD. Collaboration between these specialties is vital. In 2020, Japan made a significant stride when the Japanese Respiratory Society and the Japanese Society of Rheumatology jointly developed the '2020 guide for the diagnosis and treatment of interstitial lung disease associated with connective tissue disease' This initiative brought together pulmonologists, rheumatologists, radiologists, and pathologists, emphasizing a multidisciplinary approach to improve the management of CTD-ILD. However, the existence of multiple guidelines for individual CTD poses challenges in achieving a cohesive understanding and ensuring consistency with existing frameworks. Additionally, the presence of various international guidelines raises questions about whether to align with them or develop Japan-specific guidelines. In managing CTD-ILD, the rapid identification of inflammation and fibrosis is crucial, especially for the timely treatment of progressive pulmonary fibrosis. This area is currently the focus of numerous clinical trials, with treatment concepts continuously evolving. Therefore, it is essential for the authors to regularly revise the guidelines based on the latest research findings. The '2025 guide for the diagnosis and treatment of interstitial lung disease associated with connective tissue disease' have now been updated. In this lecture, I will outline the specific diseases that have been revised, detail the changes made to the guidelines, and discuss effective strategies for their implementation in clinical practice.

LS35-2

The guideline for the diagnosis and treatment of interstitial lung disease associated with connective tissue disease: update in 2025

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Conflict of interest: None

Connective tissue diseases (CTD) are systemic autoimmune diseases that affects various organs to varying degrees. Especially, interstitial lung disease (ILD) associated with connective tissue disease (CTD-ILD) is one of the refractory conditions, which is a leading cause of death. The striking characteristic of CTD-ILD is its heterogeneity in high resolution CT findings, histopathological findings, the clinical course, treatment responses, and prognosis among patients diagnosed as the same disease as well as patients with each CTDs. In 2020, the Japanese Respiratory Society and the Japan College of Rheumatology cooperated to release the world's first guide focusing on CTD-ILD, based on the evidence and expert consensus of pulmonologists and rheumatologists in addition to radiologists, pathologists, and dermatologists. This guideline clarified the current understanding and unmet needs of CTD-ILD and is also useful tool to understanding the clinical features and standard therapeutic algorism of ILD in each CTD-ILD. In 2025, the revision of this guideline has been made because new information or findings were reported in terms of unsolved questions during past 5 years. In this lecture, the updated points regarding the diagnosis and therapeutic strategy of CTD-ILD are summarized from the standpoint of rheumatologist.

LS36

Mechanism of Action and usefulness of JAK inhibitors - including an interim analysis of post-marketing surveillance data in rheumatoid arthritis patients receiving filgotinib -

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Conflict of interest: Yes

The 2024 update version of the Japan College of Rheumatology clinical practical guidelines for the management of rheumatoid arthritis (RA) was published and biological disease-modifying antirheumatic drugs (bDMARDs) and JAK inhibitors were equally listed as treatment options in phase II. To date, five JAK inhibitors with different selectivities have been approved for RA in Japan. The post-marketing surveillance (PMS) of all the patients receiving tofacitinib and baricitinib have been completed and their safety profiles up to 3 years have been clarified. However, other JAK inhibitors are still being investigated and a caution has been added stating that "TNF inhibitors and JAK inhibitors are almost equally useful in short-term treatment but bDMARDs are more preferred from the perspective of long-term safety and medical economics". from Oral surveillance data. bDMARDs (currently 9 originators) have contributed to improve patient QOL and mortality with anti-inflammatory and bone destruction inhibitory effects. However, bDMARDs basically target a single molecule. Because neutralizing anti-drug antibodies are occasionally developed, there are still unmet medical needs for RA. Since JAK inhibitors have no immunogenicity and are supposed to inhibit multiple molecules, mainly IL-6 and IFN-α, their usefulness for difficult-to-treat RA (D2T-RA) has also been suggested. Filgotinib, which is thought to have high inhibition activity against for JAK1, was approved as the fifth JAK inhibitor in Japan and is currently undergoing safety investigation by PMS. At present, however, head-to-head clinical trials have not been conducted between JAK inhibitors, so no clear conclusions regarding selectivity cannot be drawn. In this seminar, I would like to discuss the inhibitory activity of JAK inhibitors and their clinical usefulness.

LS37

How to Achieve Concurrent Treatment for Rheumatoid Arthritis and Cancer? - From the Perspective of a Medical Oncologist -

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Conflict of interest: None

When rheumatoid arthritis (RA) patients are diagnosed with cancer, balancing RA and cancer treatment is an important issue. Especially in the introduction of immune checkpoint inhibitors (ICIs), the risk of RA exacerbation (flares) and immune-related adverse events (irAEs) is a concern. On the other hand, ICIs have contributed significantly to improving the prognosis of patients with advanced cancer, d application to RA patients is also attracting attention. However, patients with autoimmune diseases, including RA, have been excluded from ICI trials, and no specific guidelines have been established in Japan or other countries. Therefore, ICIs are sometimes avoided in patients with RA. Recent studies suggest that ICIs can be cautiously administered to RA patients, maintaining the effectiveness of cancer treatment while managing RA. At our institution, we have provided ICI treatments in collaboration with rheumatology specialists, based on clinical data and experience with RA-complicated cancer cases, to ensure both efficacy and safety. In this presentation, we will focus primarily on lung cancer to explore the epidemiological association between RA and lung cancer. It addresses the impact of RA medications (csDMARDs, b/tsDMARDs, and glucocorticoids) and their dosage on cancer

treatment, the management of RA activity when initiating ICIs, and strategies for addressing RA exacerbations during treatment. Specific management approaches, such as treatment modifications using IL-6 inhibitors and low-dose glucocorticoids, will be discussed based on real-world clinical cases from our institution. Furthermore, multidisciplinary collaboration, including oncologists, rheumatologists, and pharmacists, is essential for successful RA and cancer treatment. I would like to present a comprehensive treatment approach to deliver smooth treatment for patients based on our experience. Through this presentation, I hope to share practical knowledge for the optimal treatment of cancer patients complicated by RA and discuss the clinical ideas for RA specialists from my perspective as an oncologist so that we can establish a medical system that enables both cancer treatment and RA management.

LS38-1

Current status and issues in SLE Treatment in Japan

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Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center

Conflict of interest: Yes

The national database analysis (PI: Takako Miyamae, Tokyo Women's Medical University) disclosed the number of patients with SLE in FY 2019 was 74277. The prevalence of SLE is 60 per 100,000, but it is not rare among women aged 20 to 39, with a prevalence of 1 per 1,000. The prevalence of SLE patients seen at specialized facilities in Japan is high at 79.4%, but even among those seen at specialized facilities, glucocorticoid (GC) use is high at 90% (monotherapy 29%), while hydroxychloroquine (HCQ) use is low at 23%. GC has been the first-line drug in Japan for many years and complications from long-term GC use are serious concerns; 18% of patients aged 20-39 were treated for hypertension and 2.9% for diabetes, while 6.6% of patients aged 40-69 were treated with denosumab and 1.2% with teriparatide. In our department, HCQ has been recommended for all SLE patients since its approval in 2015. HCQ is initiated as soon as SLE is clinically diagnosed regardless of the classification criteria. We also actively introduce HCQ to patients who are in remission with low dose GC, aiming for GC-free remission. As of April 2024, 468 patients with SLE were identified, SLE medications were HCQ 83% (monotherapy 17%), GC 75% (monotherapy 6%), tacrolimus 28%, mycophenolate mofetil 25%, azathioprine 8%, methotrexate 6%, mizoribine 3%, belimumab 14%, anifrolumab 2%, and rituximab 1%. Although biologics use is relatively low, 90% used prednisolone (PSL) 7.5 mg/day or less, 87% used PSL 5 mg/d or less, and 25% patients were GC-free. HCQ should be used in all SLE patients, ideally started at the disease onset. Biologicals are useful, but cost-effectiveness should be evaluated. Japanese SLE treatment guideline issued in 2019 is expected to promote standardization of SLE treatment in Japan.

LS38-2

Hydroxychloroquine retinopathy: How many patients actually receive eye examinations?

Mineo Kondo
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Conflict of interest: None

Hydroxychloroquine sulfate (HCQ) was approved and widely used in Japan for systemic lupus erythematosus (SLE) and cutaneous lupus erythematosus (CLE) in 2015. The most important side effect of HCQ is retinal damage (hydroxychloroquine retinopathy). Therefore, periodic examinations by the ophthalmologists are essential for the safe use of this drug. Hydroxychloroquine retinopathy is often difficult to recover even after the drug is discontinued. About eight years after the approval of HCQ, hydroxychloroquine retinopathy is gradually being reported in Japan. It has also become clear that we Asian races are at relatively high risk for HCQ retinopathy. In this lecture, I would like to talk about the basics of hydroxychloroquine retinopathy and precautions that prescribing physicians should know for the proper use of this drug. In addition, we recently conducted a survey using insurance databases to determine the proportion of patients taking HCQ who actually receive eye examinations, and we would like to discuss the results.

LS39-1

Current issues in the management of Behçet's disease

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Conflict of interest: None

Behçet's disease is a chronic inflammatory condition of diverse lesions in various organs with a relapsing and remitting course. The use of GWAS to identify disease susceptibility genes, the search for environmental factors such as pathogenic microorganisms, and the development of the concepts of autoinflammatory disease and MHC-I-opathy have all helped to advance our understanding of pathogenesis, but there are still many unknowns. The treatment of Behçet's disease in Japan has advanced in recent years, with the approval of TNF inhibitors, the publishing of comprehensive Behçet's disease treatment guidelines 2020, and the introduction of PDE4 inhibitors. This has not only benefited patients, but also reduced the psychological burden on us, rheumatologists. However, because it is a rare disease with unequal prevalence around the world, the development of evidence for its treatment, as well as the updating of global guidelines based on this evidence are often delayed. As a result, many concerns remain to be addressed at each step of medical practice. In diagnosis, the lack of specific laboratory findings for Behçet's disease and the variety of sites, timing and combinations of symptoms can make the diagnosis time-consuming. In the assessment of activity, painful mucosal symptoms significantly impair patient quality of life, but are difficult to assess accurately as symptoms often have resolved before the consultation. In treatment, oral ulcers, the most frequent form, may be resistant to local therapy and systemic administration of glucocorticoids is unavoidable. When ocular or severe organ involvements are resistant to TNF inhibitors or immunosuppressive treatments, secondary therapy options are limited. Advances in treatment have made it possible to maintain remission in many cases, but how to reduce or withdraw therapeutic medications once remission is achieved remains a matter of debate. In this session, we would like to discuss these issues at each step of the treatment of Behçet's disease.

LS39-2

Utilizing Apremilast for PsA

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Conflict of interest: None

Psoriatic Arthritis (PsA) is a chronic inflammatory disease associated with psoriasis and is characterized by musculoskeletal inflammation, including arthritis, enthesitis, tendinitis, and axial manifestations such as inflammation of the sacroiliac joints and spine. PsA significantly impacts patients' quality of life (QOL) and has the potential to cause joint destruction, making early diagnosis and appropriate treatment essential. Apremilast, a phosphodiesterase 4 inhibitor, has demonstrated efficacy in improving symptoms in PsA patients as well as in treating psoriasis. It is included in the treatment recommendations of GRAPPA (the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) for multiple PsA domains and is recommended by the European League Against Rheumatism (EULAR) for use in cases of mild PsA with few affected joints. In 2023, findings from the FOREMOST trial were reported, demonstrating the efficacy and safety of apremilast in a randomized controlled trial involving patients with early oligoarticular PsA within five years of onset. In addition, the concept of Psoriatic Disease (PsD) emphasizes the importance of managing not only skin and musculoskeletal symptoms but also comorbidities and associated conditions. Patients with PsD are known to have a higher cardiovascular risk, as systemic inflammation accelerates atherosclerosis and increases the likelihood of cardiovascular events. Comprehensive management, including the impact on the cardiovascular system, is therefore necessary. The MOSAIC trial, presented at EULAR 2023, demonstrated that apremilast improves peripheral joint inflammation in patients with psoriatic arthritis and highlighted its beneficial effects on the management of comorbidities associated with psoriatic arthritis. As therapeutic options for PsA continue to expand, the 2023 GRAPPA meeting included an intriguing discussion on treatment strategies, specifically whether to start with biologics or to initiate treatment with targeted synthetic DMARDs, such as apremilast or TYK2 inhibitors. This presentation

provides an overview of apremilast's significance in PsA treatment, including efficacy, safety, and the latest evidence, as well as practical considerations for its use in clinical practice.

LS40

JAK Inhibitors in Rheumatoid Arthritis: A decade of Progress

Motomu Hashimoto
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Conflict of interest: Yes

Janus kinase (JAK) inhibitors were introduced for the treatment of rheumatoid arthritis (RA) in Japan approximately a decade ago. Since then, substantial evidence has accumulated supporting their efficacy and safety in RA management. Type I and type II interferons are crucial cytokines in RA pathogenesis, with signals transduced via the JAK-STAT pathway through JAK1/TYK2 or JAK1/JAK2, respectively. Recent studies, including single-cell RNA sequencing analyses, have revealed that upregulation of IFN signaling in the synovial tissue of RA patients was associated with the treatment resistance, as IFN signaling has not been targeted by conventional biologics such as TNF inhibitors. These findings provide a rationale for the use of JAK inhibitors in RA clinical practice. Another significant cytokine not targeted by existing biologics is GM-CSF, which signals through JAK2/JAK2. GM-CSF is involved in inflammation and pain perception, as well as in the formation of bone marrow edema, which precedes the development of bone erosion in RA. Recently in vitro and clinical studies have evaluated the influence of baricitinib, a JAK1/2 inhibitor, on both GM-CSF signaling and bone microstructure destruction in RA. This seminar will present recent basic and clinical studies on JAK inhibitors, focusing on their mechanism of action, efficacy, and safety in RA treatment.

LS41

Mechanisms of Bone and Joint Destruction in Rheumatoid Arthritis (RA) and Their Management: Optimizing RA Treatment through Insights from Cohort Studies

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Conflict of interest: Yes

The 2024 Guidelines for Rheumatoid Arthritis (RA) Management outline the primary treatment goals as "improving clinical symptoms (clinical remission) and preventing joint destruction (structural remission)", with further objectives of "preventing physical disability and enhancing life expectancy". Additionally, the 2020 Rheumatism White Paper reports that RA patients most expect their treatment to halt joint destruction progression (structural remission). However, in clinical practice, nearly half of RA patients in Japan are now aged 70 or older (RA Management Guidelines, 2024). This population often faces challenges in intensified treatment with anchor drugs like methotrexate due to renal or pulmonary impairment, despite high disease activity. Furthermore, some patients meet clinical remission criteria based on blood inflammatory markers and composite measures, yet still experience joint destruction and physical disability progression due to glucocorticoid treatment. This issue can be attributed to factors such as: (1) limited understanding and assessment of the mechanisms and risks of joint destruction; (2) insufficient evaluation of small joint inflammation in hands and feet or deep joint inflammation (e.g., shoulder, hip) that does not reflect in blood tests; and (3) a lack of non-glucocorticoid treatment strategies tailored for elderly patients. To address these challenges and meet RA patients' treatment expectations, it is crucial to: (1) understand the mechanisms underlying RA-associated joint destruction; (2) initiate timely interventions considering age and the risk of joint destruction progression; and (3) perform regular risk assessments of joint destruction. In this presentation, I will provide an overview of the latest insights on bone and joint destruction mechanisms in RA and optimal RA treatment strategies, drawing on data from the multi-center ANSWER cohort in Kansai.

LS42-1

CTD-PAH: Current Trends and Practical Knowledge Required for Treatment

Yuichiro Shirai
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Conflict of interest: Yes

Pulmonary arterial hypertension (PAH) is an intractable disease, but clinical trials and registry studies have shown that the pulmonary vasodilators have improved symptoms, hemodynamics, exercise capacity, and prognosis. In recent years, therapeutic options have expanded to oral, intravenous, subcutaneous, and inhalation agents, and furthermore, initial combination therapy has become the standard. In 2022, the ESC/ERS guidelines for the treatment of pulmonary hypertension (PH) has been updated, and in 2024, the World Symposium on Pulmonary Hypertension (WSPH) will provide the latest recommendations from diagnosis to treatment. Connective tissue diseases (CTD)-PAH is supposed to the same diagnostic criteria, risk assessment, and treatment algorithm as other type of PAH, including idiopathic PAH. On the other hand, CTD-PAH has a unique pathogenesis. Therefore, the 2024 WSPH has identified the following points to be considered in CTD-PAH: i) the presence of comorbidities that limit the efficacy of therapeutic agents, ii) lack of awareness of pulmonary veno-occlusive disease in systemic sclerosis-PAH, and iii) susceptibility to treatment-related adverse events. The study also included the following points: The management of cases that overlap multiple clinical classifications has been mentioned for the first time in the guidelines to date. The practical knowledge is essential for the appropriate treatment of CTD-PAH. This talk will provide an overview of the latest information required to optimize treatment for CTD-PAH. In addition, the advantages of Riociguat, a pulmonary vasodilator with a unique mechanism of action, will also be presented.

LS42-2

Up to date on treatment of pulmonary arterial hypertension associated with systemic sclerosis (SSc) and non-SSc connective tissue diseases

Masaru Kato
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Conflict of interest: Yes

Connective tissue diseases (CTD) are one of the most prevalent conditions underlying pulmonary arterial hypertension (PAH). In Europe and the US, PAH associated with systemic sclerosis (SSc) accounts for more than 60% of CTD-PAH cases, whereas in East Asia, including Japan, the proportion of PAH associated with non-SSc CTD, such as systemic lupus erythematosus and mixed connective tissue disease, is relatively high. In addition, not a small number of cases of non-SSc CTD-PAH respond to immunosuppressive therapy as well as pulmonary vasodilators. SSc-PAH often develops after a long disease duration of SSc and is histologically characterized by fibrous intimal thickening and luminal narrowing in a wide range of pulmonary blood vessels, from the pulmonary arteries to the pulmonary veins, loss of pulmonary capillaries, and little infiltration of inflammatory cells. Conversely, in cases of non-SSc CTD-PAH, PAH and CTD often develop simultaneously, with histological abnormalities resembling idiopathic/hereditary PAH, including pulmonary artery vasculitis accompanied by medial thickening, plexiform lesions, and fibrinoid necrosis due to proliferation of vascular smooth muscle cells. In this seminar, we will discuss the significance of subclassifying CTD-PAH into SSc-PAH and non-SSc CTD-PAH and introduce the current recommendations for their diagnosis and treatment.

LS43

Biosimilar biologics: a new selection in treatment of rheumatoid arthritis

Hiroaki Matsuno
Matsuno Clinic for Rheumatic Diseases

Conflict of interest: None

Biosimilar biologics: a new selection in treatment of rheumatoid arthritis A biosimilar is a biological medicinal product that contains a version of the active substance of a original biological product. The high similarity in the structural and functional properties and biological activities between biosimilar and original product has been demonstrated. Many clinical studies have demonstrated that switching from original product to biosimilar has no problem with efficacy or safety. EULAR recommendations indicate that there are no problems with treating rheumatoid arthritis with biosimilars. In Europe, when a reference product has a biosimilar, treatment is replaced the reference product with the biosimilar almost 100%. The price of a biosimilar is lower than that of the reference product, biosimilars contributes to reducing medical costs. However, our clinical study of switched from one biosimilar to another demonstrated that there was no difference in efficacy between biosimilars but safety was a difference. Therefore, be careful when switching biosimilars. This lecture will also introduce the nocebo effect of biosimilars.

Evening Seminar

ES1

Optimizing Treatment of RA: Achieving Treatment Goals with Upadacitinib

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Conflict of interest: Yes

Rheumatoid arthritis (RA) management has evolved with a focus on achieving early remission to prevent joint damage, improve patientreported outcomes (PROs), and reduce the risk of major adverse cardiovascular events (MACE) and serious infections. This lecture will highlight the importance of early, targeted treatment, emphasizing findings from the SELECT program, including SELECT-COMPARE, EARLY, and MONO 5-year studies. These trials demonstrated the superior efficacy of the JAK-1 inhibitor Upadacitinib (UPA) in achieving remission compared to Adalimumab. While JAK inhibitors, including UPA, offer benefits, they are associated with an increased risk of Herpes Zoster (HZ). This underscores the importance of vaccination, particularly with the adjuvanted recombinant zoster vaccine (Shingrix), which is becoming routine clinical practice. The presentation will cover new 60-week immunogenicity results from a randomized substudy evaluating Shingrix in RA patients treated with UPA, providing critical insights into vaccine efficacy in this population. Additionally, real-world evidence (RWE) from the OPAL study and other recent analyses will be discussed, demonstrating the clinical profile, persistence, and effectiveness of UPA compared to other JAK inhibitors and TNF inhibitors. These findings offer practical help for treatment selection in daily clinical practice. By integrating clinical trial data with real-world insights, this presentation aims to provide a comprehensive understanding of optimizing RA treatment with Upadacitinib, ensuring better patient outcomes while addressing safety considerations.

ES2-1

The awesome achievement of Tofacitinib during the 12 years~The novel strategy for RA treatment to the future by Rheumatologist~

Kenta Misaki
Department of Rheumatology, Kita-Harima Medical Center

Conflict of interest: Yes

Tofacitinib (TOF) appeared in the world of the region of rheumatoid arthritis (RA) *1 in 2013 after just 12 years when the first biologics (Bio) was approved in Japan in 2003. TOF is one of the JAK inhibitors (JAKi) focused on multiple cytokines led to severe inflammation of RA unlike the mechanism of Bio: just targeted to one cytokine. The approve of JAKi in RA-clinical setting made a huge paradigm-sift to RA treatment also in terms of the route of administration. Most of Rheumatologists gingerly prescribed TOF to the Bio-IR of RA patients because there was no appropriate treatment-guideline about JAKi in 2013. Nevertheless, we were able to obtain a newly insight by using TOF to Bio-IR cases at that time. Fortunately, TOF was listed as the one of the treatment agents in domestic RA treatment guideline published in 2014, moreover JAKi including TOF were also conditionally elected in Phase II of the 2024 Japanese guideline as well as those of abroad. Additionally, TOF is also approved to inflammatory bowel diseases*2 under the medical insurance in Japan. Just 12 years have passed since TOF is available as RA treatment. TOF has attracted lots of attention as one of the JAKi with greatest number of clinical evidence concerned with both efficacy and safety during the 12 years. These evidence definitely make it possible to list up the TOF as one of the useful treatment agents in this new era. I'll introduce the novel track-history of TOF during the 12 years including the provisions of RA treatment led to the future one especially focused on the efficacy and safety of TOF based on the evidence of ORAL trials in this session. *1rheumatoid arthritis with inadequate response to existing therapies *2 remission-induction and maintenance therapies for moderate to severe ulcerative colitis (only in the case of inadequate response to existing therapies)

ES2-2

Positioning of JAK inhibitors for rheumatoid arthritis (RA) with pulmonary involvements leading to Difficult to treat (D2T) RA

Hiroto Tsuboi, Nana Uematsu, Akiyoshi Rai, Hirofumi Toko, Toshiki Sugita, Ayako Ohyama, Masaru Shimizu, Ayako Kitada, Saori Abe, Haruka Miki, Hiromitsu Asashima, Yuya Kondo, Isao Matsumoto
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Conflict of interest: Yes

RA with pulmonary involvements (PI) is often associated with disease activity and treatment limitations. This seminar focuses on PI in RA, discussing 1) PI as predictors for D2T RA, 2) the pathogenesis of PI in RA and MOA of biologics and JAK inhibitors (JAKi), and 3) the usefulness of JAKi for RA with PI leading to D2T RA. 1) Approximately 30-40% of RA patients develop some forms of PI. Shared risk factors between ILD and airway disease in RA include advanced age, smoking, prolonged disease duration, and elevated RF and anti-CCP antibodies (Ab). High disease activity has been linked to both the onset and progression of RA-ILD, with 34.5% of RA-ILD cases reportedly exhibiting PF-ILD. In IORRA cohort, RA with ILD had a lower likelihood of achieving remission compared to those without ILD. Additionally, in Japanese two clinical studies, prolonged disease duration, high RF, anti-CCP Ab positivity, high DAS28-ESR, and pulmonary disease were identified as predictors for D2T RA. 2) Sustained autoimmune inflammation in lungs involving T cells, macrophages, neutrophils, inflammatory cytokines, and JAK2 signaling promotes fibroblast-myofibroblast transition and fibrosis in RA-ILD. These cells, cytokines, and JAK can serve as potential targets when considering MOA of therapeutic agents. 3) In our cases, 75% of patients treated with JAKi experienced no progression nor emergence of PI. Recently, there has been an increasing number of reports on the administration of JAKi for RA-ILD. However, JAKi might increase the risks of MACE and malignancies, particularly in older patients and smokers who had high risks for PI in RA, necessitating cautious decision-making.

ES2-3

Understanding the Safety Profile and Mechanisms of JAK Inhibitors

Satoshi Kubo
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Conflict of interest: Yes

Since the approval of tofacitinib as a first JAK inhibitor for rheumatoid arthritis* in 2013, evidence regarding its clinical efficacy and safety has been gathered. Nonetheless, concerns about the risk of major adverse cardiovascular events (MACE) and malignancies, as highlighted by the ORAL surveillance study, have led to a reduction in the usage of JAK inhibitors[1]. In contrast, the post-marketing surveillance of tofacitinib in Japan showed that the incidence of major adverse cardiovascular events (MACE) and malignancies per 100 patient-years was 0.31 and 1.12, respectively. In the long-term extension study[2] of the tofacitinib clinical trial, the combined major adverse cardiovascular events (MACE) were 0.4/100 person-years and malignancies other than NMSC were 0.8/100 person-years. By exploring differences from ORAL surveillance study, it is hoped that more appropriate use of JAK inhibitors can be identified. This lecture will focus on the adverse events associated with JAK inhibitors, their mechanisms, and insights into their safety profile. *Rheumatoid arthritis with inadequate response to existing therapy.

ES3

Importance of Shingles (Herpes Zoster) Prevention in Rheumatic Diseases

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

Conflict of interest: Yes

Shingles is a disease caused by reactivation of the varicella virus and occurs mainly in the elderly and people with weakened immune systems. The incidence of shingles is high in patients with collagen diseases, not only in the elderly but also in young people. The risk of developing the disease is known to be very high, especially in SLE. In addition, immunosuppressive drugs and glucocorticoids increase the risk of developing herpes zoster, especially JAK inhibitors and biologic agents. Herpes zoster can sometimes spread throughout the body, which can be severe. Long-term persistent pain (postherpetic neuralgia) can also have a significant impact on quality of life. In patients with collagen disease, the occurrence of herpes zoster has been reported to increase the risk of disease flares. Therefore, prevention of herpes zoster in immunosuppressed patients with collagen disease is desirable. The recombinant shingles vaccine “Shingrix” induces specific humoral and cellular immunity against glycoproteins (gE) present on the surface of the varicella-zoster virus. Clinical efficacy is very high, with a 97% suppression rate in a clinical trial in the general elderly population and approximately 90% prevention at 10 years of follow-up. It is also highly effective in suppressing post-herpetic neuralgia. Because Singrix is a recombinant vaccine, it can be used in immunosuppressed patients at high risk for shingles. In fact, it has been shown that a shingles suppression rate of approximately 70% can be achieved even in patients following hematopoietic stem cell transplantation. In recent years, the efficacy of Shingrix in suppressing shingles has been investigated using reimbursement data, and its efficacy in patients with autoimmune diseases and rheumatoid arthritis has also been demonstrated. In this presentation, I will discuss the benefits of Shingrix, including the latest data.

ES4-1

The Role of Anifrolumab in the New Paradigm of Systemic Lupus Erythematosus Treatment~A Perspective on the Involvement of Type I IFN in Disease Pathogenesis~

Kimito Kawahata
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Conflict of interest: Yes

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease characterized by the production of autoantibodies. It predominantly affects young women, with the onset age commonly falling within the reproductive years of the 20s to 40s. The disease often follows a chronic course, marked by cycles of remission and exacerbation. Despite progress in the development of novel therapeutic agents for other connective tissue diseases, SLE treatment remains centered on nonspecific immunosuppression with glucocorticoids and immunosuppressants. Specific therapies targeting refractory disease conditions have yet to be developed. In recent years, Type I interferon (IFN) has been recognized as playing a crucial role in the onset and pathogenesis of SLE. Type I IFN contributes to dendritic cell maturation, autoantibody production, and inflammation. It is also known as a cytokine that bridges innate and adaptive immunity. Overexpression of IFN-inducible genes has been observed in many SLE patients, further implicating its involvement in disease pathogenesis. Anifrolumab is a human anti-IFNAR1 monoclonal antibody that binds to subunit 1 of the Type I IFN receptor (IFNAR1). It induces the internalization of IFNAR1 and reduces its expression on the cell surface, thereby inhibiting the pathological processes mediated by Type I IFN. The efficacy and safety of Anifrolumab in patients with moderate to severe SLE receiving standard therapy was confirmed in the TULIP-1 and TULIP-2 Phase III global trials and has been launched in Japan in November 2021. In this lecture, we will discuss the role of Anifrolumab in the treatment of SLE based on the latest findings on the relationship between SLE and type1 IFN, as well as clinical trials and our experience of its use.

ES4-2

Unmet medical needs of SLE and expectations for anifrolumab

Takao Fujii
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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is an autoimmune disease with serious organ damage that affects patients’ prognosis. The treatment goal is to sufficiently suppress disease activity in acute phase, prevent relapse,

reduce glucocorticoid (GC) as much as possible (and discontinue them if possible), and prevent long term organ damage. The EULAR recommendations revised in 2023 shows strict control of GC dosage and state that GC is a "bridging therapy" that does not play a major role in treatment. In order to achieve such high treatment goals, early introduction of immunosuppressants and biological agents in addition to the basic drug hydroxychloroquine, should be considered. In recent years, data on biological agents in SLE has been accumulated and the possibility of modifying the natural history of SLE has been shown. Regarding anifrolumab (ANF), a biological agent that inhibits type I interferon (type I IFN), it has already been three years since its launch in Japan in 2021, and long-term safety and efficacy have been reported in TULIP clinical trials. ANF is the only drug that directly targets IFN-α signaling, a key cytokine in SLE pathology. Because ANF is not only useful for inducing clinical remission, but also has been shown to prevent relapse and reduce GC dosage, ANF may be one of the disease-modifying drugs for SLE. Although the prognosis for SLE has improved compared to the past, the 5-10 year survival rate is still low considering the age at which the disease develops, suggesting unmet medical needs. For a professional of SLE doctors, it is required to use biologics effectively to achieve the above treatment goals. In this lecture, I would like to discuss how ANF should be used to address the many unmet medical needs in SLE.

ES5-1

Hand Surgery for D2T RA

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Conflict of interest: None

D2T RA (Difficult-to-treat Rheumatoid Arthritis) is reported to occur in approximately 5-10% of RA patients. This session focuses on the treatment of progressive rheumatoid arthritis in the hands that becomes difficult to manage even when inflammation is controlled with drug therapy. Advances in drug therapy have led to an increase in the number of patients who can achieve remission of RA at an early stage. However, surgery for joint disorders in the fingers and toes-often the first affected areas-remains common, reflecting the growing need for improving patients' ADL and QOL. Even if drug therapy prevents joint destruction and subsides RA inflammation, joints that once loosen due to initial swelling may gradually deform as the soft tissue balance is lost. Such joints lose their physiological movement, potentially leading to secondary OA with cartilage damage and tendon dislocation or rupture, and can further induce deformity in adjacent joints. For example, a loosened radial deviation of the wrist may induce ulnar deviation of the fingers at the neighboring MP joint, while a loosened MP joint may promote swan-neck deformity in the fingers. In this session, panelists will present and discuss the characteristics and treatment approaches for these hand conditions with participants, aiming to support daily clinical practice. Furthermore, the special lecture will cover potential treatment and prevention strategies for D2T RA in the hands, including drug therapy.

ES5-2

Drug treatment and hand surgery for D2TRA

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Conflict of interest: None

In recent years, drug treatment for rheumatoid arthritis (RA) has changed dramatically and made remarkable progress. These changes have brought the importance of RA tight control into the spotlight and is now widely recognized. As a result, joint destruction associated with RA is suppressed and there is a possibility that it can be repaired, so orthopedic surgery is also changing, and small joint surgery such as hand joints and finger joints is attracting attention, and joint-preserving surgery is also attracting attention. However, on the other hand, there are cases where both drug treatment and surgical treatment are difficult. The theme of this edition of Rheumatic Hand Surgery 2025 is "Hand Surgery for D2T RA", and we would like to consider drug treatment for D2TRA and hand surgery. Even if disease activity is controlled by RA drug treatment, if inflammation remains in some joints, it may cause joint destruction and deformity to progress. For such synovitis, if conservative treatment such as intra-articular injections does not respond, synovectomy is considered before deformity or joint destruction appears. This is important from the viewpoint of joint preservation, and it can also prevent tendon rupture in the hand joint, so the timing of intervention is the key. In addition, even if the inflammation seems to subside, joint destruction may progress. In such cases, it is important to determine the indications for surgical treatment. If a characteristic deformity of the RA fingers occurs, the cause should be ascertained, and the surgical method will be considered depending on the situation. In the hand joint, the surgical technique is selected according to the progress of joint destruction. In view of the expectation of the joint destruction repair effect of drug treatment, joint-preserving surgery will be considered if possible. In relatively young patients, where joint destruction has not yet progressed and the degree of deformity is mild, we would like to actively consider the indications for joint-conserving surgery. In the future, it is necessary to consider the problem of D2T RA from the perspective of both drug treatment and surgical treatment. Therefore, the importance of drug selection and the significance of RA surgery, especially hand surgery, may increase. RA hand surgery is likely to change in terms of the scope of its contents, becoming more sophisticated, including rehabilitation. However, it can be said that there are still many problems to be solved. We will continue to provide appropriate and aggressive drug treatment with biologics, etc., and we will also take on the challenge of achieving higher goals for RA hand surgery.

ES6

Treatment Strategies for Osteoporosis: The Role of Abaloparatide

Ko Chiba
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Conflict of interest: Yes

In the daily clinical practice of rheumatoid arthritis and collagen diseases, osteoporosis medications play an important role. One is as a preventive for glucocorticoid-induced osteoporosis, and the other is for the prevention of secondary fractures in cases where fractures have already occurred. Currently, there are six types of osteoporosis medications: active vitamin D, SERMs, bisphosphonates, anti-RANKL antibodies, anti-sclerostin antibodies, and PTH receptor agonists. These medications are used according to the patient's bone mineral density and fracture risk. Abaloparatide is the newest osteoporosis medication to be launched in Japan. It is one of the PTH receptor agonists like teriparatide, but has a different mechanism and effects. In this seminar, I will be talking about the basics of evaluation and treatment strategy of osteoporosis, and particularly discuss the characteristics and role of abaloparatide.

ES7-1

Molecular mechanism for oathogenesis of spondyloarthritis: Bridging the basic and clinical researches

Susumu Nakae
Graduate School of Integrated Sciences for Life, Hiroshima University, Hiroshima, Japan

Conflict of interest: None

Researches using genetically engineered mice and mouse models of human disease have been very useful for elucidating the pathogenesis of chronic inflammatory diseases. Rheumatoid arthritis, for which mouse and rat models had been established, has seen dramatic progress in the elucidation of molecular mechanism for its pathogenesis since the 1990s. On the other hand, the study of psoriasis in mice took time until the mid-2000s, when imiquimod-induced dermatitis was established, followed by the late 2000s, when the importance of the IL-23/IL-17 axis in its pathogenesis became clear. The pathogenesis of spondyloarthritis, including psoriatic arthritis, is still unknown due to the lack of a suitable mouse model, although there are several specialized mouse models. Based on findings from basic studies in psoriasis using mice, I will review the involvement of the IL-17 family of cytokines in spondyloarthritis, including psoriatic arthritis.

ES7-2

Treatment strategy of psoriatic arthritis and axial spondylitis based on pathophysiology

Kei Ikeda
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Conflict of interest: Yes

Spondyloarthritis (SpA) encompasses multiple diseases and is a spectrum of peripheral SpA and axial SpA. Psoriatic arthritis (PsA) is the most prevalent type of SpA in Japan, which 10-30% of patients with psoriasis develop. Musculoskeletal lesions of SpA consist of arthritis, enthesitis, dactylitis, and spondylitis, but enthesitis is considered to be the most characteristic to PsA/SpA. Recently, consensus-based sonographic lesions of dactylitis were published. Although methotrexate has been recommended for the peripheral lesions of PsA/SpA, ultrasound findings have been suggested to predict the responsiveness of PsA/SpA to methotrexate. As IL-17 producing cells have been shown to reside in human entheseal tissues, IL-23/17 axis is implicated in the pathophysiology of enthesitis. On the other hand, the involvement of IL-23 in axial lesions may be low, causing debates over the mechanistic differences. Recently, bimekizumab, which inhibits IL-17F as well as IL-17A, was approved for the treatment of PsA/SpA. The results of multiple clinical trials of bimekizumab, have shed light into the roles of IL-17A and IL-17F in the pathophysiology of PsA/SpA.

ES8-1

The Future of VHH Antibodies: Insights from Existing Antibody Therapeutics

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Conflict of interest: None

Recent advances in antibody (Ab) engineering have been remarkable, and it is desirable to produce Abs with more added value. In the field of pharmaceutical development in particular, the commercialisation of 'Ab drugs' is under way, but there are still many problems to be solved, such as high development and production costs, and the lack of productivity and long-term shelf life. As one solution to these problems, there are high hopes for the use of VHH Abs, which are ultra-low molecular weight versions of Abs consisting only of heavy chains possessed by camelids. In this context, we are conducting research aimed at the practical application of VHH Abs based on 'a low-cost, highly sensitive and storage-stable Ab production technology using camelid VHH (variable domain of heavy chain of heavy chain Ab) Abs'. The VHH Ab, which is said to be the 'smallest unit of Ab', has many advantages, including stability against heat, denaturing agents and changes in pH, and the ability to be produced in large quantities at low cost in bacteria such as *Escherichia coli*. We have constructed a phage library of VHH Abs, which enables rapid production of VHH Abs against a wide variety of antigens; VHH Abs can be used for a variety of applications and are beginning to be utilised as therapeutic Abs when humanized. Under these circumstances, the TNF inhibitor ozolalizumab was approved as the first Nanobody (VHH Ab) drug in Japan. It is a bispecific Ab capable of binding specifically to human TNFα and human serum albumin, and has been called a next-generation Ab product because of its novelty. Ozoralizumab contains two anti-human TNFα Nanobody molecules, which bind bivalently to TNFα. It is also reported that binding to serum albumin has been shown to increase the half-life of the drug in studies using mice. In this seminar, the advances and challenges in Ab engineering will be outlined and the future of VHH Abs will be considered.

ES8-2

The Potential of Next-Generation Small-Molecule Antibody Ozoralizumab in Revolutionizing RA Treatment

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Conflict of interest: Yes

Advances in pharmacotherapy have made clinical and structural remission a reality in the treatment of rheumatoid arthritis (RA), and TNF inhibitors have been at the core of the standard of care with biologic agents due to their pioneering role and the wealth of evidence they provide. Recent studies have revealed the central role of TNFα in bone and cartilage destruction, reaffirming the importance of its control in the face of remaining challenges, such as the presence of elderly rheumatoid arthritis, in which joint destruction progresses rapidly. joint destruction in RA is mediated by matrix metalloproteinase (MMP) and other enzymes that cause cartilage destruction by MMP and others, and bone destruction by osteoclasts. Since TNF-α and IL-1 induce chondrocyte apoptosis in a concentration-dependent manner, and MMP-3 levels in the blood of RA patients have been shown to correlate with the progression of joint destruction, it is necessary to control joint destruction by Therefore, early, potent, and safe suppression of MMP-3 is required to control the progression of joint destruction. In the treatment of RA, various molecular targeted drugs have become available, and their therapeutic outcomes have improved. On the other hand, more than 20% of patients have failed to achieve low disease activity in the last decade, and cases of progressive joint destruction and physical dysfunction have been observed. This is presumably due to the aging of RA patients with joint fragility and large joint disease, high disease activity due to immune aging, and drug ineffectiveness due to comorbidities that make it difficult to use methotrexate (MTX) in combination, and there are still many issues to be resolved. To overcome these issues, development of next-generation antibodies with lower molecular weight, faster absorption speed, lower immunogenicity, and less dependence on MTX has been promoted. In this context, ozoralizumab, a TNF inhibitor, was launched in Japan for the first time as a next-generation antibody formulation based on Nanobody technology. Unlike conventional biologics, ozoralizumab has structural characteristics such as small molecular size, lack of Fc region, and binding ability to human serum albumin. This is expected to lead to early control of disease activity and effects on large joints and reduced dependence on MTX due to earlier intra-articular transfer of the drug. In this seminar, we will reconsider the issues in the treatment of RA based on various recent research evidences, and outline the evidence and future potential of ozoralizumab.

ES8-3

Latest Findings regarding a Novel TNF Inhibitor, Ozoralizumab

Tsutomu Takeuchi
Saitama Medical University / Keio University

Conflict of interest: Yes

With the advent of biologic agents, the realistic goal of treating rheumatoid arthritis is to effectively inhibit the progression of joint destruction and enable many patients to achieve structural remission. Furthermore, JAK inhibitors, oral small-molecule drugs that show efficacy comparable to that of biologics, have emerged, leading to the establishment of treat-to-target treatment strategies. On the other hand, while biological agents and JAK inhibitors are highly effective, their high drug costs have given rise to new challenges, such as predicting the therapeutic effect of each drug, and considering whether to suspend or reduce the dose after achieving remission, or to extend the administration interval. In this situation, it is necessary to consider long-term treatment strategies for how to use the wide variety of existing anti-rheumatic drugs. The first molecular targeted drugs to appear in the field of rheumatoid arthritis were TNF inhibitors, and due to their long history of use and abundant clinical evidence, they are positioned as the first-choice drug for standard treatment with biologic agents in the rheumatoid arthritis treatment guidelines. It is no exaggeration to say that the use of TNF inhibitors has already been established based on their efficacy and safety, but much research is still being conducted and new evidence continues to be reported. In this context, ozoralizumab, TNF inhibitor, has emerged. Its efficacy and safety have been investigated in two Japanese clinical trials: the OHZORA study conducted in MTX-IR patients with MTX, and the NATSUZORA study conducted in MTX-naive patients. In addition, the results of the HOSHIZORA study, a two-year follow-up study after the completion of the above two studies, have been published and are attracting much attention. The HOSHIZORA trial has shown excellent results in terms of long-term efficacy and safety, like those of other TNF inhibitors. In this presentation, I would like to review the development of rheumatoid arthritis treatment and the role that TNF inhibitors have played in the treatment of rheumatoid arthritis and summa-

rize the evidence and clinical use of TNF inhibitors including ozolalizumab.

ES9-1

The major role of interleukin (IL) -6 receptor (R) blockade in Rheumatoid arthritis (RA) and inflammatory conditions

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Conflict of interest: None

Before the advent of modern therapeutic approaches and strategies, RA has been regarded a relentlessly progressive disease that caused cartilage and bone damage and led to irreversible disability. When looking back at the first two decades of the new millennium, patients with RA and rheumatologists as well as other stakeholders can be quite pleased with the advances made since the 2000. While at the end of the preceding century, only conventional synthetic disease-modifying antirheumatic drugs (DMARDs) were available and many patients with RA and other inflammatory diseases often could not attain optimal disease control, the last 20 years have allowed tumour necrosis factor inhibitors, IL-6R blockers, a T cell co-stimulation inhibitor to become approved and successfully applied. In addition to these biological DMARDs, most recently, Janus kinase inhibitors (JAKi) have been developed for treating RA, designated as targeted synthetic DMARDs that can be taken orally. Many therapeutics successfully applied in patients with inflammatory rheumatic diseases target proinflammatory cytokines, their receptors or their signal transduction. Among these cytokines IL-6 stands out by virtue of its very high serum concentration and its pivotal role in the induction of the acute phase response. A humanized monoclonal antibody targeting IL-6Rα, tocilizumab, was licensed more than a decade ago for RA, more recently for Giant cell arteritis and Takayasu arteritis and has been used successfully. Additionally, new indications for IL-6R inhibition have been approved, such as CART-cytokine release syndrome and severe COVID-19, and data have become known of efficacy in polymyalgia rheumatica, although this is not (yet) a licensed indication. Much more information on the long-term adverse event profile both from clinical trials and registries is available today than a decade ago, providing reassurance of the safety of IL-6R blockade, also in comparison with JAKi. Today, we will discuss the importance of blocking of IL-6R focusing on RA and glance at other diseases in this symposium.

ES9-2

Celebrating 20 years of Ineterleukin-6 signal blocking therapy

Tsutomu Takeuchi
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Conflict of interest: Yes

In rheumatoid arthritis (RA), we have achieved clinical remission or low disease activity by using a typical DMARD MTX, TNF inhibitors and IL-6 receptor inhibitors that selectively suppress inflammatory cytokines, or tsDMARDs. Since an approval of Tocilizumab in Japan, which is blocking interleukin-6 receptor, we have developed not only clinical data but also translational research. Using blood samples, we have investigated the analysis of factors that influence clinical efficacy, the relationship between inflammatory cytokines and bone or cartilage destruction, and data at the molecular level. Recently, a relationship between changes in functional regulatory T cell subsets and clinical efficacy has also been clearly reported. Patients with an early increase in resting regulatory T cells showed a favorable treatment course, and this increase in resting Tregs may reflect molecular remission induced by IL-6 signal inhibition. In this symposium, to commemorate the 20th anniversary of the launch of anti-IL-6 receptor therapy in Japan, we will highlight the importance of IL-6 inhibition, and the relationship between inflammatory cytokine and pathological conditions based on the research with TCZ.

ES10-1

Design rationale for ozoralizumab and medical applications of VHH antibodies

Kohei Tsumoto
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Conflict of interest: Yes

Antibody drugs have brought about significant progress in the treatment of cancer and immunological diseases. However, in recent years, the depletion of target antigens has become an issue, and research and development of next-generation antibody drugs with new functions is underway. Next-generation antibody drugs are constructed by utilizing antibody engineering technologies, such as the addition of low-molecular-weight compounds, mixing multiple types of partial structures, and using easily engineered low-molecular-weight antibodies, while utilizing the partial structures of IgG antibodies. Among these, VHH antibodies (variable domain of heavy chain antibodies) are attracting attention, which are produced by cutting out the variable domain of heavy chain antibodies that do not have light chains, which are possessed by animals of the camelid family. Although VHH antibodies have some issues such as short blood retention, lack of effector function, small binding surface, and low target affinity, they have advantages such as high tissue invasiveness, epitope structure different from that of IgG, and easy utilization of antibody engineering technology. VHH antibodies are also known as Nanobody molecules, and ozoralizumab contains two anti-human TNFα Nanobody molecules and one anti-human serum albumin Nanobody molecule. It is a humanized fusion protein with a trimeric structure with one anti-human serum albumin Nanobody molecule and is a low molecular weight antibody of approximately 38 kDa, about 1/4 the molecular size of a conventional IgG antibody. In this talk, I will give an overview of VHH antibodies as next-generation antibody drugs, which are attracting attention as a new format for drug development and discuss their potential for the future.

ES10-2

A New Era of Rheumatoid Arthritis Treatment: The Potential of Ozolarizumab, a Next-Generation TNF Inhibitor

Ryu Watanabe
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Conflict of interest: Yes

The advent of biologic agents and Janus kinase (JAK) inhibitors has markedly advanced the management of rheumatoid arthritis (RA), enabling many patients to achieve clinical, structural and functional remission. However, a subset of patients continues to exhibit active disease despite these therapies, underscoring the necessity for individualized treatment strategies that consider each patient's unique pathophysiology and therapeutic response. Additionally, the long-term management of adverse effects remains a critical concern, particularly in the context of Japan's aging population, which necessitates the development of safer therapeutic options. In this context, ozoralizumab, a novel tumor necrosis factor (TNF) inhibitor, has emerged as a promising therapeutic candidate. TNF inhibitors have long been the mainstay of RA treatment in Japan, with extensive evidence supporting their efficacy and safety. Ozoralizumab is a bispecific antibody that binds both TNF and human serum albumin, administered subcutaneously once every four weeks. While its mechanism of action aligns with existing TNF inhibitors, its unique binding properties and pharmacokinetics, particularly its albumin-binding capability, distinguish it as a potential advancement in RA therapy. A notable feature of ozoralizumab is its utilization of variable domains of heavy-chain antibodies (VHH) and lacks the Fc region present in conventional TNF antibodies. We have previously examined whether elevated rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibody titers influence the drug's efficacy. Our study results demonstrated that ozoralizumab has consistent efficacy irrespective of baseline RF titers and has been associated with reductions in both RF and anti-CCP antibody levels. In this presentation, I would like to introduce the therapeutic potential of ozoralizumab and discuss its optimal use.

ES11-1

A New Era in Rheumatoid Arthritis Treatment: Unveiling the Potential of MTX and Advancing a Multidisciplinary Therapeutic Strategy

Shigeki Momohara
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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic inflammatory disease requiring a multifaceted treatment approach, including immunomodulator-based pharmacotherapy, structured exercise therapy, and surgical intervention in advanced cases. Among pharmacologic treatments, methotrexate (MTX) remains the first-line therapy due to its anti-inflammatory and disease-modifying effects, effectively suppressing disease activity in many patients. MTX exerts immunomodulatory effects, playing a pivotal role in remission induction and disease progression control in RA. However, challenges remain, particularly in managing extra-articular manifestations such as pulmonary involvement, vasculitis, and renal impairment, which often persist despite MTX treatment. Dose limitations may also be required due to age-related risks, including renal dysfunction, bone marrow suppression, and hepatotoxicity. Nevertheless, the introduction of subcutaneous MTX formulations has allowed for higher dosing with reduced adverse effects, decreasing reliance on additional medications. RA frequently presents with multiple comorbidities, necessitating an integrated treatment approach. A comprehensive management strategy should include optimized combination therapy with MTX, JAK inhibitors, or biological agents, alongside the development of novel immunomodulators targeting extra-articular disease and elderly patients. Beyond pharmacotherapy, exercise therapy and rehabilitation play key roles as non-pharmacological interventions. Personalized rehabilitation programs should aim to balance pain management and functional maintenance, while osteoporosis and fracture prevention strategies are particularly important in elderly RA patients. Moreover, interventions for cognitive decline could offer additional benefits. While MTX-based pharmacotherapy has advanced RA treatment, unmet needs remain, including extra-articular disease control, optimized treatment for elderly patients, and osteoporosis and fracture risk management. Moving forward, developing more effective therapeutics, refining exercise and surgical indications, and establishing a comprehensive disease management framework will be essential. Advancements in personalized medicine are expected to further improve RA patients' quality of life.

ES11-2

Optimizing Methotrexate Treatment in Rheumatoid Arthritis ~Considering the Role of MTX Subcutaneous Injection formulation~

Kimito Kawahata
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Conflict of interest: Yes

The treatment of rheumatoid arthritis (RA) has significantly improved due to the use of methotrexate (MTX), molecular-targeted therapies, and the implementation of the treat-to-target (T2T) strategy. However, many challenges remain in RA management. In addition to improving the rate of early remission, attention is being focused on treating patients with special backgrounds, such as those with interstitial lung disease or a history of malignancy, as well as those with difficult-to-treat RA (D2TRA). MTX use has a significant impact on the treatment of these patients. Successful first-phase treatment is crucial in early intervention, and in cases with comorbidities, MTX usage may often be limited. Furthermore, it has been suggested that sufficient early treatment with MTX may reduce the risk of progression to D2TRA. Thus, treatment optimization to safely and adequately use MTX at necessary doses is required in various clinical settings. In Japan, a subcutaneous injection formulation of MTX became available in November 2022. This formulation is expected to reduce gastrointestinal symptoms and liver dysfunction compared to oral administration, thereby improving tolerability. Additionally, its bioavailability is higher, and its therapeutic effects are considered equivalent or superior to oral administration. As a result, optimizing MTX treatment now involves not only dose escalation but also changes in the route of administration. On the other hand, treatment decisions must also consider factors such as medical costs and the need for injection procedures. This presentation will cover a wide range of topics, from the latest pharmacological insights on MTX to treatment optimization using the subcutaneous injection formulation.

ES12-1

Unraveling the pathology of psoriatic arthritis from the perspective of cytokines and the potential of IL-17A/F inhibitor therapy

Ippei Miyagawa, Yoshiya Tanaka
The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan

Conflict of interest: None

PsA is thought to be primarily caused by enthesitis. Activation of the IL-23/IL-17 axis plays an important role in the pathogenesis of PsA. In fact, the results of our FLOW study confirmed the involvement of Th17 cells and IL-17A in PsA. Currently, various molecular-targeted drugs are available for PsA. However, the achievement rate of minimal disease activity, the treatment target for PsA, is still only 30-40%, even when treated with bDMARDs. PsA is a highly heterogenous disease. This heterogeneity is seen in the clinical features and the pathology of each involved organ/tissue. For example, IL-23-dependent IL-17 is strongly involved in the skin, but IL-23-independent IL-17 is strongly involved in enthesitis. This is also shown by the high therapeutic efficacy of IL-17A inhibitors and IL-23 inhibitors against skin involvement, the equivalent efficacy of TNF inhibitors and IL-17 inhibitors against peripheral arthritis/synovitis, and the difference in reactivity between IL-23 inhibitors and IL-17 inhibitors against spinal involvement. The IL-17A/F inhibitor bimekizumab is expected to be a treatment option that can cover this heterogeneity. IL-17A and IL-17F, which have about 50% structural homology, form homodimers or heterodimers and transmit their signals through the IL-17RA/RC complex, resulting in various physiological and pathogenic activities. On the other hand, the variable domain of bimekizumab can selectively bind to both IL-17A and IL-17. IL-17A and IL-17F have high structural homology and can independently induce inflammation, act synergistically with TNF, and are expressed differently in different organs/ tissues. In addition, there is an IL-17A-IL-17F autocrine loop in Th17 cells and an IL-17F signaling pathway independent of IL-17RA. Based on these findings, IL-17A/F inhibition may be able to cover a broader range of pathologies.

ES12-2

Treatment of axial spondyloarthritis to learn from a case

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

Conflict of interest: Yes

Spondyloarthritis (SpA) is an inflammatory disease concept, which exhibits not only enthesitis but also arthritis or spondylitis. SpA which shows sacroiliac joint or spine involvement is roughly classified into axial SpA (axSpA). AxSpA consists of ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) which is thought as a pre AS. Although there are classification criteria, we have some trouble to make a diagnosis. We should know that back pain is not always caused by inflammation, and distinguish inflammatory back pain from mechanical pain or others. When we look at images, we should try to find not only cross-sectional changes but also longitudinal reaction. Spinal fusion does not always mean axSpA. We should distinguish axSpA from other diseases such as diffuse idiopathic skeletal hyperostosis (DISH), psoriatic arthritis (PsA), pustulotic arthro-osteitis (PAO) or osteitis condensans illi (OCI). STIR high lesions in MRI simply suggests inflammation, but not axSpA. We distinguish it from insufficient fracture or infection. In this lecture, I would like to focus on imaging and read longitudinal reaction from it.

ES13

Mastering osteoporosis treatment for patients with rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is well-known a risk factor of osteoporosis. RA patients have an increased susceptibility to fragility fractures, and when such fractures occur, physical function can deteriorate rapidly. Osteoporosis in RA involves not only glucocorticoid-induced bone loss but also primary osteoporosis mechanisms, such as postmenopausal osteoporosis. Therefore, a thorough and accurate diagnosis is essential as a first step. It is important to identify the contributing factors to osteoporosis and educate patients not only about medication but also about necessary lifestyle improvements. We require an understanding of factors such as exercise, nutrition, and sunlight exposure, and providing guidance accordingly. Furthermore, it is critical to assess whether osteoporosis has reached a high fracture-risk status. While bone mineral density (BMD) tests are commonly used, they have certain limitations; for example, high BMD does not necessarily equate to low fracture risk. Thus, reviewing the results is important including discrepancies between BMDs at spine and hip. When we select pharmacological treatment, an awareness of goal-directed treatment approaches is essential. These approaches have been updated in 2024, with higher treatment targets recommended. Additionally, a new guideline for glucocorticoid-induced osteoporosis was published in 2023, and understanding how to apply it is crucial. When selecting medications, it is essential to understand the potential of each treatment option, not only in terms of BMD improvement but also regarding the impact on bone structure as suggested by changes in bone metabolism markers. Treatment options include bisphosphonates, selective estrogen receptor modulators (SERMs), active vitamin D_3 formulations, denosumab, teriparatide, romosozumab, and abaloparatide. Romosozumab, a monoclonal antibody targeting sclerostin, has a dual effect; it increases bone formation by activating and differentiating osteoblasts via inhibition of canonical Wnt signaling, and it also decreases bone resorption by reducing the NF-κB receptor ligand (RANKL)/ osteoprotegerin (OPG) ratio through inhibition of RANKL expression. Due to these dual effects, romosozumab is used as a treatment for osteoporosis at high risk of fractures. This presentation aims to provide a comprehensive overview of essential diagnostic and treatment points, along with common pitfalls, to equip attendees with the practical knowledge needed for mastering osteoporosis treatment in clinical practice.

ES14

Diagnostic and therapeutic strategies for EGPA focusing on eosinophilic inflammation

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Conflict of interest: Yes

Eosinophilic granulomatosis with polyangiitis (EGPA) is an autoimmune disease characterized by the pathogenesis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis and eosinophilic inflammation, which can lead to multi-organ damage. As the role of eosinophilic inflammation in the pathogenesis of EGPA becomes clearer, new classification and diagnostic criteria, as well as treatment strategies, are being proposed and revised. It is important to note that the presence of small- to medium-sized vasculitis is used as an entry criterion, but the 2022 ACR/EULAR classification criteria have shown excellent properties, with a sensitivity of 85% and specificity of 99%. On the other hand, distinguishing EGPA from other eosinophilic systemic diseases remains a clinical challenge. In this regard, the presenters have developed the E-CASE score, a diagnostic criterion for EGPA among eosinophilic patients with organ involvement. A genome-wide association study has found associations with genetic variants involved in the regulation of eosinophils and mucosal damage in ANCA-negative EGPA, and EETosis (eosinophil extracellular trap cell death) also plays a role in the disease's development. Controlling eosinophilic inflammation is a treatment strategy that aligns with the disease's pathophysiology. Mepolizumab, an anti-IL-5 monoclonal antibody that inhibits IL-5 signaling pathway involved in eosinophil differentiation, proliferation, and activation, has demonstrated efficacy and safety in treatment-resistant or relapsing EGPA in the international clinical trial. Reports from clinical trials and real-world data have shown that mepolizumab can reduce steroid doses and prevent relapses, making it a key drug in the management of EGPA. This presentation will provide an overview of the latest developments in the pathogenesis, diagnosis, and treatment of EGPA, focusing on eosinophilic inflammation and exploring the potential for personalized treatment approaches.

ES15

Challenges of Rheumatoid Arthritis Treatment in a Super-aging Society

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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.

ES16

Looking Ahead to the Future of PsA Patients -The Importance of IL-23 Inhibition and the Potential of Guselkumab-

Tadashi Okano
Osaka Metropolitan University, School of Medicine Department of Medical Science and Graduate School of Medicine

Conflict of interest: Yes

The onset of psoriatic arthritis (PsA) often occurs after the development of skin lesions, enabling early diagnosis and treatment in patients with psoriasis. Peripheral arthritis frequently occurs in the fingers, while enthesitis is commonly observed in the lateral epicondyle and the Achilles tendon. Therefore, focusing on these areas may facilitate early diagnosis. In recent years, ultrasound has been recognized as highly useful not only for rheumatoid arthritis but also for PsA. It is now widely used as a screening tool. At our institution, we collaborate with dermatologists to conduct ultrasound screening for PsA in psoriasis patients who do not exhibit joint symptoms. This approach has revealed numerous instances of inflammatory findings even in asymptomatic psoriasis patients. In some cases, treatment interventions targeting subclinical inflammation identified by ultrasound have led to improvements in inflammatory findings. Furthermore, biologics and JAK inhibitors are available as targeted molecular therapies for both psoriasis and PsA. Notably, the use of targeted molecular therapies for psoriasis has been suggested to help prevent the onset of PsA. Among the biologics, IL-23p19 inhibitors may be the most effective for preventing PsA onset. Additionally, basic research data suggest that IL-23 inhibition in the early stages of spondyloarthritis can prevent the development of spondylitis and arthritis. This highlights the potential utility of IL-23p19 inhibitors in the treatment of psoriasis and early-stage PsA. Guselkumab, an IL-23p19 inhibitor, demonstrated inhibitory effects on peripheral arthritis, enthesitis, and dactylitis in the DISCOVER trials, showing results comparable to those of TNF inhibitors and IL-17 inhibitors. Particularly in early PsA patients, its use may have long-term benefits. In this seminar, we will explore the positioning of IL-23 inhibitors for

PsA treatment.

ES17

Screening, evaluation, and treatment of systemic autoimmune rheumatic diseases based on recently published guidelines

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Conflict of interest: Yes

The 2023 American College of Rheumatology (ACR)/CHEST Guidelines provide a roadmap for screening, monitoring, and treatment of systemic autoimmune rheumatic disease (SARD) related interstitial lung disease (ILD) in general while the recently published American Thoracic Society guidelines (ATS), as well as European Alliance of Associations for Rheumatology (EULAR) recommendations focus specifically on systemic sclerosis (SSc). The vast majority of recommendations were conditional because high level certainty of evidence that would lead to strong recommendations was lacking. The ACR/Chest guidelines recommended high-resolution chest CT (HRCT) Chest over history and physical examination alone for ILD screening in patients with SARDs at increased risk of developing ILD. There was a recommendation against open lung biopsy or bronchoscopy for screening, although these procedures can be used to rule out alternative diagnoses. For monitoring, pulmonary function tests at the interval of 3-12 months (depending on the type of SARD and disease duration) were recommended. ACR/Chest guidelines provided a list of first-line treatments for SARD-ILDs. In all diseases, mycophenolate* was conditionally recommended over the other listed therapies for the initial therapy. In case of ILD progression, switching to or adding another immunosuppressive treatment such as rituximab* or anti-fibrotic treatment with nintedanib was recommended. There was a strong recommendation against glucocorticoid use in SSc-ILD. In ATS guidelines, mycophenolate was strongly recommended for treatment of SSc-ILD while there was also a conditional recommendation for cyclophosphamide, nintedanib, rituximab, and tocilizumab**. EULAR endorsed cyclophosphamide, mycophenolate, rituximab, as well as nintedanib (alone or in combination with mycophenolate) as treatment options for SSc-ILD. For SSc-ILD patients with high inflammatory markers in early disease, tocilizumab was also recommended as a treatment option. *Approved only for SSc-ILD in Japan **Not approved for SSc-ILD in Japan

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PL .... **Presidential Lecture**

RS .... **Representative Session**

SS .... **Special Symposium**

TS .... **TREG Session**

S .... **Symposium**

EL .... **Educational Lecture**

MTE .... **Meet the Expert**

ICW .... **International Concurrent Workshop**

W .... **Workshop**

EP .... **English Poster Session**

P .... **Poster Session**

MS .... **Morning Seminar**

LS .... **Luncheon Seminar**

ES .... **Evening Seminar**

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Modern Rheumatology Abstract Supplement

The 69th Annual Scientific Meeting of the

Japan College of Rheumatology

Publishing date: April 1, 2025

Publishers: Japan College of Rheumatology (JCR)
Modern Rheumatology Editorial Board

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Production

Hidejima Inc.
Toshin Nishi-Shinjuku Bldg. 2F
7-18-16 Nishi-Shinjuku, Shinjuku-Ku, Tokyo, 160-0023, Japan
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